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Exploring the Human Gut Microbiome

Promises, Limits, and Future Perspectives for Personalised Nutrition and Health

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ABSTRACT

Microbes are everywhere. Humans have always been greatly affected by their presence and we are only recently beginning to understand to what extent: the microbial world is not just in us; it is part of us. Indeed, it is the myriad patterns of causality, interconnection and mutualism with microbes what ultimately makes us who we are. In the last few decades, such a groundbreaking change of perspective has sparked a robust interest in scholars and professionals alike towards the study of the microbial communities – the microbiome – that inhabit the human body.

In particular, a remarkable increase in the number of startups operating in the gut microbiome sector in relation to food and nutrition has been registered in the past few years. What is the correlation between microbes living in our guts and the food we eat? How could we benefit from a thorough study of the human gut microbiome, and what are the possible risks associated with it? This dissertation aims at analysing the premises and promises of the gut microbiome within the field of nutritional sciences, imagining plausible future scenarios and reflecting on the role of microbes in human health.

This work has been largely based on field data and interviews from an EU-based Health Science company and various members of the bioinformatics lab – also based in EU – cooperating with it.

CHAPTER ONE INTRODUCTION

To be one is always to become with many.¹

Through these words, philosopher and writer Donna Haraway deconstructs the individual identification of self in favour of a more co-dependent and interactional perspective. A process of becoming which rests not on the single unit, but on the myriad entities that constitute the whole – although, claims Haraway, their existence does not precede their relating. The subtle implication of such claim is that identity – and the "ability to exist" ceases to be a trait intrinsically attached to the individual, and becomes a defining feature of, and emerging from the active interaction with what Haraway calls "companion species."

Macroscopic entities with which we interact – that is, other human beings, but also animals, plants and objects – exist, in truth, as complex biomolecular networks featuring a substrate which we call "host" and other, extremely varied, microbiological networks, which we call "guests." From such perspective, the concepts of self and non-self lose much of their significance and, rather than opting for reductive terms such as "hosts" and "guests," it may be wiser to embrace Margulis's concept of holobiont. That is the assemblage of a central (human) host and the many other species living in or around it, which together form a discrete ecological unit through symbiosis.²

¹ Haraway, Donna. When Species Meet. Minneapolis: University of Minnesota Press, 2008.

² Margulis, Lynn, and René Fester, eds. Symbiosis as a source of evolutionary innovation: speciation and morphogenesis. MIT press, 1991.

Such reflections prompt the individual to abandon their preconceptions about life as they know it and challenge the common understanding of human nature and selves.³ Redefining the human as a collective of different species rather than a single, perfectly unitary individual, paves the way to a significant number of social and cultural implications. In the last few decades, scholars from various fields have increasingly been interested in exploring such posthuman⁴ perspectives. Their goal has been to establish horizontal relations between different forms of life, and building on the assumption that these are not defined through hierarchies, but rather by an inextricable mutuality of action. One such field of research is that of the human gut microbiome.

The human gut microbiome⁵ is a complex ecosystem comprising of all the bacterial communities, viruses and fungi living inside the human gastrointestinal tract.⁶ While it remains largely under-appreciated in its structure and functions,⁷ recent technological progress and innovative laboratory techniques, i.e. metagenomics, have led to an exceptional growth in the knowledge and comprehension of such vast microuniverse rooted within us.⁸ Metagenomics is a

⁶ Berg, Gabriele, et al. "Microbiome definition re-visited: old concepts and new challenges." *Microbiome* 8 (2020): 1-22.

⁷ The Human Microbiome Project Consortium. A framework for human microbiome research. *Nature* 486 (2012): 215–221.

⁸ Wirbel, Jakob, et al. "Meta-analysis of fecal metagenomes reveals global microbial signatures that are specific for colorectal cancer." *Nature medicine* 25.4 (2019): 679-689.

³ Rees, Tobias, Thomas Bosch, and Angela E. Douglas. "How the microbiome challenges our concept of self." *PLoS biology* 16.2 (2018): e2005358.

⁴ As their re-definition goes beyond what is traditionally defined as "human."

⁵ In developing my research, I have tried not to be overly scientific to better reflect the multidisciplinary nature of my anthropological inquiry. However, it should be noted that the microbial diversity on Earth is, in truth, staggeringly more complex than what I present here. Microbes are found in each of the three domains of life: Archaea, Bacteria, and Eukarya. Microbes within the domains Bacteria and Archaea are all prokaryotes (meaning that their cells lack a nucleus), whereas microbes in the domain Eukarya are eukaryotes (meaning that their cells do have a nucleus). Roughly put, this means that all bacteria are microbes but not all microbes are bacteria – as the latter configure as single-celled microbes that lack a nucleus. For this reason, when addressing the human but microbiome in this work, I have decided to adopt the larger-umbrella term "microbes" over the more limited term "bacteria." For further information see Woese and Fox (1977), Curtis (2007), Sadava and Hillis (2012) and Hug (2016).

fairly new method that studies the structure and functions of entire genomic nucleotide sequences isolated and analysed from all the organisms (typically microbes) in a bulk sample. Metagenomics is often used to study a specific community of microorganisms, such as those residing on human skin, in the soil or in a water sample.⁹ Due to reduced costs¹⁰ and sequencing time, metagenomics is today the most commonly used practice to comprehensively study the human microbiome. Owing to the staggering research engagement in the field over the past few decades, we now know that the human gut microbiome – which is unique to each individual – has a degree of complexity higher than that of the genome¹¹ and weighs equally on human health, by playing a pivotal role in host metabolism, immunology and behaviour.¹²

For such reasons, although much research still needs to be done,¹³ the microbiome has certainly risen up to become one of the most studied and popular areas in Computational sciences, biotechnology, nutritional studies and pharmaceutics,¹⁴ as innumerable studies have linked its composition and activity to a relevant number of serious human diseases.^{15,16} Some scholars have even

⁹ For further information see "METAGENOMICS," National Human Genome Research Institute, accessed 9 January, 2023, <u>https://www.genome.gov/genetics-glossary/Metagenomics</u>.

¹⁰ It should be noted that these costs are much lower today than twenty years ago. However, sequencing is still a pretty expensive practice for some laboratories and research centres. For further information see subsection 1.2 of the present chapter.

¹¹ Grice, Elizabeth A., and Julia A. Segre. "The human microbiome: our second genome." *Annual review of genomics and human genetics* 13 (2012): 151-170.

¹² Shi, Na, et al. "Interaction between the gut microbiome and mucosal immune system." *Military Medical Research* 4 (2017): 1-7.

¹³ Cresci, Gail A., and Emmy Bawden. "Gut microbiome: what we do and don't know." *Nutrition in Clinical Practice* 30.6 (2015): 734-746.

¹⁴ Sharma, Anukriti, et al. "The future of microbiome-based therapeutics in clinical applications." *Clinical Pharmacology & Therapeutics* 107.1 (2020): 123-128.

¹⁵ Clemente, Jose C., et al. "The impact of the gut microbiota on human health: an integrative view." *Cell* 148.6 (2012): 1258-1270.

¹⁶ Wang, Baohong, et al. "The human microbiota in health and disease." *Engineering* 3.1 (2017): 71-82.

described the human gut microbiome as a vestige to a forgotten organ^{17,18} which, if thoroughly studied and researched, could constitute the missing link in medicine to better diagnose and treat a wide number of incurable diseases and conditions. Over the years, and especially in the last few decades, such "turn to the microbiome" has made thousands of well-established companies and newly-founded start-ups¹⁹ focus their attention on it.

Whilst, as I have mentioned, interest in the field has been steadily growing in the last few decades, the in-depth study of the human gut microbiome is a relatively new area of research, which was started by the Human Microbiome Project in 2007.²⁰ Since then, the number of academic publications and granted patents linked to the microbiome has grown significantly,²¹ reaching a first historical apex in 2014,²² and every subsequent year after that (figure 1):²³

¹⁷ O'Hara, Ann M., and Fergus Shanahan. "The gut flora as a forgotten organ." *EMBO reports* 7.7 (2006): 688-693.

¹⁸ Spector, Tim. Spoon-Fed: The# 1 Sunday Times bestseller that shows why almost everything we've been told about food is wrong. London: Penguin, 2020. P. 9.

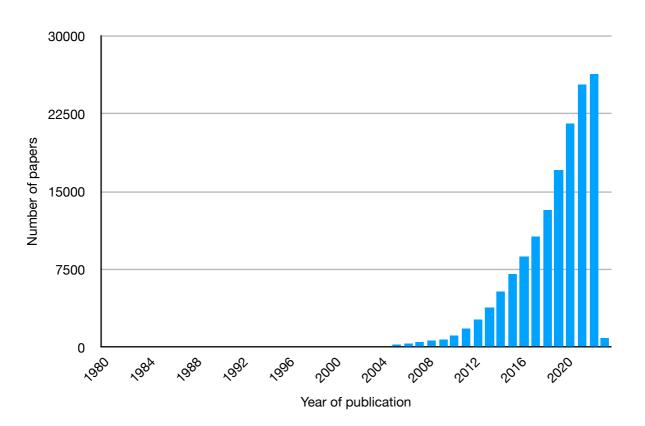
¹⁹ With the term "startup" I intend what Natalie Robehmed described in 2013 as "a company or project undertaken by an entrepreneur to seek, develop, and validate a scalable business model." For further information see: Robehmed, Natalie, "What Is A Startup?" *Forbes* (16 December 2013).

²⁰ Funded by the National Institute of Health (NIH) Common Fund from 2007 to 2016 and aimed at characterising the microbiomes of healthy human subjects at five major body sites, using 16S and metagenomic shotgun sequencing. The overarching mission of the HMP was that of generating resources to facilitate the compiling of the human microbiota to further our scientific understanding of how the microbiome impacts human health and disease. For further information see: <u>https://hmpdacc.org/hmp/</u>

²¹ The same is true for the Impact Scores (IS) of journals that have a strong body of publications related to the (human) microbiome and which are showing a rising trend when compared to preceding years. For further information see: <u>https://www.resurchify.com/impact/details/</u>21100401152; <u>https://www.resurchify.com/impact/details/21100788431</u>.

²² Gosálbez, Luis. "The microbiome biotech landscape: an analysis of the pharmaceutical pipeline." *Microbiome Times* (2020).

²³ "PubMed Timeline Query: Microbiome," <u>pubmed.gov</u>, accessed Jan 6, 2023, <u>https://pubmed.ncbi.nlm.nih.gov/?term=microbiome&timeline=expanded</u>.



PubMed: number of academic publications showing "microbiome" as keyword. 1980 – 2023

Figure 1: Timeline results by year. Search query: "microbiome." Total results: 132,896.

Such powerful this wave of research and investments was, that in 2019 Forbes nicknamed the 2010s as the decade of the microbiome,²⁴ since the most important discoveries in microbiota²⁵ research had happened during that period.²⁶

However, the innovative character of the subject leaves lots of unexplored areas and gaps in research, which often needs more time to catch up with

²⁴ Cat, A. Linh, "The decade of the microbiome," Forbes (2019).

²⁵ Although at times used interchangeably, the terms "microbiota" and "microbiome" have slightly different meanings. "Microbiota" refers to the collection of microorganisms (such as bacteria, fungi and viruses) that inhabit a specific ecological niche or environment. In other words, "microbiota" specifically refers to the community of microorganisms themselves. "Microbiome," on the other hand, refers to the collective genomes of all microorganisms, including their genes and genetic material, found within a particular habitat or ecosystem. Thus, "microbiome" identifies both the microorganisms themselves, but also their genetic information, as well as the functional interactions among them and with their environment.

²⁶ Pariente, N., et al. "Milestones in human microbiota research." *Nature* (2019).

innovation. In particular, I am referring to the world of emergent startups operating in the nutritional sector, which employ the study of individual gut microbiomes to develop precision medicine and personalised nutrition approaches to food and diet. My keen interest in investigating the social, cultural and economic implications of such process has led me to engage with the present thesis' inquiry. I strongly believe that researching the microbiome and its relations with food and nutrition from an anthropological perspective, constitutes an invaluable asset to understand the dynamics governing the interplay between the microbiome and the preservation of human health. Particularly, I am interested in understanding how such dynamics contribute to shaping new trends in healthcare and health governance, e.g. personalised nutrition from an angle that sees the microbiome as an essential part of what is commonly defined as "human."

To achieve my goals, I have come in contact with one such company and thoroughly studied – both internally and externally – its mission, philosophy, ideals, methods, organisation, science and people. I have conducted a form of digital ethnography²⁷ complemented by semi-structured interviews²⁸ with field experts, lab members, project's investigators and startup's employees to get direct insights and a varied degree of perspectives about the different beneficial and controversial aspects of microbiome research. As such, I focus both on microbiome research in general and on my case study, in particular. My institution of choice to conduct such research has been a EU-based company which I will be naming Foodomics for the remainder of the present thesis.

Foodomics is a personalised nutrition startup operating in the nutritional sector, which employs microbiome technology to deliver personalised dietary

²⁷ Digital ethnography is a relatively new and evolving subfield within the social sciences, which studies the cultural and social domains of human interaction through the internet technologies that they use.

²⁸ Depending on the native language on the interviewee, some of the interviews were held in Italian e.g. Prof. Rossi and Dr. Bianchi. In such cases, I have reported the related English translation.

advice to its customers. It was founded in 2017 by author and Professor of Genetic Epidemiology Dr. Smith, data science leader J. Johnson and entrepreneur G. Brown. Foodomics' mission, as it is reported in the company's whitepaper, is to helps users to better understand their body and its response to food, working at the intersection of diet, lifestyle and health.²⁹

The core materials I used in my research were data uncovered from digital ethnography and semi-structured recorded interviews, as well as a thorough review of the state-of-the-art and study of the available literature from the fields of medical anthropology, microbiology, economics and environmental humanities. Digital ethnography was a critically important research tool to better understand the socio-cultural context within which Foodomics – and other companies like it – operate, as well as the public response to it. Secondly, the semi-structured interviews provided me with extremely precious insights directly from the scientists and researchers involved in the field. Finally, thoroughly reviewing the state-of-the-art was crucial to situate my project within an existing framework of raising anthropological engagement with the bacterial world,^{30,31,32} from which to draw essential theoretical knowledge and upon which attempt at producing new insights.

The methodologies and principles I employed for my data analysis include: content coding, which allows for systematic, qualitative or quantitative analyses of information; saturation of data, meaning that no additional data are being found whereby the researcher can develop properties of the category; thematic analysis of qualitative data, which uses *themes* – or actively constructed patterns for meaning – derived from data sets to address research questions in a

²⁹ "Whitepaper: An overview of our science," Foodomics, accessed March 25, 2023.

³⁰ Hird, Myra. The origins of sociable life: Evolution after science studies. Springer, 2009.

³¹ Davis, Mark, et al. "Immunity, biopolitics and pandemics: Public and individual responses to the threat to life." *Body & Society* 22.4 (2016): 130-154.

³² Raffaetà, Roberta. Metagenomic Futures: How Microbiome Research is Reconfiguring Health and what it Means to be Human. Taylor & Francis, 2022.

six-step process. Particularly, some of the questions I will try to answer in my dissertation are: what are the impacts of microbes on human health in relation to food and diet? What is personalised nutrition and how does it work? Are there any risks to it and, if so, of which nature and scale?

From an ethical standpoint, in compliance with GDPR and ethical considerations on potential sensitive data being handled as part of my ethnographic research, I ensured that my research would comply at all times with EU Regulations on protection and safeguard of personal and sensitive data in terms of: privacy rights; data tracking; data processing and storage; data protection and erasure; data usage. In addition to that, each interviewee has been duly informed about their privacy rights and have been given the possibility to maintain their anonymity. To this end, the real names of scholars, employees, doctors, companies and labs that have taken part in my research have been anonymised and changed into invented ones.

My goal is that of exploring the current state of research into the gut microbiome and its applications within the field of food and nutritional studies. In particular, I am interested in exploring how microbes directly contribute to the preservation and enhancement of human health, and how innovative approaches such as personalised nutrition are trying to incorporate the microbiome into pre-existing paradigms of health and well-being. Building on such topics, I am also interested in debating the meaning of "being human" in a world that is progressively characterised by inextricable action-reaction networks and species intersectionality.

I firmly believe that the task of anthropology is to defy barriers and go beyond the mere observation of a nested, multiscalar reality. On the contrary, the biosocial awareness sprouting from anthropological inquiries must be the starting point of a much deeper analysis which needs to focus on the social, cultural, ethical and political consequences of a new kind of reality. Posthuman takes on science, anthropology and social sciences might prove essential in

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fostering a post-anthropocentric stance for the future of our planet and societies. However, one must also be wary of the potential risks embedded in it. In such regard, further research aimed at redefining who (or what) the contemporary human is, could prove paramount in constructing a new and renovated starting point for anthropology.

1.1 Why are microbes so important?

The world around you is swarming with microbes. Trillions live on your phone, in your food, on your hands before you wash them, on your hands after you wash them, on any surface and literally everywhere else on top of you too. Microbes are omnipresent at any moment of our lives, and there is nothing we can do about It. Due to such inevitability of intersection, millions of years ago the first humans and microbes had to come an evolutionary agreement: our ancestors would give them shelter, and they would work for us.

For nine months spent inside your mother's womb you experienced your best, most pristine and sterile life:³³ there was no sign of any viruses or microbes living in your gut, and your entire body was covered in a protective oily covering which allowed no parasite to contaminate it. Then, you were born. Almost instantaneously, you were besieged by billions of the most varied microbes infesting your mother's birth canal,³⁴ the nursing personnel and every possible surface in the hospital delivery room. Unaware of such apocalypse-like scenery,

³³ It should be noted that contrasting papers have been published on this topic. Computational scientists are generally convinced the uterus is indeed a sterile environment for the foetus, while many obstetricians and gynaecologists have doubts about it. Definite consensus still has to be reached due to the lack of compelling, rigorous experiments. For further information see Wassenaar, T. M., and Pinaki Panigrahi. "Is a foetus developing in a sterile environment?." *Letters in applied microbiology* 59.6 (2014): 572-579.

³⁴ Magne, Fabien, et al. "The elevated rate of cesarean section and its contribution to noncommunicable chronic diseases in Latin America: the growing involvement of the microbiota." *Frontiers in pediatrics* 5 (2017): 192.

you proceeded to be breastfed for the first time in your life, and the sieging was complete. An unimaginable number of microbes started to flow inside your mouth and down towards your stomach and intestines: you were completely overrun. Billions of tiny aliens grew, multiplied and inexorably spread throughout your body. Within weeks, your pristine and sterile baby skin was covered entirely, and your intestines were swarming with trillions of different microbes.

Surprisingly, you survived this invasion. In fact, as counterintuitively as it may seem, this is a completely normal process that all newborn humans undergo at birth and it is an essential part of human health. Studies have shown a significant increase in contracting rates – from 20% up to 50% – for diseases like asthma, type 1 diabetes (T1D), immune diseases and even leukaemia in children born via C-section as opposed to vaginal delivery.³⁵ Such findings tell us that not only does the human body accepts and survives the invasion of microorganisms: it welcomes it. There is an ancestral and partially unexplored interplay here; an intimate relationship we maintain with our microbes throughout all our lives and from time immemorial. Over millions of years, humans and microorganisms have co-evolved to make the best out of a necessary relationship of co-dependency. Mother's milk – the most natural food an infant could ingest – contains special sugars meant to feed and support the development of certain strains of microbes, work as decoys for others, and help adjusting the immune system of the newborn child.³⁶

It takes up to two years until a healthy microbial community has formed – we call this "the microbiome" – and up to three to five years of life³⁷ for the microbial diversity to fully develop and converge towards an adult-like

³⁵ Magne et al., "The elevated rate of cesarean section."

³⁶ Le Doare, Kirsty, et al. "Mother's milk: a purposeful contribution to the development of the infant microbiota and immunity." *Frontiers in immunology* 9 (2018): 361.

³⁷ Rodríguez, Juan Miguel, et al. "The composition of the gut microbiota throughout life, with an emphasis on early life." *Microbial ecology in health and disease* 26.1 (2015): 26050.

microbiota.³⁸ The microbiome varies greatly depending on the habitat taken as reference. Hence, the skin, mouth, vaginal and gut microbiomes, for instance, will largely differ in their composition and functions. Due to the nature of the present work, my research has focused solely on the gut microbiome. Indeed, what is truly surprising is that each individual has their own personal and unique gut microbiome – made up of trillions of different microbes, fungi, viruses and other organisms living in the gut.³⁹ Each person on planet Earth has their own, exclusive microbial composition and balance, which heavily shape the responses to external stimuli and disturbances.^{40,41} Studies have shown, for example, that individuals have repeatable and predictable nutritional responses to different foods depending on the proportions of nutrients – protein, fat and carbohydrates – but with potential wide variations between people, up to tenfold. This also included stark differences between identical twins, who are biological clones sharing 100% of their genes and a vast part of their environment.⁴²

Essentially, the microorganisms living on and inside our bodies can be divided in three main categories: firstly, there are microbes that maintain a commensal relationship⁴³ with humans. Although these species have no interest in harming the human body, as it often times constitutes their only favourable habitat, their presence can sometimes be harmful to us. Take *Helicobacter*

³⁸ Although the terms 'microbiome' and 'microbiota' are often used interchangeably, there is a slight difference between the two. Whilst the term 'microbiota' refers to the different types of microorganisms living in a specific environment, 'microbiome' describes the different types of microorganisms living in a specific environment alongside their genes – or genetic material.

³⁹ Gilbert, Jack A. "Our unique microbial identity." Genome Biology 16.1 (2015): 1-3.

⁴⁰ Gilbert, Jack A., et al., "Current understanding of the human microbiome," *Nat Med* 24, (2018): 392-400.

⁴¹ Spector, Spoon-Fed, 20-21.

⁴² Berry, Sarah E., et al. "Human postprandial responses to food and potential for precision nutrition." *Nature medicine* 26.6 (2020): 964-973.

⁴³ In biology, commensalism happens when there is an association between two organisms in which one benefits and the other derives neither benefit nor harm.

pylori, the recently discovered (1982) microbe that causes ulcers and of which humans are the only known hosts: about 50% of middle-aged Americans is known to host this microbe in their gut. However, the incidence of the infection resulting in actual ulcers is around 20% – which means that only one in five people carrying the microbe will develop the disease.⁴⁴ *H pylori* has changed over thousands of years to co-evolve with humans and become – in most cases – a friendlier microbe, thus preserving and boosting its own survivability.

Secondly, we find microbes that could potentially harm us, but with whom we have learned to live. Take *Streptococcus mutans*, one of the 300 microbial species living in the human oral cavity and one amongst the main causes of dental decay through polysaccharide storing and extra acid secretion. We cannot dispose of *S mutans* entirely, so we had to invent dentifrices to coexist together.⁴⁵

The third and last category is made of microbes that are beneficial to our human health. Most of these make up a community of approximately 380.000 billion microbes, from up to 5.000 different species all living in the gut.⁴⁶ To give a rough idea of scale, it is estimated that the number of stars in the Milky Way could vary between 100.000 and 400.000 billion, which means that we host a number of microorganisms in our gut that spans from as many microbes as there are stars in our galaxy to four times as much. Such microorganisms aid human digestive processes and even enhance them by augmenting the harvest

⁴⁴ Brown, Linda M., "Helicobacter pylori: epidemiology and routes of transmission," *Epidemiologic reviews* 22, no. 2 (2000): 283-97. What is really interesting, however, is how these percentages can vary up to ten times if we travel to the other side of the globe: Korea, for instance, has one of the highest rates attesting at over 90% of incidence – which means nine out of ten people will develop the disease. This can be the result of other factors such as different hygiene, diets and external modifiers, all of which will be later analysed in this thesis.

⁴⁵ Loesche, Walter J., "Microbiology of Dental Decay and Periodontal Disease," in *Medical Anthropology. 4th* edition, ed. Baron, Samuel (Galveston, TX: University of Texas Medical Branch at Galveston, 1996). Chapter 99. Available from: <u>https://www.ncbi.nlm.nih.gov/books/NBK8259/</u>.

⁴⁶ Rodríguez, "The composition of the gut microbiota."

of calories from foods we would not be able to digest ourselves.^{47,48} It is towards this last group of microbes, which constitutes the human gut microbiome, that I will now turn my attention.

As I have briefly mentioned, the human gut microbiome is extremely diverse and unique to each individual. But what does it do, exactly? What is its function? I will cover this more extensively in later chapters, but to provide a brief yet exhaustive answer now, I will use the words of Professor Rossi – full university professor in Northern Italy and founder of the Rossi Lab of Computational Metagenomics located at the same institution – whom I had the luck to interview as part of this research. When asked for a definition of the gut microbiome, Professor Rossi replied:

"The microbiome represents the primary and most important interface between the food we eat – our diet so to speak – and our body, as it is the first processor of any food we insert in it. Its critical importance lies in its direct link with our health as individuals."⁴⁹

When the variability of individual responses to different food is analysed at the metabolic level, this variability owes its *raison d'être* to the microbiome itself. Generally, the degree of influence can be negligible, but when certain parameters such as blood glucose spikes are considered, which correlate with a higher risk of diabetes, heart attack and other diseases, it becomes crucial to know more about the topic. Rossi claims that a more thorough, in depth and comprehensive study of the microbiome is of paramount importance to improve dietary regimes and consequently act directly on the cardio-metabolic health of

⁴⁷ Ursell, Luke K. et al., "Defining the human microbiome," *Nutrition reviews* 70, Suppl. 1 (2012): S38-44.

⁴⁸ Valdes, Ana M. et al., "Role of the gut microbiota in nutrition and health," *BMJ* 361, k2179 (2018).

⁴⁹ Prof. Rossi, interviewed by Luciano Ferrari, November 30, 2022.

individuals.⁵⁰ Here, however, the issues of uniqueness and diversification come to the fore, but I will address these in later chapters.

Apart from housing billions of friendly microbial species, the human gut is also the perfect point of entrance for other, more dangerous organisms. To face this threat, evolution has provided us with the deadliest and most efficient army we could ever hope for: the immune system. The immune system is responsible for blocking off potentially harmful intruders and eradicate them before they can cause any damage. When it comes to microbes, however, while extremely effective in its tasks, the immune system is often unable to differentiate between friend or foe. Such inaccuracy could easily turn out to be detrimental to the health of the individual.

Therefore, to survive in such a hostile environment, whilst ensuring the health of its host, the human microbiome had to co-evolve with humans, that is it had to learn to directly communicate with our body. Indeed, studies have shown that:

Interactions between the microbiota and the host immune system are numerous, complex, and bidirectional. The immune system must learn to tolerate the commensal microbiota and respond appropriately to pathogens, and in turn the microbiota is integral to educating the immune system to function properly.⁵¹

Even more surprisingly, more recent studies have shown how the influence exercised by the gut microbiome could go much further, with a growing number

⁵⁰ Rossi, Interview. Moreover – and unsurprisingly – the degree of variability varies greatly across different cultures, eating habits and geographies. For further information see Segata, Nicola. "Gut microbiome: westernization and the disappearance of intestinal diversity." *Current Biology* 25.14 (2015): R611-R613.

⁵¹ Shreiner, Andrew B., John Y. Kao, and Vincent B. Young. "The gut microbiome in health and in disease." *Current opinion in gastroenterology* 31.1 (2015): 69.

of studies outlining the presence of a direct line of communication between the gut microbiome and the human brain:

In more recent years, the concept of a 'gut-brain axis' has been introduced. The endocrine system may be modulated at the intestinal level in a sort of neuro-entero-endocrine system. This system interacts with the immune system at the mucosal level in order to maintain a homeostasis but also to enhance defence against microbial invasion in pathological states.⁵²

Other scholars have built on this by theorising that alterations in the microbiome composition are associated with marked changes in behaviours relevant to mood, pain and cognition.⁵³ For instance, a study conducted in mice has recently been published,⁵⁴ suggesting that certain gut microbes can regulate motivation to exercise by increasing dopamine levels in the brain during physical activity.

Dysfunction of the gut-brain axis – which basically functions as a two-ways communication system between the central nervous system and the gastrointestinal tract – has also been directly linked to stress related disorders the likes of depression, anxiety, and neurodevelopmental disorders such as autism.⁵⁵ Evidence has been found on how the 90% of serotonin, a crucial neurotransmitter substance used by neurones to communicate through our body, is produced in the gut.⁵⁶ Furthermore, a recently discovered neuron circuit

⁵² Cianci, Rossella, et al. "The microbiota and immune system crosstalk in health and disease." *Mediators of inflammation* 2018 (2018).

⁵³ Borre, Yuliya E., et al. "The impact of microbiota on brain and behavior: mechanisms & therapeutic potential." *Microbial endocrinology: The microbiota-gut-brain axis in health and disease* (2014): 373-403.

⁵⁴ Dohnalová, Lenka, et al. "A microbiome-dependent gut-brain pathway regulates motivation for exercise." *Nature* (2022): 1-9.

⁵⁵ Ibid.

⁵⁶ O'Mahony, Siobhain M., et al. "Serotonin, tryptophan metabolism and the brain-gutmicrobiome axis." *Behavioural brain research* 277 (2015): 32-48.

has shown how the human gut is lined by more than 100 million nerve cells, making it practically a small brain unto itself.⁵⁷

Scholars believe that our gut microbiome uses serotonin to establish a contact with the vagus nerve, which is a sort of informational highway of our nervous systems.⁵⁸ Once inside the systems, microbes can send all kinds of message to our brain by stimulating the immune cells in the gut to force them to send electric impulses to our cerebral cortex:

[...] As a result, modifications of microbiota composition may be associated to several disorders of the nervous system, including neuropsychiatric, neurodegenerative, and neuro-inflammatory disorders.⁵⁹

The aforementioned instances of human-microbial intersectionality are but few examples of the intricate interplay between humans and the living microuniverse they carry inside, and which directly impact their health. When considering the meshwork of factors determining what we simplistically label as "health," the very concept behind the word seems to lose its unitary character in favour of a more organic, comprehensive and multispecies-oriented complexity.

Indeed, in the light of the microbiome's significant interaction with its host's metabolic processes,⁶⁰ immune system,⁶¹ brain activity⁶² as well as its ability to

⁵⁷ Emily Underwood, "Your gut is directly connected to your brain, by a newly discovered neuron circuit: find could lead to new treatments for obesity and depression," *Science*, Sep 20, 2018, <u>bit.ly/40I31Yq</u>.

⁵⁸ Fülling, Christine, Timothy G. Dinan, and John F. Cryan, "Gut Microbe to Brain Signaling: What Happens in Vagus...," *Neuron* 101, no. 6 (2019): 998-1002.

⁵⁹ Cianci, "The Microbiota and Immune System Crosstalk."

⁶⁰ Martin, Alyce M., et al. "The influence of the gut microbiome on host metabolism through the regulation of gut hormone release." *Frontiers in physiology* 10 (2019): 428.

⁶¹ Cianci, "The Microbiota and Immune System Crosstalk."

⁶² Mayer, Emeran A., Kirsten Tillisch, and Arpana Gupta. "Gut/brain axis and the microbiota." *The Journal of clinical investigation* 125.3 (2015): 926-938.

directly affect the absorption of nutrients from digested food,⁶³ its participation in preserving its host's healthy state appears evident.⁶⁴ From such perspective, health stops being an intrinsic feature tied to a body, and is reshaped as an emergent property arising from a state of balance between the human and other-than-human components of that same body.⁶⁵ This reformulation of health as a bodily condition at once defined and participated by both human and more-than-human actors, shapes a new, posthuman health paradigm that rests on non-hierarchical interactions between the different constituents of a body.

Thus, if the meaning of human health is to be reformulated as a transversal feature emerging from the encounter and coexistence with more-than-human species, rather than an intrinsic property of human bodies, debating about health means to investigate the modes and alternative scenarios of living and thriving together in a world characterised by the inescapable intertwining of relationships between humans and more-than-humans.^{66,67}

By now, I hope to have made clear how important microbes really are. They can adapt to extreme conditions and hostile environments. They were here long before humans and will continue to thrive long after our species will have gone extinct.⁶⁸ Microbial importance, however, lies not only in their staggering adaptability and omnipresence, rather in their largely underestimated

⁶³ Berry, E. Sarah et al., "Human postprandial responses."

⁶⁴ Hansen, Tue H., et al. "The gut microbiome in cardio-metabolic health." *Genome medicine* 7.1 (2015): 1-16.

⁶⁵ Raffaetà, Metagenomic Futures.

⁶⁶ Raffaetà, Roberta, "Caring across borders. The politics of belonging and transnational health," *Anuac* 8, no. 1 (2019): 59-83.

⁶⁷ With the expression "more-than-human" I refer to those organisms who exceed the definition of "human." Such organisms are also referred to as "other-than-human," however, I have deliberately decided to adopt the former definition to underline its ethical, social and cultural standpoints and implications.

⁶⁸ O'Malley, Maureen. Philosophy of microbiology. Cambridge University Press, 2014.

transformative potential. Microbes have the power – if observed, studied and interpreted carefully – to reshape our culture, our consideration of the morethan-us and ultimately our vision of the world and of those who inhabit it. Microbes constitute an integral and crucial part of our "being human," both conceptually and factually.⁶⁹ Their presence is essential to us and constitutes the foundation of our well-being. In light of this, our own "human body" loses its unitary form and can be redefined as an intricate ecosystem – or holobiont – in which the human and more-than-human factors merge as complementary parts of a single whole.

As such, reflecting on the role of microbes becomes essential to a deeper understanding of the human nature in a world that is increasingly scarred by human-induced global changes and on the brink of climatic collapse. This is especially true in light of the gigantic monetary traction that microbiome companies have been gaining globally, thus shaping the nature of multiple research areas and public as well as private investments.⁷⁰

1.2 Mining for microbes: the proliferation of microbiome startups.

Before entering the world of a microbiome startup, is it crucial to understand what a startup is. Author and entrepreneur Paul Graham describes it as:

A startup is a company designed to grow fast. Being newly founded does not in itself make a company a startup. Nor it is necessary for a startup to work

⁶⁹ Studies have shown how the human-microbial cell ratio seems to be as high as 1:1. For further information see Abbott, Alison, "Scientists bust myth that our bodies have more bacteria than human cells," *Nature* (Jan. 2016).

⁷⁰ Gosálbez, "The Microbiome Biotech Landscape."

on technology, or take venture funding [...] the only essential thing is growth. Everything else we associate with startups follows from a fast and steady growth.⁷¹

Consistency and speed: these are the two essential parameters. Due to the focus on growth as "the only essential thing," it appears evident how the laws of supply and demand play a critical part for such a business model to successfully develop and retain its efficiency over time. If the supply is lower than the demand, the unitary price for a particular good or service will go up and more actors will be looking to join the market while they still can. This will be done through the use of investments which can be internal or external, and that are aimed at generating a future return from the invested asset, be it time, money or effort. The process will play itself out until the quantity demanded will equal the quantity supplied and an economical equilibrium will be reached. These laws form the theoretical basics of modern economics. When it comes to connect economic theories to the world of microbiome, however, there are other factors e.g. scientific advancement to consider.

Indeed, new discoveries and research create innovative practical applications, herald unexplored futures and mould new collective imagination. In the case of the microbiome, establishing new patterns and constructing knowledge linking microbes and health have set the perfect conditions for a favourable economic and investments environment. Intellectual property tutelage in the internet age also played a key role. This led to the explosion of microbiome related biotechnology startups all throughout 2010s, reaching a peak in 2014, when 28 companies operating in the sector were born in that year alone.⁷²

⁷¹ Graham, Paul. "Startup = growth," Internet access: http://www. paulgraham. com/growth. html (2012): 1.

⁷² Gosálbez, "The Microbiome Biotech Landscape."

Professor Rossi, whom I have already mentioned, identifies three main propellers that can justify the staggering increase in popularity and consequent waves of national and international investments in the microbiome field, which, more often than not, take the shape of new startups operating in the sector:⁷³

- Better technologies
- Reduction of the associated costs
- The raising awareness amongst specialised and general public that the microbiome has a crucial impact on human health.

Whilst the improvement of obsolete technologies was essential to propel research in the field, by providing new and efficacious ways to observe microbes at heightened resolutions, the greater computing power was not enough by itself.

If scientists were finally able to study microorganisms with much more precision and in much greater detail, what they lacked now was context. As I will further explain in later chapters, studying microbes' genetic characteristics comes with great difficulties, the first of which has to do with sample complexity. That is the high degree of diversity embedded within the human gut microbiome, which consists of trillions of microorganisms from different taxonomic groups. In addition to that, a community of microbes is much more than the sum of its parts, and a mere taxonomic classification is thus not useful to make successful predictions on the overall functions.

Suddenly, scientists and researchers had a new goal: they had to extrapolate meaning from otherwise dull data, uncovering new biological implications and establishing new patterns of relations. This was not easy to

⁷³ Rossi, Interview.

achieve. DNA sequencing was extremely slow⁷⁴ and expensive⁷⁵ compared to today (figure 2), which brings me to the second point raised by Professor Rossi: the reduction of sequencing costs.⁷⁶

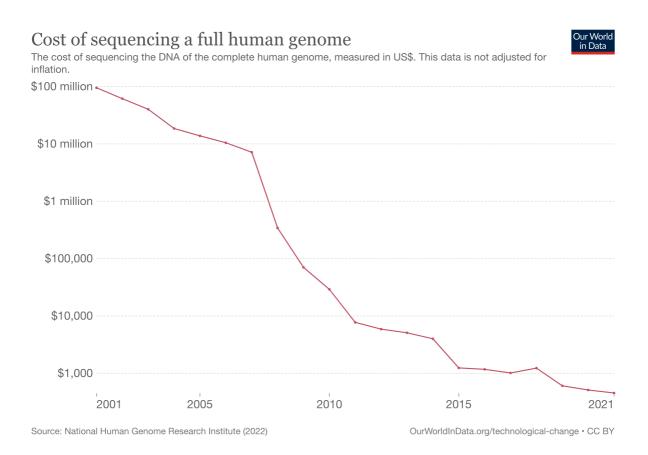


Figure 2: Courtesy of <u>OurWorldInData.org</u>: Cost of sequencing a full human genome through the years.

Author and university Professor Young recalls that in the 90s the cost of sequencing was around 6.000\$ per megabase (MB),⁷⁷ which is the unit of

⁷⁴ Emily Mullin, "The Era of Fast, Cheap Genome Sequencing Is Here," *Wired*, September 29, 2022, <u>https://bit.ly/3vMiKIL</u>.

⁷⁵ "The Cost of Sequencing a Human Genome," National Human Genome Research Institute, accessed 9 January, 2023, <u>https://www.genome.gov/about-genomics/fact-sheets/Sequencing-Human-Genome-cost</u>.

⁷⁶ "DNA Sequencing Costs: Data" National Human Genome Research Institute, accessed 9 January, 2023, <u>https://www.genome.gov/about-genomics/fact-sheets/DNA-Sequencing-Costs-Data</u>.

⁷⁷ Professor Young, interviewed by Luciano Ferrari, January 6, 2023.

measurement used to help designate the length of DNA, where one megabase is equal to 1 million bases.⁷⁸ With time, technology slowly became more effective and cost-efficient. The rate of improvement followed Moore's Law⁷⁹ for about a decade until next-generation sequencing came out in 2006-2008,⁸⁰ and the cost plummeted from the 6.000\$/MB to 0.03\$/MB.⁸¹

Such drastic change in the market made DNA sequencing extremely faster and much more affordable, leading to an explosion in related research.⁸² Phylogeny and other evolution scholars⁸³ – who had not necessarily been trained as molecular biologists – could observe firsthand the genetic basis of relatedness amongst living organisms.⁸⁴ Whilst the relationships of relatedness they observed in plants and animals were consistent with the pre-existing literature, this was not at all the case for microbes. In fact, microbial observational studies powered by next-generation sequencing (NGS) opened a

⁷⁸ "MEGABASE (MB)" National Human Genome Research Institute, accessed 9 January, 2023, <u>https://bit.ly/3ZIVheZ</u>.

⁷⁹ In 1965, Gordon E. Moore, co-founder of Intel made the observation that the number of transistors on a microchip doubles every two years, making their growth exponential. Moore claimed that we can expect the speed and capability of our computers to increase every two years because of this, yet the cost of computers will be halved after that same interval. His observations became known as Moore's Law.

⁸⁰ Kulski, Jerzy K. "Next-generation sequencing—an overview of the history, tools, and "Omic" applications." *Next generation sequencing-advances, applications and challenges* 10 (2016): 61964.

⁸¹ "DNA Sequencing Costs: Data"

⁸² Kulski, "Next-Generation Sequencing."

⁸³ In biology, phylogenetics is the study of the evolutionary relationships among or within groups of organisms. These relationships are determined through phylogenetic inference methods which focus on observed heritable traits such as DNA sequences or morphology. The results of such analyses are condensed into a phylogenetic tree, or a diagram depicting a hypothesis of relationality that reflects the evolutionary history of a group of organisms. For further information see: https://www.biologyonline.com/dictionary/Phylogeny.

⁸⁴ Kulski, "Next-Generation Sequencing."

whole new world that scientists could not possibly have imagined (figure 3):^{85,86,87}

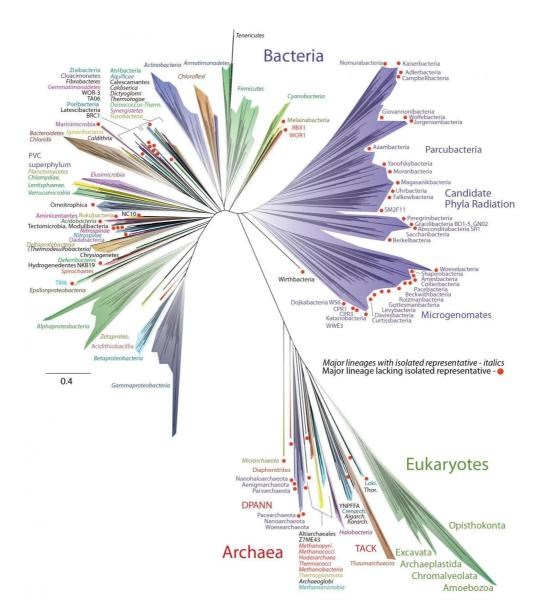


Figure 3: Updated representation of the tree of life. This diagram clearly shows that much of Earth's biodiversity is of bacteria I origin, half of which includes *Candidate Phyla Radiation*, whose members have yet to be studied. Human beings can be found in the bottom branch of eukaryotes. Credit: Hug, Laura A., et al. "A new view of the tree of life." *Nature microbiology* 1.5 (2016): 1-6.

⁸⁵ Pasolli, Edoardo, et al. "Extensive unexplored human microbiome diversity revealed by over 150,000 genomes from metagenomes spanning age, geography, and lifestyle." *Cell* 176.3 (2019): 649-662.

⁸⁶ Woese, C. R., Kandler, O. & Wheelis, M. L., "Towards a natural system of organisms: proposal for the domains Archaea, Bacteria, and Eucarya," *Proc. Natl Acad. Sci. USA* 87, (1990): 4576–4579.

⁸⁷ Zimmer Carl, "Scientists Unveil New 'Tree of Life'," *The New York Times*, April 11, 2016, <u>https://www.nytimes.com/2016/04/12/science/scientists-unveil-new-tree-of-life.html</u>.

In the words of Professor Young:

"It was like someone opened Pandora's vase. And this was 2006-2008, so fifteen years ago. But it was probably about 2017-2018 when we really started marvelling at the thing. At all the vastness of it and the immeasurable and unexpected diversity of the microbial world."⁸⁸

When asked about that same vastness, Professor Rossi mentioned how data from the Human Microbiome Project, which was terminated in 2016, are still producing new results even today.⁸⁹ Hence, the discovery of data ceases to be the point of arrival, functional in so far as corroborating element of the starting hypothesis, rather it becomes the starting point for an inquiry that is much more profound and articulated.

Since 2008, technological advancement has done nothing but speeding up and evolve into new and groundbreaking applications. Metagenomics is a prime example of such trend. In turn, innovation has led to the astounding decrease in the time and costs of sequencing, which today amount to one tenth of where they stood just five years ago.⁹⁰

Finally, the third point raised by Professor Rossi mentioned the raising awareness that the microbiome directly impacts human health. When individual metabolic responses to different foods are analysed, it becomes undeniably clear that the microbiome has a crucial and direct impact on the individual's cardio-metabolic health. The community of microorganisms living inside a person's gut can and will influence the metabolic responses (glucose, metabolites, triglycerides, etc.) of that particular individual towards specific foods. Discovering more about the dynamics regulating these interactions – which still remain vastly unknown – could greatly improve prevention and

⁸⁸ Young, Interview.

⁸⁹ Rossi, Interview.

⁹⁰ Ibid.

treatment of diseases associated with the gut microbiome or parts of it, i.e. diabetes or irritable bowel syndrome (IBS).⁹¹

There is perhaps a fourth reason that can explain the relentless blooming of microbiome startups: microbiome composition is changeable; science, but also individuals can intervene on it:

Rossi: "Its crucial importance [of the microbiome] lies in its direct link with our health as individuals. But perhaps even more than that, it lies in its ability to be adjustable. When you combine 'adjustability' and 'crucial impact on health' – although the 'how' is still unclear – you get the importance of this new research field."⁹²

To really understand the scale of this revolution we need to think back to the human genome. Just like the microbiome, the human genome is of paramount importance for someone's health. Differently from the microbiome, however, a person will never be able to alter their own genome. This is where the true heart of microbiome research lies: in the liminal spaces of known and unknown interactions between microbes and humans.

What does this practically mean, though? How can the microbiome be adjusted? And what mission do the companies operating in this sector have for the future? To answer all of these questions, we will have to enter Foodomics, a personalised nutrition startup dealing with the microbiome and which analyses personal metabolic responses to different food in order to provide individual, real-time dietary advice that best suit each of its customers' microbiomes.

⁹¹ Shreiner, "The Gut Microbiome."

⁹² Rossi, Interview.

CHAPTER TWO INSIDE THE WORLD OF FOODOMICS

This chapter, which stands at the heart of the present work, is the result of extensive research, digital ethnography and several interviews conducted with internal employees and external collaborators at Foodomics, a personalised nutrition startup operating in the microbiome sector and based at King's College London. Specifically, I will take up Foodomics' work and research into the microbiome as a case-study to thoroughly analyse what personalised nutrition is, how it can affect our health as individuals and how it can be used to move beyond a limited, anthropocentric and ultimately detrimental vision of food and personal well-being.

In order to construct a solid and comprehensive basis for my research, I will focus both on the practical and the conceptual sides of my case study, dealing with the services offered by Foodomics, unpacking their product line and analysing users' experiences. I am particularly interested in understanding which role does the individual play within a personalised nutrition dietary programme.

To this end, I will deconstruct the concept of personalisation to understand if and how it can be truly beneficial to the individual, while also looking at the bigger scheme of implications of such research into the microbiome. The primary goal of this thesis is not to endorse personalised nutrition and/or personalised medicine practices. My aim is to explore the social implications as well as the benefits and limits associated with such technoscientific innovation, investigating its practical applications and potentially problematic implications.

For such reasons, I will start by exploring the relatively small reality of Foodomics to later broaden the scope of my research to a comparative analysis

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of the potentials and limits linked to personalised nutrition – which seem to apply to the field of personalised medicine as well, trying to assess both positive and negative aspects for each of the topics I will cover. My aim is to showcase the premises and promises of microbiome research and its medical applications in the field of food and nutrition. In this regard, particular attention will be dedicated to the political and economic aspects of healthcare governance vis a vis the personalisation of medical treatment.

2.1 The philosophy of Foodomics: understanding how food affects your body

In Q1 2021, personalised nutrition app-based startup *Foodomics* closed his Series B financing round⁹³ with 20\$M raised, bringing the total amount of funding received to 53\$M.⁹⁴ The company is both UK and US based and, although it was founded in 2017, it nearly only conducted research into the microbiome for the first three years of its life.⁹⁵ Foodomics' main founder is academic Professor Smith, from a very prestigious UK-based University. Professor Smith originally became interested in the connection that food and the microbiome maintain with health, after spending decades researching identical twins to uncover the role of nature vs. nurture factors on human health.⁹⁶

⁹³ Series B financing is the second round of funding for a company that has met certain milestones and is past the initial startup stage. Series B investors usually pay a higher share price for investing in the company than Series A investors.

⁹⁴ This source cannot be disclosed due to privacy rights.

⁹⁵ Over this time, Foodomics has collaborated with illustrious scientists and researchers from prominent institutions such as King's College London, Harvard T.H. Chan School of Public Health, Stanford Medicine, Massachusetts General Hospital and others.

⁹⁶ Over the years, this has led Professor Smith to the publication of several academic papers and books, as well as to be one of the most renowned scientific public figures in the UK.

To delve into the microbial mystery of the human body and understand how it affects our health, Foodomics uses large datasets derived mainly from two large-scale microbiome studies – while a third one is currently ongoing. The two studies, named PREDICT1 and PREDICT2 constituted two complementary halves of the PREDICT program (figure 4), which configured as the largest indepth nutritional research program of its kind in the world. The program was aimed at measuring biological responses to specific foods in 2,152 and 987 people respectively. PREDICT1 ran over a period of 14 days, and it was carried out between January 2018 and February 2020. Scientists measured blood glucose, fat levels, activity, inflammation, sleep and gut microbiome diversity of each of the participants. The final results were published on *Nature Medicine* in June 2020.⁹⁷ PREDICT2 configured as an expanded home-based study which opened in June 2019 and was completed in March 2020. 987 volunteers were recruited across the U.S. and nutritional responses to food over a period of 11 days was measured.⁹⁸

⁹⁷ Berry, "Human postprandial responses."

⁹⁸ For further information see "WHITEPAPER: THE PREDICT PROGRAM," Foodomics, accessed 10 April, 2023.

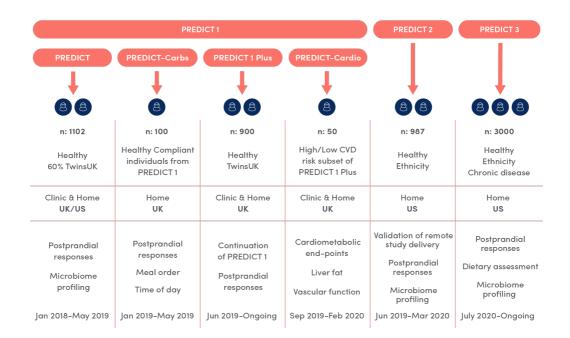


Figure 4: An overview of the entire PREDICT program. Courtesy of Foodomics. For further details see Appendix A.

With the massive amount of biological data extrapolated from their observational studies, Foodomics' IT experts engineered a first algorithm, which then constituted the primal skeleton of their personalised nutrition app. The commercialisation of such app took place in September 2020, alongside the launch of Foodomics' first tangible product on the U.S. market: a home testing kit which enabled customers to find out more about their individual metabolic responses to different foods, by joining Foodomics' program to get personalised nutrition advice based on individual test results.

This first testing phase requires customers to undergo a series of selfadministered tests designed to assess their own biology, metabolism and gut health. The results of these tests are then sent back to Foodomics' labs where more specific tests are run by professional personnel and a report is produced. Before delving too deep into Foodomics' science, however, I will take a few steps back and have a look at the premises and main assumptions underlying their work.

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Professor Rossi and his research team at the Rossi Lab in Trento actively collaborate with Foodomics by leading all the microbiome research side of the company. As part of my research, I have had the honour to interview postdoctoral fellow and bioinformatician Dr. Bianchi, who joined the Rossi Lab in March 2014 and deals with the development of computational tools for metagenomics and phylogenetic analysis.⁹⁹ In particular, Bianchi has given me interesting insights on some of the difficulties associated with microbiome research:

Ferrari: "What is the engine that propels this huge wave of microbiome research and why is the cooperation with a reality like Foodomics so important to you as a research team?"

Bianchi: "I believe this microbiome craze sprouts from the need to explain why something works – or doesn't – in different individuals and improve human health as a result. [...] The potential of this research has been widely acknowledged. The key to unlock it, however, is to study a lot more people and to gather a lot more data: the microbiome is simply too large and too unique. This is why working alongside a company like Foodomics constitute an optimal condition for us: they get to improve their product, and we get to study the microbiome at a scale that wouldn't be possible with any research grant, due to economical and practical limitations."¹⁰⁰

Precisely from such need of studying a lot more and gathering a lot more data to give meaning to observational studies, PREDICT1 was launched in 2018, and 1.102 people spent a day at the hospital giving out urine, blood and stool samples. These samples were then tested to "provide detailed measurements of individual metabolic responses to standardised muffin-based meals engineered to contain carefully controlled amounts of calorie, fat, protein, carbohydrate and

⁹⁹ In biology, phylogenetics is the study of the evolutionary history and relationships among or within groups of organisms.

¹⁰⁰ Dr. Bianchi, interviewed by Luciano Ferrari, November 21, 2022.

fiber."¹⁰¹ The cohort included 660 identical and non-identical twins from the TwinsUK database, which were chosen to prove that even individuals carrying the exact same genome can have completely different microbiome compositions, resulting in contrasting responses to the same food. Such findings have important epistemological implications, as they neatly separate the microbiome from the notion of something that it inherently acquired by the individual at birth and can never be modified.¹⁰²

The results PREDICT1 clearly revealed strong connections between numerous microbial species living inside of some people's microbiomes and correlated sets of metabolic responses to specific foods. When asked about the scientific relevance of such findings, Bianchi commented:

Bianchi: "For us, this was a huge turning point: if the microbiome is associated with a particular kind of diet, food or metabolic response, *then* people with similar microbiomes might have, by association, similar responses. [...] In turn, this can lead us to develop personalised nutrition guidelines and directives that would greatly improve the health of each individual."¹⁰³

Indeed, one of the core assumptions standing at the heart of Foodomics' work is that one-diet-fits-all paradigms are scientific nonsense, in that they neglect the astounding variability of metabolic responses that diverse individuals have towards specific foods. For instance, studies have shown how normal people can vary tenfold in their blood sugar responses to identical food.¹⁰⁴ Surprisingly, as the PREDICT1 successfully showed, this is true even for

¹⁰¹ "PREDICT: The world's largest in-depth nutritional research program," Nutrition, Foodomics, accessed January 19, 2023.

¹⁰² Berry, E. Sarah et al., "Human postprandial responses."

¹⁰³ Bianchi, Interview.

¹⁰⁴ Berry, E. Sarah et al., "Human postprandial responses."

identical twins, who are biological clones sharing all of their genes and much of their external environment. In particular, studies have found that identical twins share on average just 37 per cent of their gut microbe species, which is only slightly higher than the percentages shared by two unrelated people, underscoring the rather modest effect of genes in nutrition. Interestingly enough, most of the differences in metabolic responses were due to individual factors, such as microbiome composition, different circadian rhythms in individual body clocks, physical activity, amount of sleep and other factors that have yet to be studied:¹⁰⁵

The assumption that we are all identical machines responding to various foods in the same way is the most prevalent and dangerous myth about food. [...] The idea we can all follow the same advice and calories limits no longer makes sense, in the same way that we wouldn't all be comfortable in a standard car seat without adjusting it, just because it was designed for an average person.¹⁰⁶

The bottom line is that each individual faces extremely complex and endless food choices every day. These choices do not happen in a void and when it comes to food, very rarely people can just freely "choose" their behaviours. What we eat is also heavily influenced and shaped by how our social, political and economic system is organised, that is whether healthy food is easily obtainable, whether it is affordable, its quality, and whether we have the luxury to care about it.¹⁰⁷ Our microbiome, unsurprisingly, seems to be heavily affected by that. Thus, healthy-eating appears increasingly less to be a fully individual choice. Rather, it is something that should be fostered at the societal level. I believe this to be especially true in the prospect of an overcrowded and

¹⁰⁵ Spector, Spoon-Fed, 21-22.

¹⁰⁶ Ibid., 10.

¹⁰⁷ Ibid., XI.

overheated planet where nearly 40% of the global population today is obese¹⁰⁸ – with reports warning about the possibility of such figure raising over 51% by 2035.¹⁰⁹ I believe that, in such a scenario, we cannot afford the luxury to interpret the world through simplistic dichotomies. Understanding how the science of everyday-food directly impact our individual lives is of paramount importance¹¹⁰ to learn more about ourselves and find new allies to face contemporary crises:

As food choice is incontrovertibly linked to our environment, this is no longer just important for our own sake, but for the sake of our planet and future generations too. [...] Diet is the most important medicine we all possess. We urgently need to learn how best to use it.¹¹¹

Therefore, Foodomics positions itself as a mediator figure between each person's microbiome and its host. Its mission as a company is to help customers solving their major metabolic health issues caused by inflammation, while also empowering them with the most up-to-date scientific knowledge about the microbiome, so as to allow them to make more informed, personalised, individual choices. But how does this work, exactly?

¹⁰⁸ Campbell Denis, "More than half of humans on track to be overweight or obese by 2035 – report," *The Guardian*, March 02, 2023.

¹⁰⁹ Mahase, Elisabeth. "Global cost of overweight and obesity will hit \$4.32 tn a year by 2035, report warns." (2023).

¹¹⁰ While I acknowledge that food-science is not the only determinant that plays a role, I still believe it is one of the most important and underestimated factors when it comes to investigate human health and individual everyday-life. In truth, there would be many other non-technological ways to approach this issue. Such as banning the consumption of junk food worldwide, limiting the production and selling of animal products, fostering daily physical exercise, shortening working hours, etc. All of which, however, as Spector points our in his book *Spoon-Fed*, are very unlikely to happen, as they would clash with the enormous economic interests of international lobbies and corporations.

¹¹¹ Spector, Spoon–Fed, 17.

For starters, joining Foodomics is not as easy as one would expect. Due to long waiting lists¹¹² of thousands of new aspirant members wanting to partake in the program each week, it could take weeks – if not months, to actually gain access. Once a prospective customer receives notice of acceptance from Foodomics and pays the related fees, they will receive the initial testing kit at their doorstep. Buying the testing kit, necessary to join Foodomics' services and gain access to their app, at the time of writing (April 2023), costs \$294.00 in the U.S. – payable upfront or in six monthly instalments (\$49 each) – and £299.99 in the U.K. – payable upfront or in monthly instalments of variable amounts.

After the customer has paid, they will have to complete the initial sixweeks-long testing phase of food login, food tracking, food-weighing and other data collection. This includes, for example, eating artificially engineered muffins whose goal is to benchmark and compare individual nutritional responses to a specific and controlled amount of calories, carbohydrates, fats and proteins. Furthermore, a continuous glucose monitor to optimally track the participant's blood sugar must be worn at all times during this period.¹¹³ Finally, the acquisition of a stool sample is required for a detailed analysis of the gut microbiome. Once this first testing period has ended, customers will send all the relative samples and results back to Foodomics' labs and wait for their final report.

After two more weeks, customers finally receive their individual insightreport comparing their own personal results to hundreds of thousands other people. This passage is essential because, as we have mentioned, each person's response to different food may differ greatly, including significant variations in blood sugar and blood fat levels. Based on the data extrapolated from the individual's responses, then, a table is generated and attached to the report. This

¹¹² During our interview, Professor Rossi reported that 250.000 people are currently registered in Foodomics' waiting list whilst 2.000 more ask to join the program every week.

¹¹³ "How Foodomics Works," Foodomics, accessed January 22, 2023.

table lists each food originally logged-in by the user during the initial testing phase, with a small addition. Each of the foods listed in the table is associated with a tolerance score from 0 to 100, which should reflect how effectively the individual's metabolism and microbiome have responded to each food.

Finally, each participant's personalised gut health report also includes a "microbiome health score," which is associated with the presence and quantity of 30 specific microbial species. Based on past findings from the PREDICT research program linking them to metabolic health, 15 of these 30 microbes have been tagged as "positive," whilst the other 15 have been tagged as "harmful" to human health. Depending on each user's score, they will receive personalised recommendations for specific gut boosters – that is foods positively linked to the beneficial microbes detected, thus helpful in reducing gut inflammation states in that specific individual – and gut suppressors – that is foods negatively linked to the detrimental microbes detected, which should thus avoided or limited in consumption.¹¹⁴

What Foodomics seems to offer its users is an all-round, thoughtful and rich gut health guidance, attentive to the each customer's own individuality and backed up by solid scientific research. To this end, Foodomics' support to its members extends to a large number of free educational materials on the microbiome and the nutritional sciences, which are easily accessible even without specific sectorial knowledge on the subjects. This approach, in particular, seems to be in stark contrast with numerous companies operating in the microbiome sector, which often tend to neatly separate the underlying scientific knowledge from the resulting products, not leaving their customers the possibility, if they so wish, to dive into the dynamics that regulate the functioning of the product they ultimately pay for.¹¹⁵

¹¹⁴ Bianchi, Interview.

¹¹⁵ Spector, Spoon-Fed.

However, empowering users with actual knowledge about the functioning of their bodies, and how a state of health can be achieved and preserved through food and dietary choices, can constitute a fundamental element in the process of individual enhancement and societal training. The customer who embraces this will be strengthened by the newly acquired knowledge, which, in turn, will provide them with a greater level of agency in making more accurate and thoughtful dietary choices, with less risk of falling victim to a standardised industrial food industry that increasingly values parameters like sales growth and economic gains way more than customers' health.

This guidance leading to the understanding one's own microbiome, and the ways in which its microbial communities can be powerful allies in preserving our health, finds its most concrete form in the construction of personalised nutrition programs, which Foodomics uses to translate each client's insights into tangible, actionable dietary advice. Once the testing phase is over and the personalised reports have been returned to each customer, access to Foodomics' official companion app is granted and the true personalised dietary programme begins. By accessing the app, each user is provided with a weekly eating-plan that is tailored on their individual biology and lifestyle.

In order to make the process more interactive and stimulating, the app is structured as a sort of mini-game, with daily, real-time changing eating-scores provided to the user, and which are thought to be rough indicators of how well they are faring through the day. This personal score can be raised or lowered based on what foods are eaten, in which quantities, eating and fasting windows, as well as other parameters. Everything – and this is one of the fundamentals of Foodomics' service – is always related and closely linked to the composition of each individual customer's own microbiome. Thus, no two programs are perfectly identical, and each user can experience a very high, if not unique, level of customisation. Foodomics' goal in structuring its service in such a way is to

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maintain a high level of individual engagement, whilst at the same time fostering healthy eating habits.

The theoretical framework that stands behind such approach is called "gamification" and it consists on adding game-elements to non-game activities. The rationale behind gamification is to offer a sense of reward to the user, who feels periodically gratified by a positive comment or score, received as a by-product of their activity.¹¹⁶ In turn, such gratification triggers feelings of enjoyment and satisfaction, both of which encourage the release of dopamine, which further boosts user's engagement and prompts them to reiterate the target activity.¹¹⁷ Much like gaining new perks when levelling up in a game, or earning points for completing specific game goals incite you to play more.

Technically speaking, such induced reiteration is called behaviour reinforcement, and is based on the idea that people tend to enjoy being in control.¹¹⁸ If *they* are the ones choosing how to interact with any proposed activity towards the completion of a task or the realisation of a goal, they will be more likely to feel in control and thus to enjoy the experience overall.¹¹⁹ Furthermore, studies have shown how human beings are inherently competitive with themselves and others.¹²⁰ Therefore, adding competitive elements to an activity can stimulate personal commitment and dedication to the activity itself.

¹¹⁶ Krath, Jeanine, Linda Schürmann, and Harald FO Von Korflesch. "Revealing the theoretical basis of gamification: A systematic review and analysis of theory in research on gamification, serious games and game-based learning." *Computers in Human Behavior* 125 (2021): 106963.

¹¹⁷ Dopamine is a compound present in the body as a neurotransmitter and a precursor of other substances such as adrenaline, thus acting as a sort of "reward center" to the brain as well as having a role in many other bodily functions.

¹¹⁸ Krath, "Revealing the Theoretical Basis."

¹¹⁹ Chris Wingfield, "All the World's a Game, and Business Is a Player," *The New York Times*, December 23, 2012.

¹²⁰ Leibbrandt, Andreas, Uri Gneezy, and John A. List. "Rise and fall of competitiveness in individualistic and collectivistic societies." *Proceedings of the National Academy of Sciences* 110.23 (2013): 9305-9308.

In the case of Foodomics, creating weekly goals and personal scores that users will be encouraged to complete and improve is a great way for them to stimulate competition with themselves. In addition, this process offers a tangible way – through the real-time changing score – for users to visualise their progress, hopefully gaining even more motivation and momentum as they approach their goal. In the meantime, the feeling of progression generates gratification, which boosts dopamine levels and the cycle begin anew.

On the other hand, not everyone reacts the same way to competitive environments, and a minority of users reportedly experienced feelings of discomfort and emotional distress originating from the competition-triggered anxiety they felt through the gamification of their dietary journey. In some cases, such feeling of distress then translated into a partial detachment from the programme, whilst, in fewer instances, it caused certain users to interrupt their personalised dietary journey altogether.¹²¹

Perhaps the greatest feature of such service is its extremely high level of personalisation. Indeed, not only will the personal score be different for each individual and vary according to their own, unique microbiome composition, but the impact of the same food on the daily score too will be different, even across similar patterns. Such level of detail is reflected in a system of real time feedback prompts evaluating diverse parameters to give personalised meal suggestions based on the data logged in by the user.

Indeed, by processing the individual data collected during the day, as well as the huge database available to the algorithm empowered by machine learning (ML) and employed by Foodomics, the application will then proceed to provide targeted suggestions to each customer of supposedly ideal foods and/ ore recipes that are most beneficial to them, at any particular moment of the day. Such suggestions are provided always taking into account the personal tastes, culture, habits and preferences of each individual, as well as the

¹²¹ This data has been provided by an internal source who wished to remain anonymous.

biological parameters related to their own microbiome. Again, the goal is to help people achieve and maintain a state of well-being, by proposing valid and healthier alternatives that are scientifically designed to improve each customer's metabolic responses and to benefit their own unique microbial identity:¹²²

"Through the personal scoring you are assigned based on Foodomics' analyses, Foodomics' official companion app gives you real-time suggestions on which foods are most suitable to your individual biology. So, through the app, you can easily plan your day and meals. In the long run, the idea behind this is to accompany you on a journey and direct your dietary choices towards what the AI model processing your individual data has suggested is best for your metabolism and gut health."¹²³

As Dr. Taylor, University Reader in the UK and lead nutritional scientist on the PREDICT program explained to me during one of our interviews, one of the main points behind Foodomics' work is that:

"No food needs to be off limits. Our [Foodomics'] main goal is to empower our users with the information and tools they need to make the best realtime decisions for their own body and health."¹²⁴

2.2 Being a customer at Foodomics: the centrality of the individual

One dimension that perhaps constitutes one of the most important aspects of a company like Foodomics is their consideration of the complex human being

¹²² "How Foodomics works."

¹²³ Bianchi, Interview.

¹²⁴ Dr. Taylor, interviewed by Luciano Ferrari, November 25, 2022.

that stands behind the customer. If, at any time, feelings of frustration, doubt, anxiety or the general sensation of being stuck are experienced by a member of Foodomics' community, they may access a one-to-one weekly coaching service included in the price of their membership. Such form of continuous individual support is provided through a live chat system that each customer can easily access from the companion app, and which allows them to be put in touch directly with a specialist from the company.¹²⁵

The meticulous attention to the diverse lifestyles of each Foodomics member is one of the strongest points of the company's service, which – according to Taylor – still manages to dedicate the proper amount of time and attention to each and every one of them despite the very high – and rapidly growing – volume of new customers. Unsurprisingly, such attention translates into a stream of overwhelmingly positive feedback response coming from those who are already participating in the program.¹²⁶ In turn, this has led to the stacking up of extremely long waiting lists where hundreds of thousands of aspirant new customers are waiting to get accepted in the programme – with an average of two thousand new names being added each week.¹²⁷ But there is more.

The constant support and consideration of customer's needs and feelings are the reflections of one of Foodomics' founding principles, that is the commitment to always put the customers' own interests first. Whilst, as one may expect, such care towards the client appears to be a common trend amongst other companies operating in the field of personalised nutrition, a peculiar

¹²⁵ Jones, Interview.

¹²⁶ Here, I am temporarily overlooking a series of complaints about the general costs of service and occasional lack of clarity reported by some users, which at any rate constitute but a small part of the overall feedback. I will address these complaints further in the next section. Such feedbacks – both positive and negative – were reported to me by Jones, Head of User Satisfaction at Foodomics. Furthermore, several video interviews with Foodomics members can be found on the company's website in the subsection "Results & Reviews."

¹²⁷ Rossi, Interview.

philosophy is in place at Foodomics, which translates, I believe, in crucial practical differences.

However, in order to fully grasp the differences that make Foodomics' approach unique, we first need to look at the underlying premises that have laid the foundation for the company's work. One of the core ideas upon which Foodomics' research is based is that "we are living at a very unique and fortunate moment in time, where three things have come together like never before:"¹²⁸

1. The appreciation of the importance of food and diet and their impact on human health.

2. The discovery and evolution of the understanding of the microbiome and its overlapping with the field of nutritional science.

3. The technologies necessary to measure the individual biology and the microbiome at the right scale needed to provide good scientific knowledge, while giving something back to participants in return.

Furthermore, as Dr. Taylor argued during our interview, the tragedy of the COVID-19 pandemic has brought to the forefront of everyone's mind the importance of health and science, forcing people all over the world to face their own mortality and that of their loved ones directly, as well as accustoming them to undergo periodic testing in the process.¹²⁹ Indeed, Taylor claims, the brutal clash with daily images of death and suffering has prompted many people to raise the value they attribute to a condition of personal well-being, seeking healthier lifestyles, in contrast with the frenetic and suffocating pre-pandemic society.¹³⁰

- ¹²⁹ Ibid.
- ¹³⁰ Ibid.

¹²⁸ Taylor, Interview.

Such newfound interest in the preservation of a robust health state – according to Spector – has inevitably affected the food and nutritional spheres of individuals, as such dimensions are part of a larger array of basic activities the importance of which can be easily forgotten, but that truly have enormous impacts on our health, in that eating healthy, unprocessed, diverse foods undeniably improves health.¹³¹ And when the greater awareness of the role that food and diet play on human health is combined with the techno-scientific advancements that allow us to observe these phenomena in detail, such union inevitably leads to an explosion in the discipline of personalised nutrition, which attempts to combine all of the above elements to the betterment of the human condition through science and research.¹³²

Here, I believe, is where the big jump occurs. Indeed, although the single individual remains the focus of such process, the inquiry into the multiplicity of dimensions that composes them proves crucial to the detachment from an individualistic vision of life, in favour or a transversal, multispecies and systemic one. The valuing of such multidimensionality is inherent in the transversal approach that identifies the importance of both human and non-human elements as fundamental in the achievement and maintenance of an healthy state for the individual.

As explained in the introduction, the boundaries between what can be defined as "human" and "non-human" are not neat, nor factual as it used to be argued until a few decades ago. On the contrary, that of life is a porous and discontinuous border, on the edge of which it appears no longer important to be able to distinguish "us" from "them," but rather to ask questions about the entities that make up such borders and how they work together to maintain a state of equilibrium.

¹³¹ Spector, Tim. Food for Lie: The New Science of Eating Well, (London: Penguin, 2022).

¹³² Taylor, Interview.

For such reasons, the focus of microbiota studies has increasingly been shifting towards the concept of "ecological community" of specific microorganisms, rather than on the agency that each single member has within it:

Bianchi: "Even if you zoom in to the single species, this will not be completely useful for drawing accurate conclusions: it is rather necessary to have an overall, more holistic vision of the microbiome: a vision that takes into consideration the ecosystemic nature of this reality rather than the individual nature of the individual species that compose it. In fact, the ecosystemic nature, the aggregation and the internal dynamics that emanate from it [the microbiome] can potentially lead to the expression of completely different and distinct functions from those of each single species taken in its individuality."¹³³

It therefore serves a limited taxonomic purpose to categorise every single element found within the human gut microbiome, if that same microbiome is not also considered as an organic, complex system, whose elements interact and maintain functional relationships with each other.

Maybe, the time has come to embrace more holistic visions of the human being, and to attribute the right degree of philosophical and epistemological importance to such a fundamental element of our being human as the microbiome is. Perhaps the time has come to (re)consider the human entirely also in terms of its non-human components, bringing us closer to a symbiotic vision of life that rejects the concept of humans as unitary bodies and embraces that of holobionts.¹³⁴ Seen from such perspective, the "functional whole" is nothing more than a substrate underlying a set of distinct and biologically

¹³³ Bianchi, Interview.

¹³⁴ Gilbert, Scott F., Jan Sapp, and Alfred I. Tauber. "A symbiotic view of life: we have never been individuals." *The Quarterly review of biology* 87.4 (2012): 325-341.

different biomolecular networks that compose it, and within which the concepts of "self" and "non-self" totally lose their meaning.

Following such reasoning, it is essential to integrate this newfound conceptualisation of "ecological body,"¹³⁵ as well as its huge diversified complexity, with the dimensions of food and diet. But how can this be achieved? Foodomics' answer to such question – which brings us back to its peculiar philosophy – seems both obvious and cryptic at the same time: "by using the multifold character of personalisation."¹³⁶

As the different approaches chosen by various companies operating in personalised nutrition clearly show,¹³⁷ there is no set of pre-made instructions or fixed formulae on how to achieve true personalisation. Some companies focus on certain aspects and parameters pertaining to the individual, while others will look at different variables. Thus, the concept of personalisation turns out to be variable, different depending on who is putting it into practice. So how should personalisation be achieved? Is it enough to stop at the observation of biological data and use the information extrapolated from it to construct personalised interventions, or is there also another dimension, which reaches beyond biological parameters and directly concerns the individual from whom that same data was collected?

During our interview, Dr. Taylor explained to me the vision of personalisation that drives Foodomics' research:

"When we talk about personalised nutrition we need to think about two factors. We need to think first about attirance, and then secondly about efficacy. And people don't often think about the attirance side. There's lots of

¹³⁵ Gilbert, "A symbiotic view of life."

¹³⁶ Taylor, Interview.

¹³⁷ See, for instance, the case of the app-based US startup Pinto as opposed to the more DNAoriented Canadian startup Gini, focused on nutrigenomics as the core part of their personalisation process.

good diets and lifestyles, recommendations out there that we know *do* work for people, even at a population level [...]. The problem is people don't follow them. So we know that in the UK, for example, less than 1% of people follow all our seven main dietary guidelines. What we do know from published evidence is that if you deliver dietary guidance [...] in a personalised way to that individual, we know that it improves diet quality. So if there is one thing we know, is that personalisation is really powerful in bringing about change in people."¹³⁸

Delivering advice in a personalised way. From Dr. Taylor's words, it is clear how personalisation should not and cannot stop at the purely biological study of individual samples. Attitudes, preferences, habits, living conditions, psychology and any other elements that give individuality to the person must be taken into consideration. In other words, human societies are not laboratory-grown colonies of microbes. Human life does not take place in conditions of controlled sterility and isolation from the outside world. On the contrary – as Taylor emphasises – the "external" factors mentioned above will have a strong impact on the daily choices made by individuals and, therefore, they cannot be neglected.¹³⁹

Therefore, I believe that pretending to apply the same aseptic lab criteria to the process of personalisation – whereby a biological sample should be analysed, fed to a super advanced artificial intelligence, translated into an algorithm and returned as a clean and applicable outcome – without considering any other external factor, is like trying to carry out an open heart surgery in the middle of a swamp, expecting not to run into collateral hygienic problems. What emerged from my research is that personalising solely on the basis of biological data appears to be totally useless, as it neglects the fact that life does not happen in a sterile vacuum. On the contrary, several extremely

¹³⁸ Taylor, Interview.

¹³⁹ Ibid.

complex systems appear to be constantly interacting with each other, and it is precisely from their interactions that new balances are born and the process of individual ontogenesis unfolds. Indeed, Taylor stresses that personalising without taking into account everything that is not necessarily biological would mean leaving the "real person" outside of personalisation. ¹⁴⁰

Instead, according to Taylor,¹⁴¹ the two complementary sides – biological and environmental – that make up the individual must both be taken into consideration when constructing an intervention that truly aims at improving health through a personalised nutrition approach. Only then can the incredible technology allowing us to study the microbiome in such detail be effectively used to bring about real change in people's life.

Taylor: "Now the second thing about personalisation is efficacy. And the question about efficacy is: does delivering personalised advice based on someone's biology like the microbiome or their genetics improve the effectiveness of the intervention? Can that help in bringing about a *better* change in weight, or blood pressure, etc.? There's not much evidence on this because it's a new area. We believe, based on that little evidence we have, that yes: delivering personalised advice not just in a personalised way but personalised in the sense that it is based on your biology will improve health outcomes. I think both of these sides are very valuable and we mustn't underestimate the first one as delivering advice in a personalised way really improves outcomes, and this applies across all medicine, not just food and diet."¹⁴²

Here is the ambitious goal fostered by Foodomics. Through their innovative and unique multifold approach to personalisation, Foodomics' scientists, technicians, bioinformatics, physicians and researchers are attempting to

¹⁴⁰ Taylor, Interview.

¹⁴¹ Ibid.

¹⁴² Ibid.

construct new and unexplored scenarios, whereby the processes of achieving, preserving and improving individual health are framed to take into account of the full complexity of the natural world, while attempting at providing a practical tool to deal with it:

Taylor: "[...] On the subject of personalisation in order to improve outcomes, something that I think has not been acknowledged before and it's what we're doing at Foodomics thanks to the goldmine of data offered by our users, is that as well as personalising on someone's biology – microbiome, genetics, age, sex, etc., we also need to personalise on how people live their lives. We need to personalise on what *truly* is their individuality. And my individuality isn't just my genes or my microbiome, but it's also how I live my life: how much I sleep at night, how often I do exercise or how stressed I am, for instance. And all these things are of crucial importance and this is what we're seeing with our data [...] so we know for instance that for some people sleep is really important, while for others it's eating windows. [...] That's where I think the exciting future lies and it is what we're doing at Foodomics."¹⁴³

True personalisation, then, requires a 360-degree view on the individual. Personal, social and even cultural factors can play a crucial role in the choices of a person and, perhaps even more importantly, in why they make such choices. When asked about the importance of individual motivations in this formula, Dr. Taylor replied:

Ferrari: "How important are individual motivations in this equation?" Taylor: "Certainly a lot. That is why we also need to personalise on the why you make those choices. I might choose my breakfast depending on how well I slept the night before or based on my religion, or culture, etc. [...] So it's really important we consider the 'why' as well. And I think, based on the

¹⁴³ Taylor, Interview.

data we're collecting, that for *true* personalised nutrition and *true* personalisation, we have to consider four factors. One: the complexity of the food we eat. Two: the complexity of us i.e. what we eat, who we are, etc. Three: how we eat. And four: why we make those choices. And I think the game changer going forward is going to be delivering reliable and actionable real time advice to people based on all those factors."¹⁴⁴

Obviously, such a goal is far easier said than done. This is especially true when different demographics and social classes are taken into consideration: many people do not have the luxury to afford free, unbiased choice due to situations of social inequality, precarious economic resources or the necessity to work late-night shifts. As some scholars point out,^{145,146} even when these segments of the population were equipped with personal nutritional advice, they would most likely not follow them due to lack of means to do so – yet it could be argued that they would be the ones benefiting most from it.¹⁴⁷ Thus, as the critical medical anthropology debate on personalised nutrition – and medicine – clearly shows,^{148,149,150} it appears crucial to also invest on the structuring of efficient harm reduction and/or prevention systems so as to encompass the lower and poorer strata of society as well.

¹⁴⁴ Taylor, Interview. Original emphasis.

¹⁴⁵ Frank, Arthur W. "What's wrong with medical consumerism." *Consuming health: The commodification of health care* (2002): 13-30.

¹⁴⁶ Shinn, Leila M., and Hannah D. Holscher. "Personalized Nutrition and Multiomics Analyses: A Guide for Nutritionists." *Nutrition Today* 56.6 (2021): 270-278.

¹⁴⁷ Adams, Sean H., et al. "Perspective: guiding principles for the implementation of personalized nutrition approaches that benefit health and function." *Advances in nutrition* 11.1 (2020): 25-34.

¹⁴⁸ Reardon, Jenny. "The 'persons' and 'genomics' of personal genomics." *Personalized Medicine* 8.1 (2011): 95-107.

¹⁴⁹ Savard, Jacqueline. "Personalised medicine: a critique on the future of health care." *Journal of bioethical inquiry* 10 (2013): 197-203.

¹⁵⁰ Burke, Wylie, et al. "Extending the reach of public health genomics: what should be the agenda for public health in an era of genome-based and "personalized" medicine?." *Genetics in Medicine* 12.12 (2010): 785-791.

The biology of each individual is extremely complex and its interactions with other actors at play i.e. the microbiome or external environmental factors remain largely unknown. Nonetheless, given enough time, funding and research, personalised nutrition practices supported by a more detailed understanding of the microbiome structuring and composition could prove to be a resource in preserving and improving people's health, especially for middle and high middle class and in cases where more traditional medicine should have little or no effect.

While talking about such revolution with Professor Young, her words about it were at once filled with excitement and resolution, as if she was explaining something both obvious and ineluctable:

Young: The personalisation revolution in nutrition – and medicine – will impact every aspect of our daily lives. And really, when you think that this phenomenon is so closely linked to the bacterial world, are you surprised? [...] The metabolic rate of bacterial groups is so much higher than ours, and our metabolome,¹⁵¹ is 18% derived from gut microbes. This means that every cell in your body that is serviced by blood has been interacting with the microbial world. This is just profound. It's a metaphysical thing, in that it changes and reshapes the way we think about ourselves [...] and food is our prime mean of interacting with such world. Personalised nutrition studies show that we are much more complex than we thought and we must acknowledge this change, for it truly has the transformative power to change everything.¹⁵²

Here lies the importance inherently tied to the exploration of the human microbiome. It is something that impacts every human being, with no exception.

¹⁵¹ For further information see Stephen G., et al. "Systematic functional analysis of the yeast genome." *Trends in biotechnology* 16.9 (1998): 373-378.

¹⁵² The term "metabolome" refers to to the complete set of small-molecule chemicals found within a biological sample, Young, Interview.

The microbial omnipresence in our lives is a factor that must be taken into consideration, as its intermingling with our existence is inevitable and charged with agency. Indeed, it is "a revolution that cannot simply be ignored." In turn, such realisation requires further lucubration on the very nature of the concept of health, as well as the meaning of being human, and how such concepts can be (re)defined to encompass the vast microbial complexity within preexisting cultural and societal paradigms.

We are healthy individuals because the dualistic nature of our complex multispecies organism is in balance between its human and non-human components. Following the same reasoning, we are not human only because we are the product of the paternal fertilisation of a maternal egg cell. Rather, we are human because we have chosen to call ourselves that, unwittingly bypassing infinite levels of increasing complexity, which up to a few decades ago were invisible to our limited human eyes.

However, now that science has allowed us to make up for this lack, and that we have acknowledged that a table is not just a table, but an aggregate of atoms and empty space held together by elementary forces, why not apply the same principles to the study of what makes us who we are? There is a galaxy of microbial communities living within us, which *is* us, which directly influences our mood, our habits, our preferences and our lifestyles. The easiest and most accessible point of contact to establish communication with such universe is the food we ingest every day. As Dr. Spector claims, "the future of high-quality, personalised nutrition has arrived, and there is no room for ignorance and misinformation on our plates."¹⁵³

¹⁵³ Spector, Spoon-Fed, xiv.

2.3 The potential and limits of microbes: how gut science is done and what its applications are

When I first approached the study of the microbiome during my university studies, I was immediately enthralled by its vastness, mystery and beauty. Since I was a kid, I have always had a deep passion for the study of science and physics, even though my academic life has evolved in a diametrically opposite way. In high school – scientific, of course, so as to not to break the solemn family tradition – chemistry and biology were by far my favorite subjects. I was fascinated by the unique, magical, almost dreamlike character of chemistry, while of biology I adored the fact that, if observed from the right distance, nothing was as it appeared. Smoke and mirrors and make-believe. Reality was not fixed, on the contrary, it was an unknown universe just waiting to be explored. Alas, the unfortunate presence of mathematics was a more than effective repellent in making me desist from pursuing a career in the hard sciences.

Indeed, it was the dormant love for science and biology that – when the chance presented itself – instantly got me hooked on becoming obsessed with the microbiome. For the first time in my humanist academic studies I was allowed to analyse, research and deepen a scientific topic. And, although the constraint was to approach the issue of the microbiome from a mainly anthropological perspective, I immediately decided to embark on the research that has led me to write this thesis.

Because my passion for science had never really fully materialised into a real, in-depth study of the subject, I naively assumed that the act of "doing science," also physics but especially biology, was mostly done in the laboratory. Then again, such is the idea of scientists usually shared by collective imagination: mysterious alchemists who, within the inscrutable walls of their

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labs, discover the world and the laws that regulate its functioning. Soon, I discovered that this was not the case.

Indeed, during our first interview, Dr. Bianchi confirmed what I had read in relevant laboratory ethnography literature: almost all members of the Rossi Lab actually work from an office, spending eight hours a day sat in front of their laptops. Twenty or so researchers alongside their computers. No test tubes, lab coats, counters filled with Bunsen burners or fluorescent concoctions I secretly hoped I could marvel at. Perhaps taking pity on my initial – not so well concealed – disappointment, Dr. Bianchi promptly explained to me that "the wonder" was indeed there, only it was not visible to naked eyes. It happened inside very complicated machines, called sequencers, powered by even more complicated softwares running on something called machine learning.¹⁵⁴

Thus, Dr. Bianchi proceeded to clarify the clear distinction that exists between wet and dry biology. If the first is the one which most closely corresponds to the idea I personally had of scientific research carried out in the lab, the second is the one that is mainly carried out at the Rossi Lab, as well as in other similar laboratories around the world. In such cases, the laboratory itself occupies a secondary position. Most of the science is made inside of an office, sitting casually at a desk rather than standing in front of a counter, handling keyboards rather than vials.

As a matter of fact, in metagenomics, but more generally in modern molecular biology, the laboratory has been endowed with a growingly marginal role. Rather, the technological equipment is the fundamental actor capable of amplifying and processing the collected data. So what is the role of the scientist in such new paradigm? They become interpreters:

¹⁵⁴ Machine learning is defined as "an evolving branch of computational algorithms that are designed to emulate human intelligence by learning from the surrounding environment." For further information see El Naqa, Issam, and Martin J. Murphy. *What is machine learning?* Springer International Publishing, 2015.

Dr. Bianchi: "Simplifying a lot, most of our work consists in analysing what the scientific community has decided to call *reads*. That is, DNA or RNA sequences from which we try to derive patterns, which will then be organised and curated, giving us a more or less precise vision of our microbiome."¹⁵⁵

How researchers at the Rossi Lab see microbes, their vision, is therefore not a direct, material vision, comparable to that of a landscape or an object held in a hand in front of an observer. Instead, they analyse a staggering amount of extremely high-definition images depicting strips of microbial genetic material. Working upwards from there, they attempt at rebuilding the original whole. That of researchers at Rossi Lab is a vision mediated by algorithms, sequencers, diversified methodological approaches and softwares allowing for a limited interaction with fragments of microbial genetic material. In reality, the process is much longer and a lot more complex than what Bianchi explained to me. Numerous additional steps are required – both wet and dry – including the use of specific tools and procedures. However, for reasons of space and complexity, I will not expand on such topic here.¹⁵⁶

If we were to reduce the entire process to its bare minimum, necessarily giving up much of its real complexities and challenges, we would say that everyday a huge amount of extraordinarily complex, personal – both biological and non-biological information is gathered from Foodomics' users and is fed as data to super-advanced softwares at the Rossi Lab in Trento. There, researchers use ML-supported algorithms to study the microbial composition of their samples and formulate predictions on how different people will biologically and metabolically respond to different foods. Such insights are then sent back to Foodomics, which returns them to its customers through their companion app in the shape of personalised nutritional advice. The goal is to improve individual

¹⁵⁵ Bianchi, Interview.

¹⁵⁶ For further information, see Raffaetà, *Metagenomic Futures*, chapter four.

gut health, gut microbiome diversity, and reduce inflammations caused by traditional diets.

This is Foodomics today. An impressively successful, well-oiled machine if we consider that the startup has been operating in the microbiome business for little over five years now. So, what about the future? What is Foodomics' mission and how will personalised nutrition science look like ten years from now? I asked Dr. Taylor the very same question:

Ferrari: "What is Foodomics' vision for the future? What are you trying to achieve 10–15 years from now?"

Taylor: "We hope to keep growing our service so that one day it will be able to take the shape of delivering extremely precise, perfectly accurate and truly personalised real-time dietary advice to people. [...] We want it to be the equivalent of having a dietician in your pocket. Based on the personal data you feed to the app, you will be provided with extremely accurate and personalised real-time advice about the best possible food that's available to you in that particular moment and for that specific situation, so that your individual health benefits the most from it."¹⁵⁷

Whilst during our interview Dr. Taylor and I mainly focused on the potential of microbiome studies to positively revolutionise the field of nutritional sciences, she also acknowledged some of the limits associated with it, namely that of a person's over commitment to personalised dietary guidance.

Indeed, Dr. Taylor believes that such a high level of personalisation, if not carefully contextualised, could in fact be detrimental to some people. In other words, care must be taken not to perceive an imposition of food practices conveyed through the high level of personalisation, since this would only lead to negative results for the individual. In such delicate passage, correct and precise

¹⁵⁷ Taylor, Interview.

communication, as well as constant attention to the needs of each individual customer, play a fundamental role.

Other issues, then, might come with the over-extensive digitalisation of eating habits, which, Taylor warns, could end up being devoid of their inherent pleasurable dimension and the feeling of personal freedom typically attached to it:

Ferrari: "What do you think might be some of the risks or ethical concerns of this research moving forward?"

Taylor: "Our biggest ethical concern is that with too much knowledge, at times, comes confusion, anxiety and the pleasure of simple things risks to be taken away. Food is meant to be enjoyable. To medicalise it... it is a shame. To allow people to enjoy the cultural and social aspects of it is of paramount importance to us, and for this reason we must not allow over-personalisation to take this away. Our job then becomes delivering this information in a way that is responsible and actionable, with an attention to the individual as a human being, not just a test subject. Empathy is central in this, and ethical issues become about how you impart knowledge *back to* someone, and we need to do so in a proper manner to avoid triggering terrible health anxieties."¹⁵⁸

While Dr. Taylor does not deny the potential for such scenarios to occur, identifying them as latent issues that may need to be managed in a more structured and engaged way in the future, as a scientist she also has faith in the scientific medium and believes that the transformative potential behind microbiome research amply justifies the risk of making eating habits less pleasurable which could be involved in a digitalised approach such as that of Foodomics:

¹⁵⁸ Taylor, Interview.

Taylor: "We acknowledge there may be potential risks. We are walking in an unexplored territory after all. However, all things considered, it would still be great to have enough knowledge to be able to deliver this kind of information to the people who actually want them."¹⁵⁹

Although great, life changing scientific discoveries never come overnight, the future Dr. Taylor talks about could be much closer than one might imagine. Nowadays, she says, the prospects of personalised nutrition – and thus of personalised medicine – are rosier than ever. As Bianchi observed, when we consider the fact that the technological infrastructures and sequencing practices upon which this field is grounded will keep getting better and cheaper with every passing year, there is no true limit to the things we could achieve in just a few more decades:

Bianchi: "Long-term goals surely include being able to improve and perfect personalised guides and directives that work properly from a nutritional point of view. For instance, I want to be able to say that for an individual Y it's better to eat food A and not food B because other X people with similar microbiomes to Y have had considerably better metabolic responses to food A than to food B."

Ferrari: "Does this personalisation end with nutrition or can it be transferred to other areas of medicine such as oncology or pharmacology?" Bianchi: "This is *the* golden question and one of the most important implications of stratifying the microbiome in various layers of health. This, however, is still problematic as it requires something called *causality*."¹⁶⁰

The causal relationship to which Dr. Bianchi refers to configures as a univocal relationship of causality between the microbiome – or a part of it – and a certain metabolic reaction, symptom, imbalance, condition or disease:

¹⁵⁹ Taylor, Interview.

¹⁶⁰ Bianchi, Interview.

Bianchi: "There is what we call a very high 'probability association,' that is a very strong probability, that a causal link exists. It is this very strong probability that allows me, for instance, to say that if the individual "X" has a glucose peak following the intake of the food "Y," then, *most likely*, X's microbiome will contain microbial species "A," "B," and "C," which are responsible for the recorded peak. As of today, however, it is not possible for me to affirm with absolute and incontrovertible certainty that this is actually true."¹⁶¹

Causality, then, is extremely important, as it defines a relationship of direct consequence between two elements internal to someone's biology. Establishing such causal links would allow to build targeted medical interventions specifically designed to prevent and treat any medical condition directly caused by the parameter "X," internal to the patient's microbiome. Contemporary microbiome studies have been able to observe such relationality phenomenon, but they have not yet been able to prove its existence. The reasons are manifold. Perhaps the first and most impactful is that, despite the novelty of the study, there is still a lot of heterogeneity in the research of individual microbiomes and, thus, relatively few data to work with.¹⁶² It is therefore extremely complex to prove such probability association and reflect it to the higher levels of biological causality.

Some of the cases where this phenomenon has been observed include several instances of gastrointestinal and colorectal tract cancers, whereby a significant percentage of tumours has already been linked with the presence of some specific bacterial species.¹⁶³ Further research in this direction, as well as a more accurate understanding of the mechanisms that regulate the connections

¹⁶¹ Bianchi, Interview. Original emphasis.

¹⁶² Rossi, Interview.

¹⁶³ Thomas, Andrew Maltez, et al. "Metagenomic analysis of colorectal cancer datasets identifies cross-cohort microbial diagnostic signatures and a link with choline degradation." *Nature medicine* 25.4 (2019): 667-678.

between cancers and the microbiome, would undoubtedly pave the way to a new, cutting-edge frontier of oncological and immunotherapeutic treatment, with some pilot clinical trials already showing a recovery rate of over 50%.¹⁶⁴

Furthermore, studies have shown how it is possible to predict, with more or less accuracy, which individual would – or could – respond positively to such immunotherapeutic practices precisely through the analysis of their microbiota composition.¹⁶⁵ Building on that, other clinical trials have focused on individuals who had responded positively to immunotherapy and later agreed to donate part of their microbiome to other patients, who had responded negatively or had yet to undergo immunotherapeutic treatments.¹⁶⁶ The donors and the recipients had to undergo a surgery called fecal microbiota transplantation (FMT), or "the medical procedure of transferring human fecal matter from a healthy donor to a recipient to treat a disease related to microbiome imbalance."¹⁶⁷ Following FMT, it has been observed how the recipient's microbiome was able to modify its composition significantly, leading to a subsequent positive response to the treatment cycle.¹⁶⁸ However, the fact that the entirety of a donor's microbiome needs to be transplanted to obtain such results means that, according to Rossi:

"[...] On the one hand we didn't understand anything. It would be way simpler and much more efficient to establish a causal link between the single bacterium and the respective desired application. On the other hand, this is also a great confirmation of the huge impact that the microbiome has on our

¹⁶⁴ Rossi, Interview.

¹⁶⁵ Sears, Cynthia L., and Wendy S. Garrett. "Microbes, microbiota, and colon cancer." *Cell host & microbe* 15.3 (2014): 317-328.

¹⁶⁶ Mattila, Eero, et al. "Fecal transplantation, through colonoscopy, is effective therapy for recurrent Clostridium difficile infection." *Gastroenterology* 142.3 (2012): 490-496.

¹⁶⁷ Ianiro, Gianluca, et al. "Variability of strain engraftment and predictability of microbiome composition after fecal microbiota transplantation across different diseases." *Nature Medicine* 28.9 (2022): 1913-1923.

¹⁶⁸ Mattila, Eero, et al. "Fecal transplantation, through colonoscopy."

health. So huge, in fact, as to influence our internal response to immunotherapy. And that's great."¹⁶⁹

I reckon it is important to spend a few more words on the first point raised by Professor Rossi, because where at first glance there seems to be something amiss, I believe we can identify a perfect linearity instead. The necessity to transplant the entire microbiome – rather than just one or a few microbial species – for FMT to have the desired effects is indicative of the ecological character of the microbial ecosystem. Microbial communities are structured on different functional levels directly related to each other and which, in order to "function properly," necessarily need to be embedded in such a systemic reality. In other words, the microbiome is much more than the sum of its parts, and the medical practice of the FMT demonstrates it perfectly.

I believe the main problem is that western science tends towards constant simplification, and for such reason they have become accustomed to establishing more and more univocal relationships of cause and effect. Therefore, we tend to think that such functional model is applicable across every aspect and dimension of reality, regardless of the context. The microbiome, with its convoluted, ecosystemic dimension, clearly shows that this is not the case. Thus, due to the potential that such indivisible complexity has, I would like to spend a few more words on causality, before moving on.

In the case of the microbiome, the level of complexity is much higher than that of single microbes taken singularly because bacterial species generally have what is called "horizontal gene transfer." Such transmission of genetic material occurs in contrast to other animal species such as humans, whereby genetic material is transferred "vertically," with 50% of the DNA coming from the mother and 50% of the DNA coming from the newborn's father.

¹⁶⁹ Rossi, Interview.

In bacteria, however, entire sets of genes can be exchanged between two different species at any time during their life cycle. Such unregulated exchange of genetic material is, among other things, one of the main reasons leading to the development of antibiotic-resistant super-bacteria species.¹⁷⁰ Therefore, the critical question that microbiologists, bioinformaticians and doctors have to answer has now become: "is bacterial species A the cause of pathology X, or is it the functional set Y carried by species A, but originally coming from species B?" If the answer is the latter, then, neither species A nor B would be identifiable as causes of pathology X. Rather, the culprit would be the functionality Y that they carry. Such aspect of the microbial world obviously adds several levels of complexity, which Bianchi summarises in three main point:

Bianchi: First, because we ignore the functionality of 80% of the genes in question. There is no database or laboratory test anywhere in the world that associates a given gene with a specific function or developed protein. Second, this issue results in an IT problem when it comes to actually studying these species. That is because even if we were able to analyse all the genes found in the microbiome, we would end up having 80% whose potential function we ignore. "Potential," because the presence of a gene does not necessarily mean that such gene is actually active or functioning. Whilst the third point and final point concerns metabolic functions. That is because, contrary to the other species, in the case of the microbiome I can observe a pathway of five genes A-B-C-D-E, and have a bacterial species that with two genes of my pathway starts from the molecule A_1 and arrives at the molecule A_2 and carries it to the molecule B_1 .¹⁷¹

¹⁷⁰ Von Wintersdorff, Christian JH, et al. "Dissemination of antimicrobial resistance in microbial ecosystems through horizontal gene transfer." *Frontiers in microbiology* 7 (2016): 173.

¹⁷¹ Bianchi, Interview.

Thus, to draw relatively accurate conclusions, one must adopt more holistic and systemic vision to the microbiome, in order to understand its functional dimension. If, as emphasised by Bianchi,¹⁷² a causal relationship was ever to be achieved, it would pave the way to a new era of microbiome research, whereby individual genetic signatures could be employed to herald a new age of widespread personalised medicine.¹⁷³ The stratification of the microbiome into various layers of health, today only theorised based on the aforementioned association of probability, would be definitively justified. In turn, this would allow scientists to describe with the utmost accuracy which microbial signatures would identify (and define) different generalisable levels of health, even in individuals without clinically manifest disease.¹⁷⁴ Such a step would constitute a profound revolution in medical practices and prevention techniques.

Another problematic point raised by Dr. Bianchi during the course of our interview was that of the – often ignored – importance of raw data. To explain what he means by that, Bianchi told me how when his child was born a little over three years ago, he and his partner decided to request a genetic test for the kid at various Italian companies, all of which belonged to a Californian corporation. However, Dr. Bianchi complained about the fact that, even when paying a large sum of money for such services, what he and his partner received in return was only a PDF with a list of names and values printed on it:

Bianchi: The problem with this is not knowing what the future has in store for us from a precision medicine perspective, especially when public health is concerned. If I am asked to pay 300€ for a test, I cannot be satisfied with receiving a PDF with a list of names and values. I would also like to have

¹⁷² Bianchi, Interview.

¹⁷³ Pallister, Tess, and Tim D. Spector. "Food: a new form of personalised (gut microbiome) medicine for chronic diseases?." *Journal of the Royal Society of Medicine* 109.9 (2016): 331-336.

¹⁷⁴ Asnicar, Francesco, et al. "Microbiome connections with host metabolism and habitual diet from 1,098 deeply phenotyped individuals." *Nature Medicine* 27.2 (2021): 321-332.

access to the raw data which, in any case, belong to me: they are the reads that the company I paid to test my microbiome has obtained. Furthermore, it could be that in 10 years I can provide those reads to my general practitioner and they, thanks to technological advances and a greater understanding of the microbiome, can come up with something new from re-reading them. I pay for the data, not for a PDF with different coloured stickers that supposedly mean "this is good" or "this is bad." This is a very delicate point that does not always receive the degree of attention it requires.¹⁷⁵

As Bianchi reported during out interview, it was only after several days and dozens of phone calls, that he finally managed to convince the Californian corporation to build specific protocols that would allow him to access the data he had paid for. Apparently, the American corporation explained him, no other client had ever made a similar request. When asked about it, Bianchi told me that he believes that the companies' reticence to hand over raw data can be attributable to several reasons. Keeping the actual data outside the "common reach" allows companies to maintain a position of partial ambiguity on how that specific data was produced. Thus, the PDF returned to the paying customer is nothing more than a summary containing the minimum significant information extrapolated from data analysis. In turn, customers have no other choice than to trust such reports, as they do not have the means or knowledge to do otherwise.¹⁷⁶

In the meantime, the science foregrounding the production of such document remains in the hands of a small elite who is equipped with the specific expertise required to produce it – and cannot wait to sell it on the market. Such marketisation of scientific results is made possible by a paradoxical phenomenon which Bruno Latour defines as blackboxing:

¹⁷⁵ Asnicar, Francesco, et al. "Microbiome connections with host metabolism."

¹⁷⁶ Bianchi, Interview.

Blackboxing is the way scientific and technical work is made invisible by its own success. When a machine runs efficiently, when a matter of fact is settled, one need focus only on its inputs and outputs and not on its internal complexity. Thus, paradoxically, the more science and technology succeed, the more opaque and obscure they become.¹⁷⁷

In one of his most recent publications Latour returned to the topic and added that "scientists should make explicit their interests, values, and what kind of evidence might change their minds."¹⁷⁸ Whilst this would be an important first step towards full transparency, the process cannot end there. Opening the "black box of science" and revealing its interiors cannot have the sole purpose of demonstrating that scientists are all moved by wickedness and greed – rather than the pure altruism and devotion to progress. Instead, this should be:

A reflective and rational intervention about the historical, socio-cultural and political assumptions that underlie scientific practices. [...] not in order to reveal the hidden interests or intentions of individual scientists, but to open up a space for democratic debate.¹⁷⁹

During the course of our interview, Bianchi provided a rather sympathetic explanation on why companies refrain from handing raw data over to their customers, only granting a compressed interpretation of it in the shape of a report. According to him, the decision is solely based on the fact that the average client would not be able to grasp the meaning of it anyway. In other words, even if the actual data were returned alongside the report, the vast majority of customers would have no use that they could autonomously make of

¹⁷⁷ Latour, Bruno. Pandora's hope: Essays on the reality of science studies. Harvard university press, 1999.

¹⁷⁸ De Vrieze, Jop. "'Science wars' veteran has a new mission." (2017): 159 in Raffaetà, *Metagenomic Futures*, p. 204.

¹⁷⁹ Raffaetà, Metagenomic Futures, p. 205.

it. But even if such explanation was true, it would still ignore two of the fundamental aspects of technoscientific advancement: progress and variability, which Bianchi himself mentioned during our talk:

Bianchi: "I am lucky enough to work in this sector, knowing what a read is, a sequencing, which machines are used for which tests, etc. And so I'm lucky enough to understand the value of data comparison. 99% of the people wouldn't be able to make anything off that data - or rather, they think they wouldn't, because they ignore the power of data in a future perspective as well. I decided to ask for the raw data because I have no idea about what medicine will be capable of twenty years from now. Maybe, in twenty years, that same raw data will become usable again, as opposed to the binary feedback provided by a report that does nothing but profile individuals following a pattern of "good/bad," "positive/negative," "yes/no," etc. Even today this kind of profiling means very little and, certainly, it will not be usable again in the future."¹⁸⁰

Indeed, the customer's potential ignorance of what the raw data mean cannot be the decisive parameter on which such a decision is based. It is like doing an x-ray. After the customer pays, they carry out a clinical test and receive a DVD containing the raw data of their test: the x-rays. They then go to the doctor and ask for consultation. However, that same data could also come in handy in the future, maybe to look at the patient's previous situation after a certain amount of time, or perhaps when the development of new technologies and equipment would allow for a new, more accurate analysis of it.

To support his claim, Bianchi told me that even Foodomics, following the implementation of new, more advanced softwares, found itself faced with different results from those that had previously been obtained. Indeed, one must not forget that, although microbiome studies tend to be filled with excitement

¹⁸⁰ Bianchi, Interview.

and enthusiasm, they are also inevitably prone to uncertainty and error given the novelty of the sector. Microbiome knowledge is constantly evolving. Thus, even when something new is defined, it does not necessarily mean that it will remain the same forever. It is precisely here that the importance of raw data is felt the most. Indeed, Foodomics was able to reanalyse previously collected data – even several years old – from its users, and re-profile them on the basis of the newly obtained results, which subsequently led to the production of new, more precise individual reports.

Furthermore, the discussion on the ownership of raw data turns out to be even more delicate if the use of microbiome knowledge was to be extended to the emerging field of personalised medicine, as well as to its potential to support, and perhaps one day replace, generalised medicine. The issue regarding who and how should handle and preserve personal raw data still remains open. What is certain, as Bianchi points out, is that:

First of all, we need to educate people to understand and to equip them with the appropriate knowledge. Then, you need to make informed communication. We need professionals in the field of medicine to start taking into consideration the huge impact the microbiome has on the health of their patients. They need to inform themselves, study and start doing active information about it. Microbiome studies should be normalised within medical practice, not be looked down upon with reserve. This would allow microbial knowledge to become a functional clinical tool to provide additional, unique information on patients' health. The practice may not be beautiful - analysing faecal samples may not be the best practice in the world - but in any case it turns out to be much less invasive than many other tests, which are commonly used today.¹⁸¹

¹⁸¹ Bianchi, Interview.

Furthermore, whilst the development of better and vastly more precise technologies generally sounds great, certain scholars have also raised red flags about it.^{182,183,184} In particular, they have highlighted the risks and unwanted implications that might come when individuals detach themselves too much from their own data, failing to recognise the potential consequences of handing over huge chunks of their privacy to scientific authorities and governmental bodies.^{185,186}

Sadly known is the case of African-American woman Henrietta Lacks, passed away in 1951 and whose cancer cells are the source of the HeLa cell line – or the first immortalised human cell line and one of the most regarded and important cell lines in medical research.¹⁸⁷ An "immortalised cell line" is defined as a cell line that reproduces indefinitely under specific conditions, just like the HeLa cell line, which continues to be the source of invaluable medical data even to the present day.¹⁸⁸ Miss Lacks was the unwitting source of such cells, which were extracted from a tumor biopsied as part of the cervical cancer treatment the woman underwent at the John Hopkins Hospital in Baltimore, Maryland, in 1951.

¹⁸² Joyner, Michael J., and Nigel Paneth. "Seven questions for personalized medicine." *Jama* 314.10 (2015): 999-1000.

¹⁸³ Chen, Rui, and Michael Snyder. "Systems biology: personalized medicine for the future?." *Current opinion in pharmacology* 12.5 (2012): 623-628.

¹⁸⁴ Lunshof, Jeantine E. "Personalized medicine: New perspectives-new ethics?." (2006): 187-194.

¹⁸⁵ Armstrong, Stephen. "Data, data everywhere: the challenges of personalised medicine." *BMJ* 359 (2017).

¹⁸⁶ Reardon, The Postgenomic Condition.

¹⁸⁷ Lucey, Brendan P., Walter A. Nelson-Rees, and Grover M. Hutchins. "Henrietta Lacks, HeLa cells, and cell culture contamination." *Archives of pathology & laboratory medicine* 133.9 (2009): 1463-1467.

¹⁸⁸ Zielinski, Sarah. "Cracking the Code of the Human Genome: Henrietta Lacks''Immortal Cells'." *Smithsonian. com January* 22 (2010).

The first HeLa-cells were then cultured by cell biologist George Otto Gray, who first created the cell line today known as HeLa.¹⁸⁹ As per common practice, however, no consent was required to culture the cells obtained as by-product of Lacks's treatment. As a result of that, neither she nor her family ever received any form of compensation for the extraction and usage that was made of the woman's cells throughout the years.¹⁹⁰ Moreover, even though the origins of the HeLa cell line slowly became known amongst researchers after 1970, the Lacks family was never notified of the line's existence until 1975.¹⁹¹ Today, with knowledge of the cell line's genetic origins finally public, its use for medical research and commercial purposes continues to raise vocal concerns, whilst the Lacks case often serves as a warning about privacy and patients' rights in technoscientific research.

In the United States, for instance, the genomic data relating to an individual can be freely used by third parties thanks to a law introduced in 2018,¹⁹² which effectively extends the validity of informed consents regarding the processing of personal data. Thus, by signing the consent necessary for the profiling of their genomic data, customers also automatically consent to the use of their personal, genomic data for any other study, without necessarily having to be asked about it.

Governmental authorities and supporters of such law justify what effectively configures as a shift towards a state of lower personal data protection by claiming that contemporary scientific research is to be framed in the realm of the so-called "Big Data" In light of future benefits for the entire humanity.

¹⁸⁹ Grady, Denise. "A lasting gift to medicine that wasn't really a gift." *The New York Times* 1 (2010).

¹⁹⁰ Truog, Robert D., Aaron S. Kesselheim, and Steven Joffe. "Paying patients for their tissue: The legacy of Henrietta Lacks." *Science* 337.6090 (2012): 37-38.

¹⁹¹ Greely, Henry T., and Mildred K. Cho. "The Henrietta Lacks legacy grows." *EMBO reports* 14.10 (2013): 849-849.

¹⁹² Sugarman, Jeremy. "Examining provisions related to consent in the revised common rule." *The American Journal of Bioethics* 17.7 (2017): 22-26.

Although Big Data is a trending buzzword both in the academia and in business industry, its meaning has not entirely been defined yet.¹⁹³ Without entering into too much detail, the term refers to the technological ability to store, aggregate and process diverse data at unprecedented speed, leading to the creation of Alpowered complex patterns used by science and industry alike. The true strength of Big Data, however, lies is the relatedness established within the data themselves, which allow for such patterns to emerge.¹⁹⁴

Thus, the genomic data of an individual lose all of their meaning if they are not linked to other personal data, effectively justifying a lower protection of individual privacy by virtue of progress and scientific research. The problem, however, is that such a shift holds important implications that, according to some authors,^{195,196,197} should not be minimised in the name of the "common good" or the "improvement of the collective standard of living." This is especially true in the context of a capitalist, neoliberal society whereby, in light of the growing partnership between private companies and research, the meaning of phrases such as "collective standard of living" and "common good" often remain enshrouded in strategic vagueness.

¹⁹³ De Mauro, Andrea, Marco Greco, and Michele Grimaldi. "What is big data? A consensual definition and a review of key research topics." *AIP conference proceedings*. Vol. 1644. No. 1. American Institute of Physics, 2015.

¹⁹⁴ Kitchin, Rob, and Gavin McArdle. "What makes Big Data, Big Data? Exploring the ontological characteristics of 26 datasets." *Big Data & Society* 3.1 (2016): 2053951716631130.

¹⁹⁵ Smart, Andrew, Paul Martin, and Michael Parker. "Tailored medicine: whom will it fit? The ethics of patient and disease stratification." *Bioethics* 18.4 (2004): 322-343.

¹⁹⁶ Reardon, "The 'persons' and 'genomics'."

¹⁹⁷ Feiler, Therese, et al. "Personalised medicine: the promise, the hype and the pitfalls." *The New Bioethics* 23.1 (2017): 1-12.

Back when the Human Genome Project¹⁹⁸ was completed in 2001 both the scientific community and the general public, hyped by heightened promises of a new and exciting future for humanity, had to face a harsh truth: no one in the scientific community had any idea about the meaning of what they had sequenced. In this regard, Jenny Reardon writes that "in the decade after the completion of the HGP, this turn to the question of meaning — the question of the uses, the significance, and value of the human genome sequence — marks what I call the *postgenomic condition*."¹⁹⁹ The core of Reardon's critique has to do with the inability of the scientific community to answer the question of purpose related to the sequencing of the human genome:

Now that all this data has been collected and sequenced, now that the human genome has been arranged and carefully organised in tens of thousands of columns and charts spread across 118.000 pages (figure 5), what comes next?²⁰⁰

¹⁹⁸ The Human Genome Project was a multi-funded, international research project which looked at comprehensively study all of the DNA (known as a genome) of a select set of organisms – in this case, humans. Launched in October 1990 and completed in April 2001, the Human Genome Project's signature accomplishment was generating the first sequence of the human genome. For further information see "THE HUMAN GENOME PROJECT," National Human Genome Research Institute, accessed 10 April 2023, <u>https://www.genome.gov/human-genome-project</u>.

¹⁹⁹ Reardon, Jenny. The postgenomic condition: Ethics, justice, and knowledge after the genome. University of Chicago Press, 2019, 2.

²⁰⁰ Reardon, *The Postgenomic Condition*. On a side note: the feeling of discontent and discomfort that transpires from Reardon's analysis recalls Walt Whitman's celebrated verses in the poem *When I Heard the Learn'd Astronomer*, which I believe perfectly epitomises the sense of frustration and sickness that often comes with the total and aprioristic demystification of the mystery of life and/or nature.

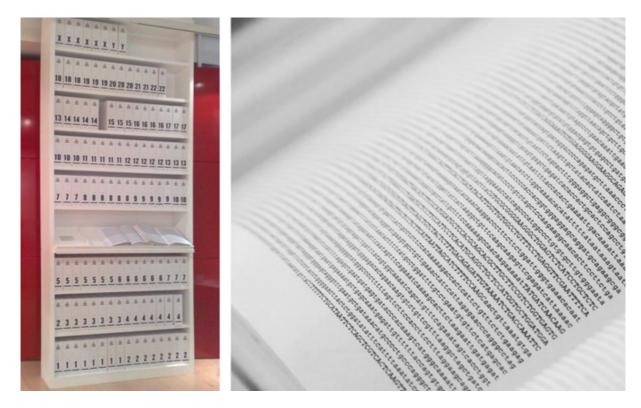


Figure 5: Courtesy of Russ London's photograph of the Human Genome in the "Medicine Now" room at the Wellcome Collection in London, 2008. The collection is made of 118 books, each one thousand pages long and reporting the human genome sequence.

In her book *The Postgenomic Condition*, Reardon also reflects on the deeper meaning of letting science collecting sensitive data on our behalf, and on the value that individual information would acquire in contemporary (un)democratic societies. In an elitist, neoliberal, globalised world, Reardon claims, inequality and discrimination could greatly benefit from the exploitation of biotechnology and life sciences' products – such as the sequencing of the human genome – as new grounds for democratic and (un)just action.²⁰¹ In such regard, genomics upholds what has been observed by social theorists in many other domains of life: the contemporary world is defined by a shift from liberal democratic government to neoliberal governance, and such shift is marked by the "economisation" of all areas of life:²⁰²

²⁰¹ Reardon, *The Postgenomic* Condition, p. 14-15.

²⁰² Brown, Wendy. Undoing the demos: Neoliberalism's stealth revolution. Mit Press, 2015.

"At its heart, bioinformatic infrastructures are built around the values of business: speed, efficiency, growth. Public genomic data today serves these ends. [...] [Thus] precision medicine paves the way for precision enterprises. In this new world, business and biology unite forces. [...] Major biomedical funding bodies direct their resources toward tailored medicine. As in the world of fashion, tailoring is an expensive affair that does not include us all. While genomics may provide leads to new drugs, those drugs will not come cheap."²⁰³

Reardon brings her harsh critique even further by claiming that:

"Rather than an emblematic public good, genomics today bears witness to the broader erosion of the meaning of the public as a domain that fosters consideration of common concerns and the creation of collective goods."²⁰⁴

Finally, in light of all this, Reardon asks an open question on whether it is right that:

"A mode of doing research so dependent on speed, technological innovation, and venture capital dominate the life sciences? Should a field that promises future – not immediate – improvements in health care move to the heart of biomedicine?"²⁰⁵

Indeed, if it is true that the prospect of using microbiome science in the employment of a 1:1 personalised medicine is quite attractive, many perplexities remain regarding its scientific solidity – mainly due to the causality problem – effectiveness, costs and role within public health plans. Indeed, whilst it promises to offer futuristic, compelling medical treatments calibrated on each

²⁰³ Reardon, The Postgenomic Condition, p. 177, 183.

²⁰⁴ Ibid. p. 189.

²⁰⁵ Ibid. p. 185.

individual, it is also true that personalised medicine costs significantly more than generalised medicine.²⁰⁶ Should personalised medicine ever become a widespread practice, the often prohibitive costs associated to it could constitute a discriminating medical care filter for all the people who cannot afford to pay the necessary money. Furthermore, such a shift towards the widespread personalisation of medicine could lead to meaningful fluctuations in funding flows, which would flow from public health care plans towards a minoritarian, elitist wing, the effectiveness of which has not been fully proven yet.

Whilst Reardon's critique might hold some truth, it also true that her analysis focuses mainly on the situation in the United States which, despite being a central actor in global politics, cannot be taken as representative of the global society, composed of a multiplicity of very different realities, which do not necessarily suffer from the same systemic, economic and political problems as the United States do.

Furthermore, building a critique on the basis of the hypothetical misuse that could potentially be made of the product of a technological advance is, I believe, the wrong way to approach the question. If anything, more attention should be paid to the systemic conditions that allow for the unjust, discriminatory, privatised exploitation of a collective resource such as health, rather than to the scientific research that produces it. Also, the fact that some kinds of research – especially the ones characterised by a high volume of technological content, thus requiring large amounts of data – are dependant on huge economic investment without being able to offer immediate, tangible applications in return, cannot be – as Reardon argues – considered the problem. Indeed, as Raffaetà argues, excluding this type of research would mean to rule out basic research, which is a fundamental component of research.²⁰⁷

²⁰⁶ Jakka, Sairamesh, and Michael Rossbach. "An economic perspective on personalized medicine." *The HUGO Journal* 7.1 (2013): 1-6.

²⁰⁷ Raffaetà, Metagenomic Futures, p. 199.

Furthermore, basic research has always required longer times to yield its results, even outside the field of metagenomics and microbiome studies.

It is right in the midst of such difficult and unstable panorama that Foodomics operates. Their service, however, differs drastically from many of the similar companies that do not share fundamental values and principles with the London startup. A notorious example is that of Ubiome, another well-known startup in the field of microbiome research, founded in San Francisco in 2012 at the end of a heartfelt crowdfunding campaign and shut down in 2019 due to bankruptcy and suspected – later confirmed – tax fraud and unpaid user insurance refunds. FBI investigations also revealed several cases of harassment on the workplace to the detriment of several employees and collaborators, who were pushed to improperly certify the scientific validity of numerous reports and results, subsequently sold to unsuspecting users of the platform.²⁰⁸

In order to avoid what has been dubbed the "overselling of microbiomehype," Foodomics takes a whole different approach to its communication. For instance, the company is very careful not to present their services and products as definitive solutions to all the food-related problems of their customers. Thus, Foodomics maintains full transparency on the science-side of its work²⁰⁹ and is attentive not to promise things that cannot be achieved yet:

Our unique microbiome test uses deep metagenomic sequencing to understand which 'good' and 'bad' microbes you have. This allows us to

²⁰⁸ United States Attorney's Office: Northern District of California. "uBiome Co-Founders Charged With Federal Securities, Health Care Fraud Conspiracies." U.S. Attorney's Office, Northern District of California Press Release. <u>https://www.justice.gov/usao-ndca/pr/ubiome-co-founders-charged-federal-securities-health-care-fraud-conspiracies</u>. Accessed 20 April 2023.

²⁰⁹ The "Discover Our Science" page on Foodomics' website is easily accessible and easy to navigate. The background science is presented to the user in various levels of complexities, from simplified summaries to external links leading to published academic papers. Furthermore, Foodomics' customers have access to a whole range of articles, blogposts and newsletter updates deepening the "science-side" behind Foodomics' work even more.

provide personalised recommendations that can *potentially* help increase the 'good' microbes that are under-represented in your gut.²¹⁰

A private company offering microbiome analysis in exchange for a major contribution to scientific research and access to the first fruits of such research through a companion app. This is Foodomics today. But Foodomics is also so much more. It is a prime example of what is commonly defined as *citizen science*, i.e. a system of collective participation based on cooperation between citizens and researchers in the collection and sharing of scientific data relating to a particular field. In Gabrys' words:

Citizen science is now being promoted by many governments, and the policy underpinning it is based on democratic values such as inclusivity and active participation to shape a world that is better for everyone.²¹¹

Indeed, the spirit animating such alternative approach of "making science together" clearly transpires from Dr. Taylor words who, with a mixture of pride and solemnity, told me how the Foodomics companion app was converted into a free access app for fighting the COVID–19 pandemic when the first wave hit the UK in March 2020.²¹² Not only was the repurposed app extremely successful, but the very high flow of data shared by nearly five million users allowed the research team to be the first to discover that loss of taste was indeed a recurring symptom in COVID-19 affected patients. This is how Tim Spector opens his best-selling book Spoon-Fed:

²¹⁰ For further information see "Why Foodomics?," Foodomics, accessed 20 April, 2023.

²¹¹ Gabrys, Jennifer. *Program earth: Environmental sensing technology and the making of a computational planet*. Vol. 49. U of Minnesota Press, 2016. In Raffaetà, *Metagenomic Futures*, p. 196.

²¹² Taylor, Interview.

In March 2020, only a few days after the first edition of *Spoon-Fed* went off to the printers, all our lives changed. When the first wave of COVID-19 hit London, my research department was shut down and we were all sent home by the university. Cycling home from work that day, feeling depressed, I came up with the idea of converting the nutrition app we had been developing with the data science company Foodomics into a free app to fight COVID. Luckily, my colleagues at Foodomics enthusiastically agreed, and within five days the team [...] had a working version ready to be rolled out. The app was an instant hit on social media and was downloaded a million times within 48 hours. [...] 18 months later it now has nearly five million users in the UK, US and Sweden, making it the world's largest citizen-science project ever existed.²¹³

Obviously, Foodomics scientists and researchers are not part of an alien monolith, completely unrelated to the dynamics that regulate the society in which they live, and solely animated by generosity and goodness of mind. The economic aspect is certainly a priority in a reality like Foodomics which, as a company, needs to have continuous income fluxes in order to keep working. However, there is a big difference between selling inflated truths – or outright lies, as in the case of Ubiome – and explore cutting-edge scientific research moved by noble ideals, whilst embracing a policy of full transparency in regards to the results and perspectives of such science. Indeed, if the economic aspect is necessarily a crucial component of the world of Foodomics, it is also true that there are extremely skilled researchers such as Professor Rossi and Dr. Bianchi, who are moved by a genuine interest towards scientific research to improve people's health and living conditions. This is especially true in the context of personalised nutrition, given that diet is one of – if not the most – effective and quickest factors to influence people microbiome's composition.²¹⁴

²¹³ Spector, Spoon-Fed, p.ix

²¹⁴ David, Lawrence A., et al. "Diet rapidly and reproducibly alters the human gut microbiome." *Nature* 505.7484 (2014): 559-563.

But what kind of value is that produced by Foodomics and what are the modes of its production? For Birch, the value in bioeconomy results to a large extent from processes of assetisation through which epistemic knowledge is reified and reshaped into private property which yields a constant stream of incomes.²¹⁵ Thus, the production of bioeconomical value is asset-based rather than commodity-based, meaning that value – be it epistemic, monetary or both – is mostly produced by the ownership and regulation of valuable assets rather than by the production of new commodities sold on the bio-market. Such observations have led Birch and Tyfield to claim that bioeconomy is grounded on a "rentier regime of accumulation," whereby knowledge is transformed into valuable assets which can be rented to extract value.²¹⁶

Pinel has expanded on this by conducting a twelve-months-long ethnographic research in two UK-based laboratories to understand the ways in which bio-value is produced, by examining in detail the activities of the laboratories taken as productive systems made of resources and assets.²¹⁷ What she found is that across the two laboratories studied, the production of value first starts by building and maintaining an accredited portfolio of valuable resources, which are subsequently turned into assets. Labs then mobilise such assets to produce knowledge and value through them. Pinel identifies two main ways in which such process unfolds. The first one has to do with the *creation* of value obtained by the mobilisation of assets and the production of results. These results are then converted into "epistemic credits," which can be mobilised in the competition for grants and fundings aimed at the accumulation of economic capital. The second has to do with the trading relationships that the two

²¹⁵ Birch, Kean. "Rethinking value in the bio-economy: Finance, assetization, and the management of value." *Science, Technology, & Human Values* 42.3 (2017): 460-490.

²¹⁶ Birch, Kean, and David Tyfield. "Theorizing the bioeconomy: biovalue, biocapital, bioeconomics or... what?." *Science, Technology, & Human Values* 38.3 (2013): 299-327.

²¹⁷ Pinel, Clémence. "Renting valuable assets: Knowledge and value production in academic science." *Science, Technology, & Human Values* 46.2 (2021): 275-297.

observed labs entertain with other research teams, to which they rent some of their own assets in return for some form of revenue – be it in the form of coauthorship or acknowledgments over resulting publications or in the form financial capital. As such, Pinel makes the distinction, this second way of producing value *extracts* it from pre-existing assets. Foodomics' production of value uses both modes at the same time.

Pinel's analysis expands well beyond what I can report here, but one crucial point she raises in her conclusion is that "the knowledge and value-making practices discussed have important implications for the type of knowledge produced."²¹⁸ To substantiate her claim, she reports how in the two laboratories studied, new research projects were considered "not just in terms of their potential epistemic value but also for the ways they could help them [the labs themselves] enhance the value of their assets. [...] In other words, what and how knowledge was produced was tightly linked to assetisation [and thus marketable] processes."²¹⁹ For my analysis, one very important implication of Pinel's observations is that entrepreneurial science, which is carried out by companies like Foodomics, being characterised by the imperative to produce knowledge that can be valuable in a variety of contexts, i.e. sold on various types of markets, "matters not only for researchers [...], but also for patients and citizens alike, in that it shapes what we know about the world and our health."220 I agree with the critical reading that Pinel's give of entrepreneurial science. Indeed, when talking about the microbiome, this can often lead to what Bianchi defined as "capitalisation craze."221 That is the obsession to find and develop all sorts of marketable applications of a technology that is often not yet mature enough. In fact, due to how western socio-economic systems are structured,

²¹⁸ Pinel, Clémence. "Renting valuable assets," p. 292.

²¹⁹ Ibid.

²²⁰ Ibid.

²²¹ Bianchi, Interview.

when something becomes a marketable trend, everybody wants to take part in it. Often, without even having the necessary skills or simply moved by the relentless pursuit of profits. Today, the field of microbiome research is perhaps amongst the ones most commonly affected by this phenomenon.

For instance, one of the claims of Viome – a startup founded in 2016 in the United States and active in the microbiome business – reads as follows:

Take the guesswork out of eating right for you to support healthy weight loss, regularity and your gut microbiome [...] Your precision supplements & Prebiotics + Probiotics are specifically formulated for you from over 250+ premium ingredients optimised to promote optimal health. Everything you need, nothing that you don't.²²²

At an initial cost of \$399, plus a monthly contribution that can vary from \$59.99 to up to \$199.99 per month depending on the program chosen,²²³ the company offers to "give you deeper insights into your microbiome, allowing us [Viome] to create a tailored food plan and custom-formulated products to *fix* your health."²²⁴ Such service, the company's website proudly states, is made possible by the ongoing collaboration with industry experts and the employment of cutting-edge technologies:

The most advanced gut health supplements – Viome's Precision Supplements, are calculated using our prime Artificial Intelligence Platform and Bioinformatics technology. [...] Thanks to that, we help you measure

²²² For further information see "Wellness," Viome, accessed 10 April, 2023, <u>https://www.viome.com/wellness/gut-health-and-weight-loss</u>.

²²³ For further information see "How much does Viome cost?," Viome, accessed 10 April, 2023, <u>https://www.viome.com/blog/how-much-does-viome-cost</u>.

²²⁴ For further information see "Homepage," Viome, accessed 10 April, 2023, <u>https://</u><u>www.viome.com/</u>. Emphasis added.

your health, adjust your diet accordingly and take the proper supplements your body needs to achieve optimal health.²²⁵

The risk, then, is that of making the wrong kind of communication, driven by economic rather than scientific interests. In turn, this could result in promoting a still flawed science, ultimately damaging the entire sector.²²⁶

That is because if economic interests can be a problematic issue, excessive enthusiasm is no different. With the discovery of new perspectives heralded by innovation in technology – especially when these become the new fashion – it can often happen that sectorial research itself becomes reductionist. Therefore, for instance, the tendency to explain *everything* through the study of the microbiota may arise, and such a positioning can be dangerous both for citizens and for science. In the words of William Hanage:

The hype surrounding microbiome research is dangerous, for individuals who might make ill-informed decisions, and for the scientific enterprise, which needs to develop better experimental methods to generate hypotheses and evaluate conclusions. Funding agencies must not let their priorities be distorted by the buzz around the field, but look dispassionately at the data. Press officers must stop exaggerating results, and journalists must stop swallowing them whole. In pre-scientific times when something happened that people did not understand, they blamed it on spirits. We must resist the urge to transform our microbial passengers into modern-day phantoms.²²⁷

²²⁵ For further information see "GUT HEALTH SUPPLEMENTS", Viome, accessed 10 April, 2023, <u>https://www.viome.com/topic/supplements/gut-health-supplements</u>.

²²⁶ Bianchi, Interview.

²²⁷ Hanage, William P. "Microbiology: microbiome science needs a healthy dose of scepticism." *Nature* 512.7514 (2014): 247-248.

Reassuming what we have seen so far, the systematic study of the microbiome is an extremely complex and at times tricky field of research. The prospects for real applications in the fields of nutritional and medical sciences exist, but are still rather early and unexplored. After having analysed various instances of companies operating in the sector, a form of continuous cooperation between scientific research and collective engagement of individuals through citizen-science projects seems to be one of the most democratic, inclusive and transparent ways of approaching the issue. Furthermore, as in the majority of human projects, economic interests play a fundamental role in driving microbiome research. They are not, however, its only engine, nor can they justify inaccurate communication or fraudulent conducts carried out in the name of progress.

In this section, I have tried to grasp the various aspects that shape knowledge and research into the microbiome, refraining from focusing on the analysis of one single perspective or critical position. Rather, I have tried to bring diametrically opposite visions into dialogue with each other, shedding a light on some of the darker areas, whilst also highlighting the huge potential hidden within microbiome research. In the following section, I will firstly focus on the reception of Foodomics' services by its users. Secondly, I will discuss one of the aforementioned grey areas in more detail, analysing the ethical and social implications that the hypothetical large-scale implementation of personalised medicine in public health plans could have in various Western realities.

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2.4 Foodomics' Customer Service and the Over-Personalisation of Medicine

Perhaps above all else, Foodomics' most important dimension is that of its users and their satisfaction with the service they are offered. As we have seen, Foodomics' customers are the beating heart of the company, not only from a monetary perspective, but also from the point of view of research. The data collected every day by the thousands of people using the app allows the algorithms to improve through machine learning and, consequently, to improve the quality of the service offered. As I was conducting interviews with some of the company's employees, the topic of users' satisfaction came out as a central one, particularly in relation to costs.

As previously mentioned, the cost of the testing kit, which can be paid upfront or in monthly instalments, is but the first expense that new customers have to bear. To access and use Foodomics' companion app, users must pay a monthly membership fee of £59.99 which can be reduced up to £24.99 per month, if payed annually. Such division of costs, however, is not always clear to Foodomics' customers.

Miss Jones, head of user satisfaction office and user researcher at Foodomics explains how, reportedly, people joining their program are sometimes confused and complain about the costs:

Ferrari: "Have there been complaints about the costs of the service you offer?"

Jones: "Yes, absolutely. [...] They [the customers] complain about our costs for various reasons. One: is confusing, because we have both the test cost and the membership cost and a lot of people don't understand and go like: 'I just wanted the test, why are you forcing me to do this membership? Why are

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you still charging me? I'm done, I did the test, right?' So that part they're sometimes really confused about."²²⁸

To be fair, the confusion reported by Jones is partly understandable. I myself initially had some problems finding my way within Foodomics' website, as locating the costs section is not exactly straightforward. Nonetheless, the actual effort that is required to find the page with the desired information is little more than zero. With a slightly more accurate search, I was able to find all the answers in the FAQ section of the website, which is also provided in a double US–UK consultation option, to clarify any possible doubts.²²⁹

Curiously, Foodomics does not allow its customers to purchase the test kit individually, i.e. without subscribing to the monthly membership. Such decision is motivated on their website as follows:

Foodomics tests cannot be bought without a membership. The scientific insights from our tests are powerful, but it's the Foodomics programme's membership that turns them into long-lasting habits. The app gives you access to your personalised Foodomics Scores for any food or meal, access to our team of expert nutrition coaches and daily bite-sized lessons designed to help you reach your goals. Taking the tests alone makes achieving long-term health goals harder for our members, so we do not recommend it.²³⁰

Whilst worded as a recommendation, customers are indeed not allowed to buy the test-kit without hopping into the program as well, essentially binding them to pay both the related costs. Although the thesis advanced by Foodomics

²²⁸ Jones, interviewed by Luciano Ferrari, December 01, 2022.

²²⁹ For further information see "Frequently Asked Questions: UK&US," Foodomics, accessed January 22, 2023.

²³⁰ "Frequently Asked Questions", Foodomics, see subsection "Can I buy the tests individually, without membership?"

seems to be that of the fundamental uselessness of the test, when this not supported by an effective follow-up via companion app, such claim resonates loudly with the unpredictability of the future of microbiome research. All things considered, I find it very challenging to identify interests – apart from the obvious economic ones – that would prevent Foodomics from selling only the microbiome screening, without necessarily binding its customers to purchase the monthly subscription as well.

Interestingly enough, the percentage of complaints coming from English and American users is not at all equal, with English customers complaining a lot more, especially about the costs. During our interview, Miss Jones attempted to explain this phenomenon:

"Our U.S. members don't complain nearly as much about the cost. Our U.K. members do *a lot*, and I think that's for two main reasons. One: they have less money, because the salaries here [in the U.K.] are less than in the U.S. And two: they have the NHS, and so their expectation is that all sorts of medical care should be free. So they'll complain a lot about the cost and their perception of how the app is *too American* and cost is one of those aspects. On the contrary, especially at the beginning, a lot of our U.S. customers came to us with the false expectation that they were going to be able to lose tons and tons of weight. But we're not a weight loss company, we're a healthy weight company. And maybe they were disappointed that they were not losing weight at such a rapid pace, so they complained about that."²³¹

Whilst cultural factors such as public health care plans or a very high concentration of overweight and obese people²³² can play a major role in how the service of a company like Foodomics is perceived from people in different

²³¹ Jones, Interview. Original emphasis.

²³² Rosenthal, Raul J., et al. "Obesity in America." *Surgery for Obesity and Related Diseases* 13.10 (2017): 1643-1650.

societies, there is a much deeper issue inadvertently brought up by Miss Jones here, which I believe deserves a far higher degree of attention.

If we wanted to perform the mental exercise of constructing new imaginaries to analyse their merits and complexities, the discontent of Foodomics' British users could be thought of as the defining feature of a future where public health care plans get replaced by personalised medicine entirely. Such shift would raise important socio-political and ethical questions which deserve to be analysed. Indeed, if today's strong push towards the digitalisation and personalisation of medical practice were to steadily keep growing to the point of being normalised within the scientific community, we could easily expect a future in which Foodomics' methods could establish themselves as new standards in the enactment of any practice and new implementation within the medical field.

In other words, if personalised nutrition turns out to be as efficient as it appears to be, there could be a tangible risk that the same paradigms governing it will be applied to other areas of medicine indiscriminately. In such a scenario, a personalised take on medical practice would permeate all aspects of our daily lives. If these new paradigms were to prove valid alternatives to effectively treat several conditions that impact human health, then, they could easily ride the wave of technological and positivist enthusiasm and replace more classical, generalised health care plans.

This transition, as it often happens within the field of artificial intelligence and technological innovations, would most likely take place at a disarming pace. Take the smartphones phenomenon for instance, which overnight have become an integral part of the lives of every human being on the planet. Precision medicine does indeed pave the way for precision enterprises,²³³ and once production facilities are in place to support the demand for innovation, change itself is always very quick to arrive, and it is often overwhelming. In the case of

²³³ Reardon, The Postgenomic Condition, p. 177.

personalised medicine, this could pose many economic, ethical, political and social problems.

In fact, if personalisation became the only medical approach available to treat any pathology or condition indiscriminately, inequality would fast bloom in countries where health care is a privatised sector. An individually tailored approach is indeed expensive, and the issue of (in)accessibility to health care and health services for people who do not have adequate financial resources – and/or reliable health insurances that can make up for this lack – could constitute a serious societal issue and a crucial ethical conundrum to overcome.

Moreover, disposable income would, unfortunately, not constitute the sole filter of iniquity in this scenario. That is because people live and act within societies, and societies do not happen in a void. Therefore, considerations on marginalised segments of the population that still suffer from heavy racial, social, economic sexual and gender discrimination should be added to such reasoning. Taking the case of the United States, for example, where finding just one black psychologist in an entire State can constitute an insurmountable deadlock for an hurting individual,²³⁴ it is not difficult to imagine how it would be the poor, the racialised, the under-represented and in general anyone belonging to a marginalised social group those who will pay the price of such transition.

Furthermore, restricting medical practice to a single paradigm, that is personalised precision medicine, also means accepting the most likely subsequent polarisation of the medical business sector. Indeed, there is the risk that the expertise, knowledge and resources to employ personalised medicine could progressively converge in the hands of a few individuals and/or companies possessing the economic and technological means to respond to such new and immense market demand. Thus, whilst personalisation promises to revolutionise medicine, I believe it is not something that should be taken

²³⁴ Horton Adrian, "John Oliver: US mental healthcare 'almost designed to prevent people from accessing it'," *The Guardian*, August 01, 2022, <u>https://www.theguardian.com/tv-and-radio/2022/</u> <u>aug/01/john-oliver-us-mental-healthcare-system</u>.

lightly, as the positive transformative potential is directly proportional to the discriminatory one.

Whose political and ethical responsibility would be to deal with such issues? Does contemporary society have the most suitable social infrastructures to cope with a change of such magnitude? Is politics sufficiently prepared to create new laws and means to protect the right to health of every individual, regardless of their ethnicity, sex, gender, origin, age or economic condition? In other words, is human society ready for the personalisation of medicine? The ones I have mentioned are just some of the risks and ethical dilemmas that we – as a global society – may expect to face in a future that might be closer than what we had initially thought.

If the practices that protect the right to health were to become a commodity, the world population would essentially split into two macrocategories defined solely by principles of inequality such as economic availability or social relevance. Those who could afford the costs of these new services would have access to a new and more effective form of medicine, whilst those who could not, would inevitably be crushed under the weight of progress. Furthermore, as various scholars in the sector have pointed out, it is not clear who should regulate the preservation of sensitive data for the users involved.^{235,236,237}

On the other hand, when I presented my concerns about the future overspread of precision medicine and its discriminatory potential to Bianchi, he promptly reassured me about it. Indeed, Bianchi believes that personalised medicine "would not *replace* general medicine. At least not completely and certainly not in the next ten or twenty years. And even if this were to happen one

²³⁵ Basu, Subhajit, and A. Omotubora. "Beyond the present: Privacy and personalised medicine." *Proceedings of 33rd Annual BILETA Conference, University of Aberdeen, Aberdeen, UK*. 2018.

²³⁶ Reardon, The Postgenomic Condition, 8-9.

²³⁷ Bollati, Valentina, et al. "Personalised Medicine: implication and perspectives in the field of occupational health." *La Medicina del Lavoro* 111.6 (2020): 425.

day, we should speak of a complementarity, rather than a replacement."²³⁸ In other words, Bianchi thinks that personalised medicine will play a marginal, supportive role to today's generalised medical approach in the future, without necessarily supplanting it. Thus, symptoms that cannot always be explained by classic diagnoses e.g. celiac disease, could potentially be explained through the analysis of the microbiome. Such a turn, Bianchi claims, will certainly require skills that the future professionals in the medical sciences are not currently been trained to face. In other words, the microbiome and its impact on human health is not studied at the faculty of medicine:

Bianchi: "I think most doctors today either don't know what the microbiome is or don't consider the microbiome to be fundamental – or even just influential – in the work they do. This will surely have to change. New generations of doctors need to understand that if they cannot explain problem X with their more classical approach, they need to keep in mind that there is literally a universe – the microbiome – that they are not considering in their analysis. And that parallel universe could provide meaningful answers to their unanswered questions. In any case, I don't think the microbiome will ever explain 100% of the complexity related to human health. It will most likely be a co-existence with classical medical sciences that will certainly require new, specific training for those working in the sector."²³⁹

Dr. Bianchi is not the only one who thinks so. Indeed, his words also resonate with those of Professor Rossi, who thinks that "the microbiome is bound to be the future of medicine, or at least a fundamental part of it."²⁴⁰ Professor Young picks up from such assumptions and goes even further,

²³⁸ Bianchi, Interview. Original emphasis.

²³⁹ Bianchi, Interview.

²⁴⁰ Rossi, Interview.

foreseeing a "fundamental role of microbes not only in the medicine of the future, but also in research, culture, society, economy and art."²⁴¹

However, it is also true that due to the novelty of the sector, very few adhoc laws or resolutions have been made to date to preserve the individual's rights within the microbiome industry.²⁴² For instance, the preservation of individual biological privacy, or the regulation of biovalue attached to users' data have not been rethought specifically for the microbiome. Rather, regulatory frameworks borrowed from other areas of medicine are applied e.g. stem cells, without modifications.²⁴³ Whilst such a thing seems to be working as of today, one must not forget that we are in the early stages of microbiome research. Hence, establishing ad-hoc framework designed specifically to address such growing field of research might be a wise thing to do moving forward.

Nevertheless, humans live in fragmented societies and there are no supranational bodies in place endowed with legislative, executive and judiciary powers. Thus, it is not clear who exactly should tackle such problems, and the risk is that each country will decide for themselves, fragmenting the global response to such techno-scientific shift and creating stark inequalities, which will be even more exacerbated across different countries.²⁴⁴

This is not to say that we, as a global society, should avoid pursuing the scientific inquiry into the microbiome. Rather, I advocate quite the opposite. The prospects related to personalised nutrition and personalised medicine promise substantial improvements in the human condition, and the novelty of

²⁴¹ Young, Interview.

²⁴² Rossi (interview) points out, however, that privacy protection remains a central issue both for scientists and people participating in the studies. Were regulations concerning individual privacy absolute, pursuing microbiome genomic studies would be extremely difficult – if not impossible.

²⁴³ Lorenzo Beltrame, "The bioeconomies of stem cell research," in *The Matrix of Stem Cell Research: An Approach to Rethinking Science in Society*, eds. Christine Hauskeller, Arne Manzeschke & Anja Pichl (London: Routledge, 2019).

²⁴⁴ Hawkins, Alice K., and Kieran C. O'Doherty. "" Who owns your poop?": insights regarding the intersection of human microbiome research and the ELSI aspects of biobanking and related studies." *BMC Medical Genomics* 4 (2011): 1-9.

microbiome studies as a substantially unexplored universe that unfolds within and before us bodes really well in such sense. However, I strongly believe that if microbiome research is to be promoted on a large scale, and far more funds are to be devoted to studying this incredible vastness that actively shapes our life on multiple levels, so too must supranational organisms like the EU, the WHO and the UN make a real, cooperative effort to build the necessary infrastructures that can effectively cope with this change, regardless of when it will happen.

An extra level of difficulty will be given by the fact that technological innovation in today's world moves at unprecedented, frightening speed. Therefore, it is difficult to predict how quickly and with what impact a technological advance can translate into a widespread, everyday-use commodity.²⁴⁵ If the implementation of new technologies derived from the microbiome were to be faster than the adaptation and tolerance capacity of human societies, we could find ourselves having to manage situations of new systematic discrimination and social inequality in the medical-scientific field.

Confronted with questions regarding this topic, both Bianchi and Rossi were showed some skepticism. The reasons given by Bianchi were mainly two: firstly, a future in which real applications of microbiome studies will be globally widespread is still too distant, and we cannot know what the world will look like when – and if – this will ever happen; secondly, Bianchi does not think that precision microbiome-based medicine will ever replace the more general medicine entirely. As mentioned above, he thinks of this scenario as of one of complementarity. Therefore, he concludes, even if microbiome studies were to yield practical results incontrovertibly significant to medicine, such results would be implemented inside a pre-existing healthcare system – without adding too much to the dynamics of power already in place.²⁴⁶

²⁴⁵ Butler, Declan. "Tomorrow's world: technological change is accelerating today at an unprecedented speed and could create a world we can barely begin to imagine." *Nature* 530.7591 (2016): 398-402.

²⁴⁶ Bianchi, Interview.

Indeed, Bianchi does not deny the possibility of a discrimination in future access to microbiome-based medical care built on a social, economic, racial and/or sexual basis. However, he does not think that such discrimination would be so distant from the one we already witness in today's private and public health care plans around the world. Besides, Bianchi extended his skepticism to the topic of extreme privatisation of healthcare too. According to him it would make much more sense, for governments and private companies alike, to implement any precision-medicine innovation in pre-existing systems, be it public or private, rather than creating new ones from scratch. Therefore, he claims, precision medicine would most likely fit equally into both pre-existing public and private healthcare plans, depending on which public health model is adopted in the various countries:

Bianchi: "Rather than an upheaval of the healthcare system, I would speak of a mutation. Which, again, would probably not even be too far from what already happens today: those who have the possibility of paying for private medical consultation will have privileged access to this new technology. But that doesn't mean that others won't have it. The same, in fact, will be true for public health, where precision medicine will be accessible but with the same limitations that we see today, for example, in the Italian public health system – long waits, conflicting opinions and a lot of bureaucracy."²⁴⁷

Rossi, for its part, relies on a more pragmatic view of the issue. To explain his position to me, Professor Rossi refers back to FMT and its potential to treat diseases related to microbiome imbalance by directly affecting the recipient's microbiome composition.²⁴⁸ Today FMT is a commonly used clinical practice in

²⁴⁷ Bianchi, Interview.

²⁴⁸ Ianiro, Gianluca, et al. "Variability of strain engraftment." FMT and its connections to personalised medical treatment has been briefly addressed in section 2.3 of the present thesis. For further references see Kashyap, Purna C., et al. "Microbiome at the frontier of personalized medicine." *Mayo Clinic Proceedings*. Vol. 92. No. 12. Elsevier, 2017.

the treatment of *C. diff.* – a microbe resistant to a wide range of antibiotics and other interventions and which, if not treated, can lead to the patient's death. However, with a mixture of anger and disillusion, Rossi told me that before being normalised as medical practice, and although promising in its early results, the first ever clinical trial involving the application of FMT in the treatment of *C. diff.* had been halted for ethical reasons. It was not "ethically just," the ethical board had ruled, to continue experimenting with FMT on a restricted number of patients.²⁴⁹

The reason was, according to Professor Rossi, that patients subjected to FMT had a successful recovery rate that peaked at a staggering 95% of the cases, whilst the ones who were not part of the clinical trial continued to suffer from higher mortality rates. The trial was therefore blocked for being "too successful", in that it was not ethically correct towards those who could not receive the same efficacious treatment.²⁵⁰ Here is how Professor Rossi commented on such issue:

Rossi: "I believe that in the light of a 90% drop in mortality rates, all other ethical problems, such as the unwanted transplantation of another pathogen in addition to the 'good' microbiome, take a back seat. It is compassionate care. If we are to cure E. Coli through the microbiome it's a form of compassion towards the patient. If it is about curing obesity, maybe the situation's bit different. In that case, are the results really worth the risks?"²⁵¹

Rossi's words are particularly representative of a common trend I have observed in almost all the interviews I conducted with experts working in the microbiome field, also echoed by Taylor's quotes in previous pages: the deep and incontrovertible trust in the scientific community's capacity for self-

²⁴⁹ Rossi, Interview.

²⁵⁰ Ibid.

²⁵¹ Ibid.

regulation. Indeed, there is an often-shared belief among scientists that science does not need any extra justification other than that which is inherently tied to its essence. Science is the study of the unknown, and its mission is to improve the living conditions of human beings as well as to lead us towards a better future for our species. Thus, the vast majority of science is often perceived as ethical regardless. If it is true that science tends to be moved by noble ends in an endless quest for truth, we can never forget that nothing is perfectly monolithic, not even science. Scientific research is made by people, whose economic interests often mix research ones, as such is the way of the world.

Therefore, I believe that entirely postponing the discussion on the potentially problematic implications that microbiome science might have on the medicine of the future, may become an issue. Neither unregulated scaremongering, nor the downplay of such issues seem the right way to approach the discussion, though. We know that the indicators are there, science is moving towards such direction. Maybe it will not be in the next ten or twenty years, or maybe it will, we have no real way to know. In light of this, I believe that our best course of action would be to approach science with transparency and collectivity, increasingly engaging citizens in science, promoting spaces for democratic debate open to anyone, with no discrimination of gender, sex, age, money or religion.²⁵²

A similar position is backed by Professor Young, who thinks that the revolution brought forth by personalised medicine should start from raising people's awareness through language. She holds that the human reticence towards embracing our microbial identity is based on the classical conceptualisation we have of the microbial world, which is mediated first and foremost by language. Bacteria, she claims, are "too often perceived as fundamentally alien to the human and mostly as an enemy from which to seek

²⁵² It should be noted that many criticise citizen science projects as means to co-opt citizens instead of engaging them. For further references see Davis, Lloyd S., Lei Zhu, and Wiebke Finkler. "Citizen Science: Is It Good Science?." Sustainability 15.5 (2023): 4577.

shelter rather companions to cooperate with.²⁵³ As feasible solution to such problem, Young proposes to "rethink the way we regard and envision microbes in our shared imaginaries, starting from the language we use to define them.²⁵⁴

The underlying idea is that if an individual is exposed to a certain lexicon linked to a specific topic, they will unconsciously interiorise specific positive or negative attributes tied to that object. To explain herself, Young resorted too to the example of *C. diff.*, stressing the fundamental inconsistency between a situation that is real, in that it can be observed, and the language used to describe such situation:

Young: "Each individual has their own microbiome but the signature of each human microbiome is the ratio and proportion of the various guilds of microbes found within it. A guild is basically a set of bacteria that do a certain job. In human populations we have guilds: teachers, doctors, engineers, etc. The same happens in the microbiome. Now, 90% of humans carry a microbe called *C. diff.* But not in all of them this microbe activates. Actually, if it doesn't activate *C. diff.* confers an advantage when it is in balance with its host. Nonetheless, we call *C. diff.* A pathogen whilst *C. diff.* is just a microbe doing its thing, really. What this tells us is that we need to apply a radical change in our lexicon."²⁵⁵

Arturo Casadevall, Professor of Medicine at the John Hopkins University and head of the John Hopkins Center for Infectious Diseases, firmly supports such position. He claims that there is no such thing as a pathogen. It is rather all about the state. There is a state of pathogenesis and then there are beneficial states where a bacterium and its host can coexist in equilibrium and both

²⁵³ Young, Interview.

²⁵⁴ Ibid.

²⁵⁵ Ibid.

benefit from that cooperation.²⁵⁶ Indeed, the human gut microbiome is full of species in perfect equilibrium with our organism. They are known as "opportunistic pathogens" and constitute a pivotal part of our normal microbiota.

The issue of language may seem light years away from what we have discussed so far. But if it is true that the words we use shape the world we know, it is necessary to provide clear definition through an adequate, objective lexicon devoid of judgments of quality. Only by doing such a thing, will we be able to normalise the microbial presence as a crucially integral part of the larger human ecosystem:

Young: "I did an experiment. I went to the US centre for disease control and I made a list of all the human 'pathogens' that are dangerous and could potentially be employed as bioweapons. Then I compared this list with the human microbiome database. Turns out that *every single* microbes on the bioweapon list are congeners – in other words related species – to at least one or more species found in the microbiome list. [...] A really good example is the bacterium Neisseria. In particular, Neisseria meningitidis causes bacterial meningitidis while Neisseria gonorrhoeae causes gonorrhoeae in their host. So Neisseria is the bad guy, right? Well, it turns out we have around twelve other Neisseria species that are part of our normal microbiota and live in perfect balance with their host. [...] How much of the language involved with Neisseria being a pathogen is the same used for beneficial Neisseria species? All of it. Even though it conveys a biased, inaccurate and shallow description of reality."²⁵⁷

In this chapter I started from my research within a restricted reality like that of Foodomics and tried to gradually broaden the focus towards more general

²⁵⁶ Casadevall, Arturo, and Liise-anne Pirofski. "Microbiology: ditch the term pathogen." *Nature* 516.7530 (2014): 165-166.

²⁵⁷ Young, Interview.

philosophical reflections on the ethics of microbiome science. In doing so, I have tried to show the hidden potential of such research but also to shed light on the grey areas of the field, maintaining a position as detached and objective as possible.

Perhaps the most important point I wished to convey was the one concerning the total and inescapable interpenetration between humans and non-humans. Such relationship should form, I believe the basis for the redefinition of the very concept of humanity. As Raffaetà states, "thanks to its unprecedented computational power, metagenomics is rewriting old ontologies, linking the microbial scale to the human one and up to the cosmic one."²⁵⁸ The research on the microbiome is defined by a constant oscillation between the study of humans and the study of the environment in which they live. And in our being inextricably linked to the environment around us, microbes play a critical role, and in fact we find the very same microbial species living in our lungs, rocks and oceans.²⁵⁹

Abandoning dichotomous visions that lead everything back to the existence of an "us" and a "them," I believe is the first step to start a process of democratic inclusion of non-humans within a humbler and more accurate (re)definition of humans. This would allow us to think more carefully and accurately about who we are, what we are doing and where we are going as a species. In 2023, faced with the dread of unavoidable environmental disaster and dozens of armed conflicts around the world, there is more than an urgent need to engage with such reflections.

²⁵⁸ Raffaetà, *Metagenomic Futures*, p. 250.

²⁵⁹ Ibid. p. 251.

CHAPTER THREE CONCLUSIONS

I started my research by trying to understand what is the anthropological role of microbes within such a basic, natural and fundamental activity as that of nutrition. The process of writing this thesis has led me to engage with anthropologists, communication experts, professors, doctors, microbiologists, virologists and bioinformatics, each of whom has provided their own invaluable contribution and an incomparable prospective richness to my considerations. I soon understood that an anthropological reflection on the role of microbes in the field of food and nutrition cannot be separated from a much broader analysis of the role they play in our everyday lives.

Such reflection moves on the edge of various disciplines, maintaining the advantages of a transversal vision that ranges across different fields. From the techno-scientific aspect of making microbiome science, to the humanistic-philosophical one, dealing with more existential questions such as "how can we redefine the concepts of health and humanity in light of the inevitable meshwork of relations with the non-human?" As I have stated in the early pages of the present thesis, microbes are everywhere. They permeate every spatial dimension of our world. They are far more resilient, adaptive and useful than us. Indeed, it is no coincidence that they were the first settling in on this Earth in and will be the last taking their leave at the end of Life:²⁶⁰

There are "one million bacteria per cm² of ocean water, and their work and their activities are crucial to the health of the entire biosphere. [...] The fact that water-to-land transition in plants was led by microbes tells us that our

²⁶⁰ Young, Interview.

world would not be as it is now if microbes didn't exist. Life as we know it wouldn't exist."²⁶¹

In light of this, and also considering the awful anthropogenic contributions given to the Earth ecosystem during the Anthropocene, the least our species could do is to just stop for a second and take the time to listen. But what should we listen to? The answer is self-evident: what microbes have to teach us. Thus, what follows are three crucial *lessons* that I believe we can learn from studying and actively engaging with the microbial world.

The first one is the lesson on collective interdependence: there is no entity, organic or inorganic, physical or abstract, which is not interdependent on the others. Animals, plants, oceans, rocks, mountains, technology, human beings, everything is connected and there is no way around this reality. It is built into the life that has developed on our planet and, as far as we know, it is a characteristic of life itself. Only by learning to appreciate the necessary cross-species interdependency of the world in which we live will we be able to appreciate its complexity, the incredible balance and the beauty that distinguishes it. Only by virtue of such realisation will we be able – hopefully – to set in motion a much needed socio-cultural, philosophical and anthropological revolution that (re)defines the concepts of disease, health and humanity, by attributing the proper importance to the foundational non-human elements of the human. To such end, I believe that a further step should be taken in approaching the study of the microbiome and its relations to health.

Indeed, if it is true that the interaction between human and other-thanhuman factors is central to medicine insofar as it is needed to restore a health state that was previously compromised,²⁶² I am interested in investigating that same interaction in the case of a non-compromised health state. My hypothesis

²⁶¹ Young, Interview.

²⁶² Shreiner, "The Gut Microbiome."

is that building microbial knowledge from data gathered from sick – or out of balance – individuals fundamentally alters the aims and results of the research due to the urge to find adequate therapies to fix the starting situation. Thus, I am interested in situating my future research in the pre-existing corpus of literature^{263,264} aimed at investigating the construction of microbiome knowledge in the context of healthy individuals,^{265,266} as I believe that this would not only provide a more comprehensive analysis, but also – as Taylor too stressed during our interview – prioritise *prevention*, as opposed to *treatment*.

For these reasons, further exploring the world of Foodomics through more lengthy ethnographic research would allow me to uncover the ways in which microbiome-based personalised nutrition can act as major factor in preserving health through daily practice. My aim would be that of destabilising the way of thinking about scientific data and knowledge, investigating how the dynamics regulating the interactions between the two affect the common perception of the microbiome, and contribute to recalibrating the understanding of the modern human. Such research, unfortunately, lies outside the scope of this thesis, but I trust I will be able to pursue it soon enough at a doctoral level.

As we saw in the last chapter, the microbial world can be filled with different meanings and, depending on the way we interpret, structure and represent it, it can acquire a deeply political connotation. Here lies the great ethical and ontological challenge inherent to the present and future study of the microbiome. As Raffaetà points out:

²⁶³ Segata, Nicola, et al. "Composition of the adult digestive tract bacterial microbiome based on seven mouth surfaces, tonsils, throat and stool samples." *Genome biology* 13 (2012): 1-18.

²⁶⁴ Zaura, Egija, et al. "Defining the healthy" core microbiome" of oral microbial communities." *BMC microbiology* 9.1 (2009): 1-12.

²⁶⁵ Nearing, Jacob T., et al. "Assessing the variation within the oral microbiome of healthy adults." *Msphere* 5.5 (2020): e00451-20.

²⁶⁶ D'Argenio, Valeria, and Francesco Salvatore. "The role of the gut microbiome in the healthy adult status." *Clinica chimica acta* 451 (2015): 97-102.

Civic sense presupposes being part of a *civitas*, but which community is *our* community? Can the microbial ecosystem be considered our 'home?' Are microbial communities part of our community? If so, [...] who or what are we willing to care for and who or what are we willing to sacrifice? A forest, a mountain, an ocean or a child?²⁶⁷

Therefore, one of the great challenges of our time will be that of combining biosecurity with biodiversity and what scales – temporal and spatial – will result from the solutions that we will envisage.²⁶⁸ In such scenario, the active role of science appears critical. Indeed, scientific research cannot stop with a detached description of the natural world and its components. Rather, I believe it should shoulder the active responsibility consequent to the development of future, unexplored imaginaries. Such new perspectives are the by-products of an extremely technologised scientific research which happens in the liminal spaces that separate increasingly porous boundaries of disciplines, species and meaning. Private or public interests, be them cultural, economic or political can then be grafted onto this epistemic paradigm. It would be anachronistic and exceedingly naive to think any different. This is the way our contemporary world works, and perhaps it is rightly so, provided that the starting point is that of an engaged science which refrains from being a mere spectator.

Microbiome studies fall within posthumanism because a horizontal relationship is established across various forms of life, rejecting the adoption of hierarchies and embracing the idea of an inextricable mutuality of action. However, one must be careful, Hinchliffe points out, not to lose sight of the existence of multiple and asymmetrical ontologies that underlie the interdependence between humans and non-humans, which is typical of

²⁶⁷ Raffaetà, Metagenomic Futures, p. 262

²⁶⁸ Howe, Cymene. "Timely." Theorizing the Contemporary. Cultural Anthropology, Fieldsights 21 (2016).

posthuman projects and reflections.²⁶⁹ It is therefore crucial – both today and in the super-technological future that awaits us – to critically analyse "the nature, limits and overlaps of such new ontologies,"²⁷⁰ in order to move "not beyond the human, but beyond anthropocentrism [...] to address the responsibilities resulting from the formidable ability that humans have to transform the environment, as well as to quickly and massively interfere with the lives of other humans and non-humans around us."²⁷¹

The second lesson that microbes can teach us is that of vulnerability, and it is about the joy that may derive from recognizing ourselves as imperfectly vulnerable. The study of the microbiome, although necessarily linked to the hard sciences, investigates an unknown universe, which has remarkable implications to all of us. For this very reason, microbiome research should involve biology as much as ethics and anthropology.

Our species has radically transformed planet Earth to make it its own. If it took two billion years from the appearance of the first multicellular organisms for the first humans to appear on Earth, culture, civilisation and space travel developed exceptionally quickly after that. Today, we live in a world that we defined as "globalised," that is deeply informationally interconnected, economically interdependent, fully dependent on the technology we have developed over the last 70 years and extremely fast.²⁷² In Thomas H. Eriksen's words:

²⁶⁹ Hinchliffe, Steve. "More than one world, more than one health: Re-configuring interspecies health." *Social science & medicine* 129 (2015): 28-35.

²⁷⁰ Niewöhner, Jörg, and Margaret Lock. "Situating local biologies: Anthropological perspectives on environment/human entanglements." *BioSocieties* 13 (2018): 681-697 in Raffaetà, *Metagenomic Futures*, p. 263

²⁷¹ Raffaetà, Metagenomic Futures, p. 263

²⁷² Castells, Manuel, and Cambridge Blackwell. "The information age: economy, society and culture. Volume 1. The rise of the network society." *Environment and Planning B: Planning and Design* 25 (1998): 631-636.

[...] Ours is a world of high-speed modernity where the fact that things change no longer needs to be explained by social scientists; what comes across as extraordinary or puzzling are instead the patches of continuity we occasionally discover.²⁷³

Such world is intrinsically subject to constant change. Boundaries are not fixed, insurmountable walls, but rather permeable membranes that allow reality to be observed from what Karen Barad would define as a sort of privileged quantum superposition.²⁷⁴

Thus, while it is true that science and technology are part of a process of positive development and emancipation of our species,²⁷⁵ we must be aware that the evolution of such disciplines will undoubtably confront us with brand new ethical and ontological questions. However, the feeling of vulnerability and despondency that comes with redefining some of our philosophical, socio-cultural and epistemological limits in response to such questions, should be experienced rather than repressed, as it is an integral part of the process leading to the answers we are seeking.

Therefore, reflecting anthropologically on the microbiome offers us the possibility to benefit from vulnerability, questioning epistemological categories and redefining key concepts such as health, interdependence, humanity, life and death. It is precisely here that microbiome studies, Foodomics and the (re)definition of health become fundamental. Until we stop thinking – and talking – about health as the abstraction of a rather vague state of being, devoid of any responsibility and falsely independent, we will not truly be discussing about

²⁷³ Eriksen, Thomas Hylland. Overheating: An anthropology of accelerated change. London: Pluto Press, 2016.

²⁷⁴ Barad, Karen. Meeting the universe halfway: Quantum physics and the entanglement of matter and meaning. Duke university Press, 2007.

²⁷⁵ Benanti, Paolo. *La condizione tecno-umana: domande di senso nell'era della tecnologia.* Edizioni Dehoniane Bologna, 2017.

health, but rather about a social, cultural, economical and politicised construct to which we have given such a name:

[Thus] Health must be rethought at the ecosystem level starting from an attitude that is not uniquely anthropocentric. And, in such process, computational biology can be a great ally, [...] helping us to bring the attention back to the internal and external balances that influence the organism's health.²⁷⁶

The last lesson, closely linked to the first, that microbes can teach us is that of the importance of disciplinary transversality, handed down to me by University Professor McFall–Ngai. Starting from the assumption that a healthy human being is a nested ecosystem where the animal–microbial cell ratio is about 50%, we can deduce – and observe – that microbial communities within our body play a fundamental role in our biology and health. Right there, according to McFall–Ngai, lies a formidable challenge, that is integrating such new, critical knowledge in our biological sciences conceptual framework:

The difficulty lies in two main points. Firstly, microbiologists are *very* resistant to change. The idea of microbes as partners in human's health is really hard to propel. Microbes make you sick, not better. That is the common thought, and reshaping it from the ground up is *really* hard. Secondly, we would need to readdress the implications of the 20th century revolution, whereby knowledge was fragmented into closed boxes we called "specialisations." We preferred a compartmentalisation of knowledge as opposed to an horizontal and holistic view of it. Well, it turns out we were wrong, and transversality is what we actually need to understand the microbiome.²⁷⁷

²⁷⁶ Benanti, Paolo. *La condizione tecno-umana*.

²⁷⁷ McFall-Ngai, Margaret, "Horizons in the study of biosystem structure and function" (ECLT and NICHE Christmas Lecture 2022, Ca' Foscari University of Venice, Ca' Bottacin 1st floor, 19 Dec 2022. Original emphasis.

Furthermore, another actor has made their entrance to the stage in more recent times. A new, unforeseen and looming character which, I believe, perfectly epitomises the incurable human tendency not to care about the connections our species entertains with the natural world: the climate crisis.

[...] The appearance of climate crisis makes everything worse. It makes pushing the revolution forward of critical importance, because we cannot possibly approach climate change and come up with effective solutions if we do not have an accurate concept of the structure and function of the biological world.²⁷⁸

In such a scenario, McFall-Ngai condemns what she calls "fundamental failures to integrate,"²⁷⁹ meaning that even if microbiologists were to talk about microbes and climate change, they usually only talk about microbes²⁸⁰ or, if they talk about mitigation of climate change, they do not talk about microbes at all.²⁸¹ Maybe the time has come to set up new goals. Some ideas could be integrating the worlds of macro and microbiology, unifying biology's conceptual frameworks, and (re)discovering the power of transdisciplinary knowledge. Whilst the first is extremely challenging, it would allow for a (re)discovery of the elements critical to life processes on Earth: "what you basically want to do is go

²⁷⁸ McFall-Ngai, "Horizons in the study of biosystem."

²⁷⁹ McFall-Ngai, "Horizons in the study of biosystem."

²⁸⁰ As it is the case of FAQ: Microbes and Climate Change: Report on an American Academy of Microbiology and American Geophysical Union Colloquium held in March 2016. Washington (DC): American Society for Microbiology; 2017.

²⁸¹ As it is the case of IPCC, 2022: Summary for Policymakers. In: Climate Change 2022: Mitigation of Climate Change. Contribution of Working Group III to the Sixth Assessment Report of the Intergovernmental Panel on Climate Change [P.R. Shukla, J. Skea, R. Slade, A. Al Khourdajie, R. van Diemen, D. McCollum, M. Pathak, S. Some, P. Vyas, R. Fradera, M. Belkacemi, A. Hasija, G. Lisboa, S. Luz, J. Malley, (eds.)]. Cambridge University Press, Cambridge, UK and New York, NY, USA. doi: 10.1017/9781009157926.001

back to each topic of macrobiology²⁸² and revise it in function of the microbial world."²⁸³

Luckily, change has already started to happen. Scholars and nonacademics alike are beginning to realise that bacteria, fungi and other microbial communities can play an essential role, for instance, in reforestation processes. Microbes can grow with plants, changing their biology and biological processes to construct new, unique and more complex nested ecosystems *with* them.²⁸⁴

Secondly, engaging physical scientists, mathematicians, anthropologists, sociologists, bioinformaticians, physicians, etc. would allow us to "leave behind the inconclusive compartmentalisation of knowledge and (re)acquire a horizontal and ecosystemic view of it."²⁸⁵ Global problems such as food, health, energy, ecology, etc. are biological and the solutions need to be sought across both the hard sciences *and* the humanities, not just in one of them. This is the reason why interdisciplinary approaches such as the Environmental Humanities are of crucial importance at this particular historical moment. There is still a lot of work to do and we will need time. We have the chance of not being alone on this journey, though, and microbes can be our very best companions.

²⁸² In this context, "macrobiology" is used by the scholar as an umbrella term for biological studies of large living organisms visible to the naked eye e.g. plants, animals and other multicellular organisms.

²⁸³ McFall-Ngai, "Horizons in the study of biosystem."

²⁸⁴ For further information see Kour, Divjot, and Ajar Nath Yadav. "Bacterial mitigation of drought stress in plants: Current perspectives and future challenges." *Current Microbiology* 79.9 (2022): 248 & Li, Jingdi, et al. "Experimental temperatures shape host microbiome diversity and composition." *Global Change Biology* 29.1 (2023): 41-56.

²⁸⁵ McFall-Ngai, "Horizons in the study of biosystem."

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APPENDIX A:



PREDICT 1	Jun 2018 – May 2019 IRAS 236407; IRB 2018P002078 NCT03479866	Main Cohort Nalidation Cohort n=1,002
Aims		
Use genetic, metabolomi	c, metagenomic and meal-	context information to predict individuals' postprandial responses to food.
Baseline Clinic Visit (Day	1)	Home Phase (Days 2-14)
Controlled Time (Mins)		Clinic Day 2 3 4 5 6 7 8 9 10 11 12 13 14 Study app; weighed records; in-study support
Metabolic challenge Other test meals	Constin	Standardized Blood Stot tests Nutritionally varied test breakfasts and lunches TAG, C-peptide assays
Metabolomics	Blood pressure and heart rate	Digital devices
Anthropometry DEXA, waist/hip, BMI	Questionnaires FFQ, Lifestyle, Medical	Stool samples Microbiome profiling

Figure 1: An overview of the PREDICT 1 study aims and protocol.

2)

PREDICT 1 Plus June 2019 – Ongoing IRAS 236407 NCT03479866	Cohort target n=900
Aims	Home Phase (Days 2-11)
 Measure glycemic responses to home-based dietary intervention, using clinic-based meals for reference Explore meal-sequence effects on glycemia/ lipemia Improve lipemic dose-response models, using 	Clinic Day 1 2 3 4 5 6 7 8 9 10 11 Dietary Dietary Assessment
test meals incrementally increasing in fat quantity Baseline Clinic Visit (Day 1)	Standardized meals
Controlled Time (Mins)	Blood Spot tests
0 30 60 120 240 300 360 Fasting	Ocontinuous glucose, physical activity and sleep monitoring
	Stocl/ urine samples
Genetics, Clinical assays, Metabolomics Clinic/home TAG assa	blood ys Metabolomics Blood pressure and heart rate Mathropometry DEXA, waist/hip, Cuestionnaire BMI

Figure 2: An overview of the PREDICT 1 Plus study aims and protocol.



Figure 3: An overview of the PREDICT-Carbs study aims and protocol.

4)

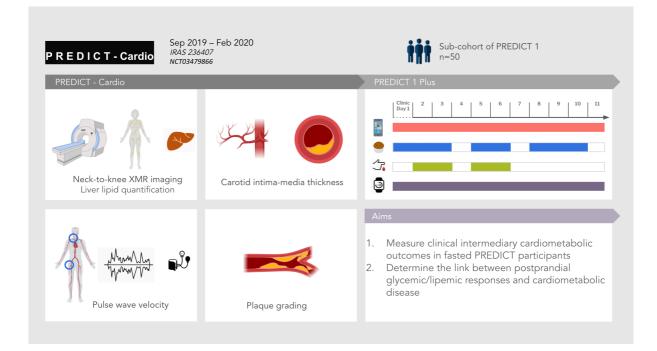


Figure 4: An overview of the PREDICT-Cardio study aims and protocol.

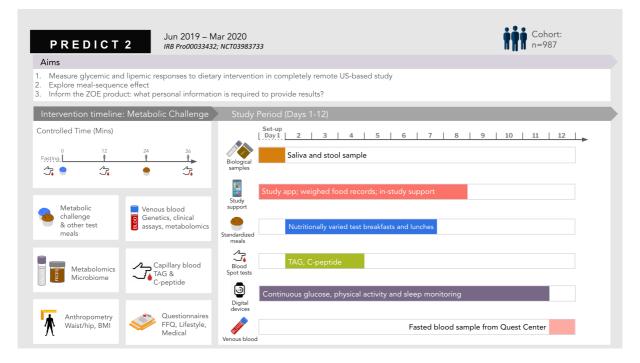


Figure 5: An overview of the PREDICT 2 study aims and protocol.