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Current Megatrends in Food Production Related to Microbes

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Abstract

The five major global phenomena or trends both in our thinking and in our societies that have strong links to the microbial kingdom:

A. Human population growth continuously increases the demand for hygienically safe and adequate supplies to prevent qualitative and quantitative malnutrition.

• Biorefineries and biotechnological techniques could be established on the basis of microbial bioengineering and understanding of natural microbial populations: this includes the reuse of food residues as well as the conversion of industrial and agricultural side streams into food sources.

B. Requirements for sustainable and climate-friendly methods have also increased considerably.

• Food ingredients can be produced from the above-mentioned additional resources which could be found within the existing processes and processes developed from them.

C. Common understanding of the vital role of soil microbes in the food production has emerged globally.

• Soil microbiota needs to be protected, and its role in the balances of carbon, nitrogen and other nutrients and elements need to be profoundly investigated.

D. Relationship between our nutrition, health and microbiome have become more and more evident to the consumers.

• Human microbiome has emerged as the core factor and contributor to our general well-being and health - the balance of the microbiome strongly influences the nutritional effects of our food, which have to be nurtured.

E. Development of novel microbiological research and production methods.

• Understanding the role of individual strains as parts of the community.

While the global developments increase the movements of people and goods, an consequently, the rise of emerging epidemics and health problems, it is possible to resist those developments by implementing the potentials of microbial strains for producing food and chemical goods, as well as for cleaning up the environment.

Keywords

Food crisis, Environmental stress, Climate change, Microbiome, Soil improvement, Vagus nerve, Bacteriological intestinal balance, Probiotics, Platform chemicals, Nutraceuticals, Side streams, Hygiene control, Undefined mixed culture, Biorefineries

Introduction

Our contemporary world has come to a point where the accumulated effects of human activities have caused serious damage to the ecosystems, climate disturbances, wild fires, melting of arctic and antarctic ice, storms, draught, floods, and various ecocatastrophes. All this has had huge impact on the local conditions as well as on the scenarios for decent living in many areas. There are increasing concerns about the soil productivity, balance of the polluted marine ecosystems, species diversity etc. From our human perspective, all these recent changes or threats influence the production of food for our societies.

Besides the global scale of environmental changes, there are many newly emerged impacts of the microbes on our diet and eating habits, which have been caused by globalization. These include the international trade of foods and their raw material, increased travelling, city life, modernization of cooking equipment, variable health trends and other cultural factors. The illustration of these current trends relating to our food practices and polices is shown in figure 1.

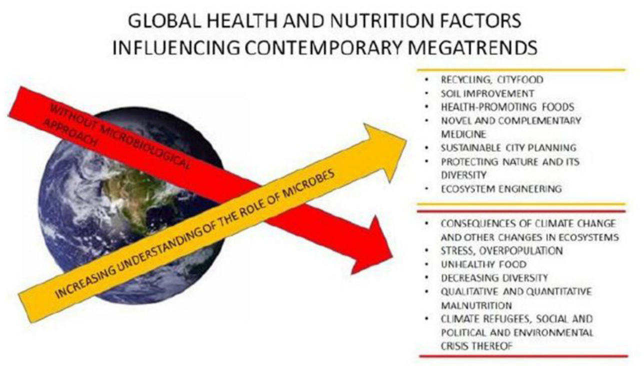

Figure 1: The food and population growth and concentration related megatrends influencing our life.

All the living things on Earth, besides the human being, can be grouped into several kingdoms. Three functionally highly important groups are plants, animals and microbes. They have their specific functions in the global ecosystem. The last one, the group of micro- organisms, is the most difficult to conceive, due to its partial invisibility. However, Mankind has always wanted to learn to live in cooperation with the unseen part of our world, although our ancestors could not observe the microbes. In any case, they could see their importance in food preparation and preservation, in environmental processes and health. In agriculture, the cultivation strategies have been developed in accordance with the soil microbiota. Human and animal health have been somehow associated with the microbiome, although it could not be seen.

Already the ancient nations had learned to use microbial cultures for food production and preservation. Even more so in today's world. We need to understand better their contribution to our nutrition, health and living. The fact of microbes being tiny ones, or microscopic in size, does not make them meaningless. Throughout the ages microbes have carried out the circulation of matter and substances in natural ecosystems. Their importance will be even more self-evident for human societies in solving the alarming problems of man and his environment.

Basic characteristics of the microbial kingdom

One inherent feature of the microbiological research and endeavor is the major issue of scale. In principle, as microbiologists or individuals interested in the mostly invisible organisms, we have to extend our thinking beyond any limits of our scales or measures. Since most microbes cannot be seen by naked eyes, this attitude is a necessity.

However, the world of micro-organisms has several most fascinating characteristics, which relate them essentially to the macroscopic world we live in (Thesis modified from the Epilogue of the Microbiological Hygiene Series of books [1]):

1 The impacts and consequences of the actions of microscopic bacterial cells and other microbes are immense in the global ecosystems, and in our human body system.

2. The microbes form communities and participate in the core functions of all ecosystems; they constitute microbiomes, which usually are wide and complex entities within microbiological systems.

3. The microbes as a functional biological group, besides plant and animal subkingdoms, comprise of versatile members [2]; unicellular and prokaryotic eubacteria and archeons, as well as eukaryotic algae, protozoa, yeasts and molds, the two latter ones belonging to so called microfungi.

4. Viruses can multiply in the cells of any other living organisms, therefore they fall between living and non-living creatures and the molecular world; as biological entities they are able to divide as like any biological cells of other organisms, producing offsprings that carry their genetic traits, but as microbial entities they do not have metabolic activities of their own, but are dependable on the other forms of life.

5. Singular molecular species, such as nucleic acids, or enzyme proteins, messenger or signal molecules of many kinds and other molecular structures, or their combinations, may extend the influence of various living forms or their communities beyond their physical boundaries; for example, the prions have been recently found out to exhibit many activities that could resemble organismal forms of life, and moreover, any forms of microbial life may interact with other forms.

6. Since we see only the outcome of the actions and activities of the ecosystems, or the microbiomes, we lack the tools to understand all aspects of the sophisticated ways, how Nature has been built up to function and sustain life on Earth; for example the gigantic viruses, (giruses), that were found about ten years ago to contain a huge proportion of the total DNA contents in the oceans, and they were shown to have big influences on the climate, and other global environmental issues.

7. Furthermore, down on the scale we actually deal in our daily life, when studying the microbes, also with phenomena that belong to the nanoscale or to the atomic scale or to the discipline of particle physics. This scale difference influences

not only us, but also our microbiota. However, the huge differences are there! When studying microbes, in our minds we need to "shrinken" ourselves down to really understand the effects of scale.

This integration of the ecosystem level effects to the various smaller scales of the universe is also bringing in the aspects of data handling into biology. Our computerized world, and related technologies, are in fact reflections of the information systems that run the natural organisms and biosphere, on the basis of the inherent characteristics of matter and its physicochemical behavior. Microbiology could be evaluated as a discipline of basic science that deals with the functions of living invisible matter organized into cellular or other entities without actual multicellular nature. All this fundamental research and thinking could open up new dimensions to the various aspects of hygienic studies. On the basis of the knowledge and understanding then acquired, we are and will be able to solve the issues in clinical, food, industrial and environmental hygiene, for the benefit of all mankind. One example of the microbiological hygiene effecting all levels of the local society was demonstrated in Burkina Faso, West Africa (Figure 2).

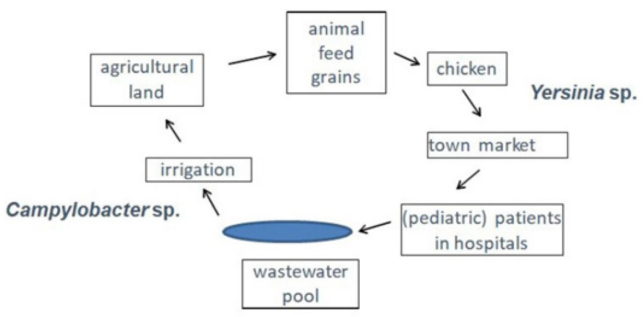

Figure 2: Monitoring of irrigation water supply and potential chain of food contamination in Burkina Faso, Africa, with the PMEU (Portable Microbe Enrichment Unit). Same genotype of Campylobacter sp. was observed in all samples. Modified from [3, 4]. The effect of micro-organisms can be seen both in good and bad developments. By our research effort we can in a way "cooperate" with the microbes and produce technologies of microbial biotechnologies which increase the production of food and improve its health qualities.

Microbes as a part of industrial and other ecosystems

Microbes include a wide variety of living organisms, united by their small scale. However, their influence in the industries, circulation of matter in ecosystems and healthcare are immense. These tiny creatures keep ecosystems functioning both inside and outside our body system. They form microbiomes in soil, intestines and elsewhere. If we could understand fully their interactions, not just classify them, we could discover the very basic mechanisms of the functions in digestive tract and other organs, pathophysiology of complex diseases, various activities of the biosphere as a whole, as well as the potential of biorefineries, or ecosystem services. In our research with the PMEU device (Portable Microbe Enrichment Unit) it has been possible to screen these events in real-time, and to simulate them. In the biorefineries, including pilot plants (e.g. European Union Baltic Sea region ABOWE biorefinery project), the interactions of the UMC (Undefined Mixed Cultures) have been utilized for the production of valuable end products, such as mannitol, valeric acid and 2,3-butanediol, from the industrial and agricultural side streams (Figure 3). We have also revealed some features of the ecological succession in the alimentary tract, and their linkage to numerous health issues, such as IBS, stroke, malnutrition etc. Understanding the strive for balance in the microbial communities could help in finding out the relevant contributions of microbes to our body functions.

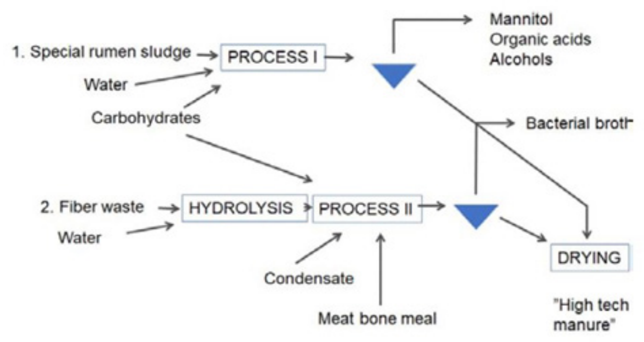

Figure 3: Schematic presentation of the treatment of slaughterhouse side streams. Example of a patented non-aceptic production unit for biorefining with rumen microbiome. See also [5].

In soil improvement we have seen, how the addition of just one strain can decisively alter the composition and function of the entire soil ecosystem. For example, the supplementation of organic fertilizers with an autonomous nitrogen fixing bacterium, *Clostridium pasteurianum* strain, Aurobion™, increases the greenhouse production of several plants by about 50% in two months [6]. Similarly, the incorporation of influential probiotic bacteria into a prebiotic product mix, could in our digestive tract attenuate trouble-making excessive microbial activities, as evidenced by simulation studies in the PMEU. Actually, the alimentary microbiome connects us with our food sources and the environment.

Hygiene monitoring in the future biorefineries

The purest form of hygiene maintenance should be based on the full recycling of organic matter from the industrial, agricultural or municipal side streams [7]. We should strive for a situation where there are no industrial organic wastes, but all side streams could be combined to each other and to fresh raw substances to form novel substrates for various new processes. The circulation of biomass wastes together with the annual increase of the global natural biomass source could provide the Mankind with adequate resources to get all the required energy, food and chemical commodities for our societies [8-10]. In order to understand the local environmental condition in different areas we should develop methods for monitoring the microbiomic structures in various geographical areas and ecosystems [3, 11].

In our food hygiene studies we have used the PCR (Polymerase Chain Reaction), sandwich immunoassays, immuno-luminescence and immuno-PCR [12]. These sensitive techniques could be enhanced by pre-enrichment with PMEU (Portable Microbe Enrichment Unit). When tap water was artificially contaminated with salmonellae, we could detect single bacterial cells by combining the PMEU cultivation in a selective RVS medium with the detection of the volatiles by the sensors of the PMEU Scentrion®. Then the detection time for a single bacterium was less than 10 hours [13]. In the confirmation of the identification (besides by the selective medium) immunological methods could be used. It is noteworthy that the expression of many microbial antigens is related to the growth phase [14].

Biorefineries in utilizing side streams

Many industrial processes further refine agricultural products and upgrade their side streams. In these kinds of "extended processes" there is a huge asset for future industries. Several products from these manufacturing lines are useful as food additives, flavors, aromas, constituents or substituents. By developing the processes on the basis of recycling organic materials from the fields and forests as well as from aquaculture or fishing industry. The overall impact on climate is positive as carbon is absorbed into the industrial ecosystem, and energy is thus effectively saved.

During the years 2012 – 2014 the author of this article was invited to be a key technology provider for European Union Baltic Sea region biorefinery project, ABOWE. Our process principle of non- aseptic UMC (Undefined Mixed Culture) strains as the biorefinery biocatalysts worked out in pilot studies in all testing sites. The natural microbial communities were fortified with inocula containing e.g. some industrial strains of lactic acid bacteria, *Clostridium* and *Klebsiella* sp. This outcome occurred regardless of the short testing periods of 2 months in all locations; for cellulosic waste in Kuopio, Finland; for potato waste in Wroclaw, Poland; and for chicken abattoir waste and chicken manure in Enköping and Västerås in Sweden [15-17]. The potato side streams we had tested already earlier as raw material for 2, 3-butanediol (2,3-butyleneglycol) (BDO) production [9].

Then we achieved top productivity of this valuable platform chemical (Figure 4). During the ABOWE testing, even more precious chemical commodity, valeric acid, was obtained in relatively high concentrations in our experiments both in Poland and Sweden. Actually, valeric (pentanoic) acid was produced as a condensation product of lactate and propionate (Figure 5). Hydrogen was generated several percentages at each testing site, and it could be combusted in so called hytane together with methane. The residual fraction from the biorefinery was 10 times better substrate for methane production than the chicken manure alone [17, 19]. Interestingly enough, in the Swedish testing it was possible to see the instant effect of trace element mix (blueberry juice) on the production of industrial chemicals (butyric acid and 2,3-butanediol) [5, 20].

The great potential of microbial technology could be seen in the media in the beginning of 2020, as the Finnish forest industry giant UPM (United Paper Mills) published their plan to build novel biochemical factory in Leuna, Germany. The investment was 550 Million Euros. This major industrial development took place 12 years after our first experiments on rapid bacterial production of glycols [21] (Figure 4). The novel industrial plant is using non-coniferous wood material. This development is an indication of the trend toward using microbial fermentation as complementary means for the mass production of industrial chemicals.

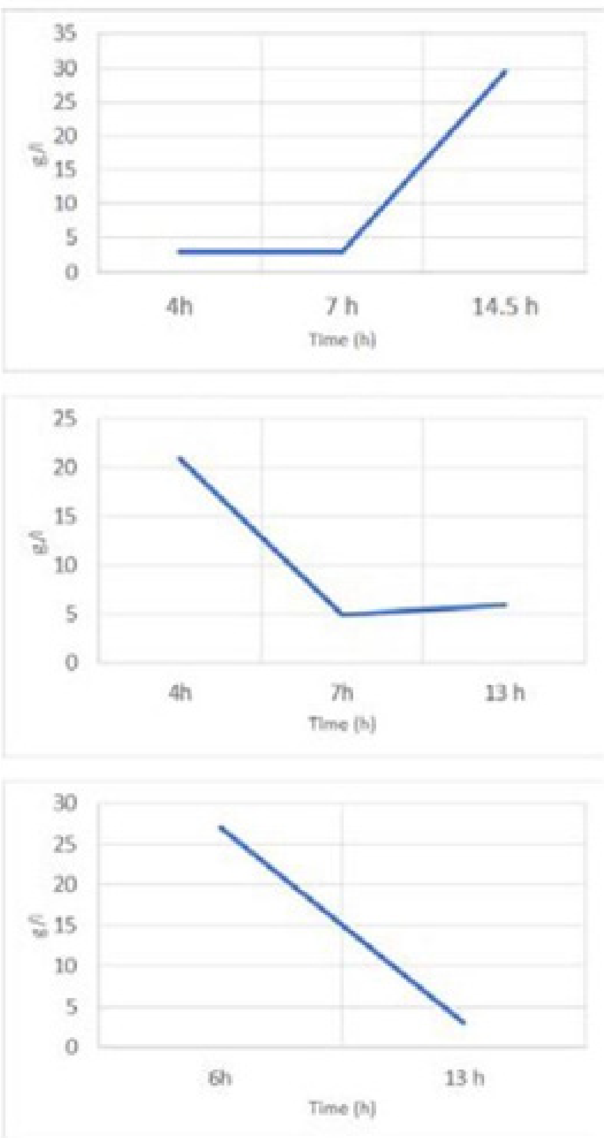

Figure 4: The record productivity of 2,3-butanediol (2,3-butyleneglycole) was 8 g/l/h already in 2007 in the lab of Finnoflag Oy [9]. In the graphs three experiments with Klebsiella sp. sultures (modified from Hakalehto et al. 2013). Production levels reached their maximum in 4-14.5 hours. On the 31st of January 2020 it was published that the Finnish forest industry giant UPM(United Paper Mills) is investing into biochemical production unit. The investment is 550 M euros, and the factory produces a variety of products, such as ethylene and propylene glycols and lignin-based filling materials from wood (according to Helsingin Sanomat magazine).

Another highly potential process for the utilization of industrial side streams was started in 2018 in the Hiedanranta area in Tampere, Finland. There the author and his company were also the key technology providers. This time we tested the production of lactate [22]. This process exploits as raw material the lake bottom deposits of the so- called zero fiber which had been dumped into the lake Näsijärvi during a

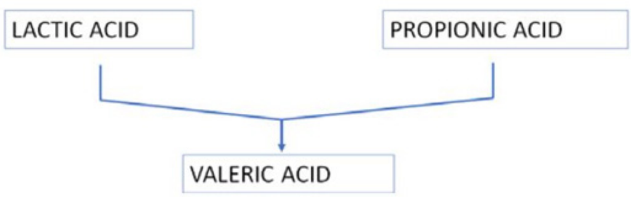

Figure 5: Condensation of lactate and propionate in UMC (Undefined Mixed Culture) biorefining process into valeric acid [17, 18].

century of operation of the factory ashore. Now this industrial area is converted into a lakeside ecological suburban area for 25000 inhabitants. Therefore, the 1.5 M tons of zero fiber needs to be removed from the lake bottom. It was proven out in our pilot project funded by the Finnish Ministry of Agriculture and Forestry, that the economical results of the biorefinery could cover up the costs of cleaning up the bay including the investments into a facility which could process 3500 tons of sludges daily (Figure 6). These calculations were validated by the global consulting company Pöyry Consulting Oy (nowadays Afry) (Figure 7). In several consecutive tests using a pilot plant of 5-10 cubic meters of effective volume. we could demonstrate the potential of a mixed microbial culture to produce elevated levels of desired chemicals, such as lactic acid.

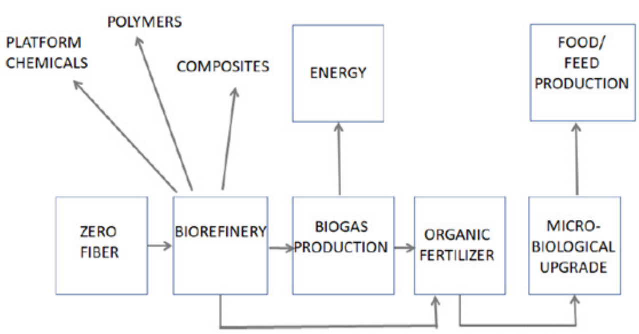

Figure 6: Hiedanranta Tampere 2018-2019 Blue Bioeconomy Project. Schematic presentation of the "Zero waste from zero fiber" project initiated by the city of Tampere, and funded by the Finnish Ministry of Agriculture and Forestry. The project was administrated by Ramboll Finland Oy, and the results validated by Pöyry Oyj (Afry). The key technology providers were Finnoflag Oy (biorefineries), University of Tampere (biogas) and DTS Systems Oy (composting).

In addition to lactate, by combining other side streams, also mannitol could be produced in the same process equipment [5]. This is an example of the great flexibility of biotechnological reactors and processes. One unit could be used for running numerous different processes. All the potential products, such as 2,3-butanediol or, 2, 3- butylene glycol, lactate and mannitol are widely used and important ingredients of various foods and food substances. We have managed to produce them in a hygienically safe way from recycled, environment-friendly and low-cost raw materials. In Tampere, the potential future plant will also carry out an important environmental engineering mission.

Bacteria and mold share molecular communication between different groups

One of the most promising form of biological interactions

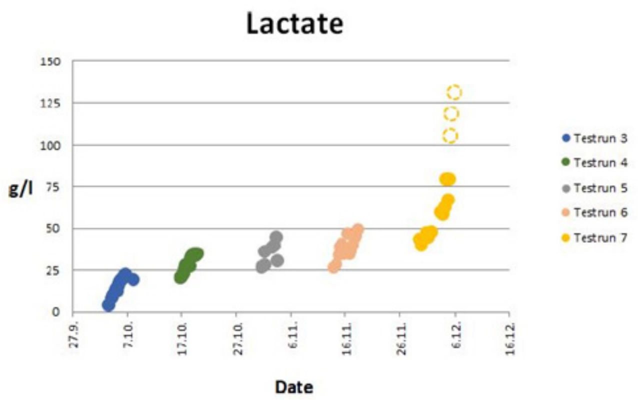

Figure 7: Example of results from the Hiedanranta biorefinery pilot in 2018 during five separate runs - production of biochemicals by mixed microbiological flora and its metabolic networks. The process runs were designed and performed by Finnoflag Oy. The metabolic interactions of natural microbes increase the yields of the biorefineries using industrial side streams or environmental deposits as raw materials. See also [22].

is the cohesive function of some bacterial and fungal strains [23]. It has been a general scientific understanding that various microbial species and strains compete for living space and nutrients in soil. This is partially true. – In fact, is this kind of situation in the microbiological communities to be found everywhere in the microbial ecosystems? It is a lucrative assumption that all living forms of microbes would rather strive for a pattern of coexistence and cooperation instead of automatically competing against each other. In this type of structured ecosystem based on mutually beneficial interactions and networking of various metabolic systems, giving much better result for all members, both energetically and by the means of discovering suitable niches for all types of microbes (Table 1).

Table 1: Role of molds in the microbial communities.

The nutrient-poor or biologically hostile environments, molds act as pioneers because
1. They can resist desiccation, heat and cold, acidity, etc. as spores..
2. They can colonize more hostile substrates by growing as aerial hyphae (thereby minimizing contact)..
3. They can reach hostile or nutritionally poor environment by transporting nutrients or modulators..
4. …and produce effective hydrolyzing enzymes.

Molds, for example, do play a role of pioneering organisms. They can reach through their mycelial mode of growth, poor or hostile environments and transport resources, signals and modulators along their hyphal structures to new areas or locations. Consequently, it would not be most unfeasible for them to engage into constant battle with the bacterial subpopulations within all microenvironments. Rather they seem to possess the antibiotic tools more than for a constant challenge, for "buying time and space" and to gain a foothold for

1. Establishing their mycelial network for
2. producing sexual or asexual spores for spreading into

new target sites, and for

3. producing their rich selection for hydrolyzing enzymes to degrade and circulate organic residues in natural ecosystems, for the benefit of the entire microbiome.

For the same reasons, it is not necessary from the bacterial perspective to ”declare a full war” against the microfungi, but to follow their routes to the threshold of ”new sources and storage rooms” of decaying biomass. Therefore, fungal activities are necessary for the bacterial mixed communities to attain a full state of metabolic flux. The opposite of it would be a stagmatic, metabolically paralyzed condition where every molecule of occasional liberated carboxylates or free amino acids or their equivalents would be instantaneously exploited by miscellaneous bacterial cells in a situation where no joint metabolism or ecological succession could be formed. In fact, we tested the development of the bioprocess technologies in the ABOWE reactor for the utilization of Undefined Mixed Cultures (UMC) together with inoculated industrial strains [6, 11, 18, 19]. The measurement techniques played a significant role in all applications where the NMR (Nucleic Magnetic Resonance) technique turned out to be suitable screening method for the surveillance of the production of the various metabolites [24]. The autoimmunity and infection aspects of the microscopic contamination are to be presented in the Autoimmunity 2020 conference in Athens, Greece [25]. One essential finding of the ABOWE experimentation was the observation of variable pathways utilized by the mixed cultures for producing various metabolites. For example, the valeric (pentanoic) acid was formed in relatively high concentrations from protein-rich chicken litter in the experiments in Sweden, as well as by the microflora from the potato waste and sorted biowaste during the Polish experimentation. The ABOWE tests were carried out in a semi-industrial pilot plant that was constructed by the Savonia University of Applied Sciences in Kuopio, Finland, according to the bioprocess design by the author of this article.

Food crisis is soil crisis

Global agricultural production is dependent on the soil quality. In long term this quality depends on the microbial community that circulates the nutrients, maintains the layer of organic matter, and the composition and texture of the soil. Without a functionable and balanced soil microbiota, the food production will decrease in long term. Even though the chemical fertilization may guarantee the crop levels for some time, in the longer run exposure to chemicals will deteriorate soil quality. Also, the cultivated food products contain less trace elements and vitamins because of long-lasting chemical fertilization of soil.

Additionally, irrigation may bring salt levels higher, which eventually makes the soil less suitable for agriculture. Loss of microbial biomass and metabolism causes drying out and erosion and removal of the humic substances. Thus, in the human agriculture, which often includes overgrazing, human influences destroy the agricultural soil by destroying its microbial balance. One modern approach for biological plant cultivation is implicated in the Arava valley, in Israel, which is one of the hottest and driest environments (Figure 8).

Figure 8: Production of pineapple according to modern principles of biological agriculture in Arava Valley, Israel. Technological advancement in combination with microbiological knowhow make agriculture possible in the most extreme environments on Earth.

Aspects of soil biological infrastructure, circulation of its nutrients, land use, and bio-fertilizers are discussed in [26]. If the soil is destroyed, and its organic materials disappeared, it is not turning into desert, whose ecosystem is usually a very diverse one. This is true also from the microbiological point of view. However, the wasted land and soil becomes a very poor and monotonous biological system [27]. Such areas exist outside cities, around big mines, in destroyed agricultural areas, landslides and waste areas, industrial premises, military zones etc. In order to return the fruitful soil and healthy microbial ecosystem, one should bring humic material with versatile microflora to the spoilt areas.

In the land recovery, as well as in any cultivation process, including gardening or greenhouse cultures, it is important to supply the soil with correct propositions of various minerals. This should not be taken into account only from the perspective of the plant growth, but also from the point of microbial ecosystem and human nutrition. The essential elements in minerals for plants and humans are listed in Table 2. The balance between these elements as well as their undisturbed microbial circulation in soil are essential for the soil resilience. The lack of specific nutritive factors may fundamentally change the composition of soil microflora, as well as its influence on the soil productivity [20].

Food as medicine

About 20-25 years ago the functional food concept was widely introduced, and the progress in health- promoting novel foods was very fast. In fact, it is the microbes which often play a central role in both health-related food concepts and nutrition-related therapies. One example is the genus *Streptomyces* which consists of mostly soil actinomycetes, which are mycelial bacteria. They produce about 95% of different antibiotics, as well as many enzymes and other products of their secondary metabolism in the biotechnology industries. For example, the first genetic vector for transferring genes from antibiotics producing bacteria to better production

Table 2: Essential elements for plants and humans.

Man	Plants
Calcium (Ca)	Phosphorus (P)
Magnesium (Mg)	Potassium (K)
Sodium (Na)	Calcium (Ca)
Potassium (K)	Sulfur (S)
Phosphorus (P)	Magnesium (Mg)
Chlorine (Cl)	Boron (B)
Sulfur (S)	Chlorine (Cl)
Iron (Fe)	Manganese (Mn)
Zinc (Zn)	Iron (Fe)
Manganese (Mn)	Zinc (Zn)
Copper (Cu)	Copper (Cu)
Iodine (I)	Molybdenum (Mo)
Fluorine (F)	Nickel (Ni)
Chromium (Cr)	
Molybdenum (Mo)	
Selenium (Se)	

organisms was carried out in year 1985 in London, England. The mission was to develop a plasmid vector by which the gene for the production of clavulanic acid was then transferred to *Escherichia coli* from *Streptomyces clavuligerus*. The former is a much more stable organism, and is also a well-known production organism for many biotechnical goods. The development of novel antibiotics is of top priority due to various emerging antibiotic resistant bacterial strains [28]. In a similar perspective Dr. Jessica C. Kissinger (Center for Tropical and Emerging Global Diseases; Institute of Bioinformatics; Department of Genetics, University of Georgia, GA, USA) introduced in MicroBio conference in Baltimore in November 2019 a novel research project funded by the Gates Foundation in order to develop rapid reaction and counter-action against the threatening local epidemics, including zoonoses. Another project in the same conference was presented by Dr. Kathleen L. Hefferon (Department of Food Sciences, Cornell University, Ithaca, NY, USA), related with the production of metabolically engineered food plants containing effective medicines. In several recent studies it has been demonstrated that various medicinal molecules can be expressed in plants [29, 30].

By broadening our understanding of the microbiome, nutrition, and their joint influence on individual health we have developed an approach for dealing with digestive disorders. In the following, find some examples of this novel concept of microbiome-based concept of therapy (MBCT) developed and used by the laboratory of Finnoflag Oy and the physicians in cooperation with the company. These treatments often relate to the regaining of shaken balance of the microbiome. The essential foundation of these procedures is the determination of the Bacteriological Intestinal Balance (BIB, see Chapter 3.8) [31]. The three examples demonstrate the ruling out of some opportunistic pathogens or otherwise unbalancing, or dominating, strains. In fact, probiotics and prebiotics have become parts of our diet, which positively contribute to our health.

A thirteen-year-old boy, suffering from abdominal pain and digestive disorders was reported to have difficulties in going to school because of his symptoms. In the microbiological analysis, the major isolate from his samples was *Morganella morgani*, which is known as an opportunistic pathogen. Its concentration in the stools was above 10 million colony forming units per gram. On the basis of the relatively high abundance of this strain in comparison with other microflora, it was supposed to play a key role in the symptoms of the patient. Since *M. morgani* strains do not utilize lactose, the patient was recommended to increase the use of milk products. This change in his diet helped him in getting rid of his digestive problems.

Some microbiological conditions relate to the patient's anatomical or physiological situation. One example is the occurrence of bacteria of the genus *Sarcina*, which are commensal or generally harmless members of the intestinal flora. However, in case of a patient, a middle-aged man with recently removed biliary glands, there was a substantial increase in the number of *Sarcina* sp. cells in his stools after the operation. This bacterium produces acetaldehyde, which is a potential carcinogen in high concentrations. Its peaking after the meals, and consequent formation of carcinogenic acetaldehyde could be mitigated by AcetiumTM, a product of Biohit Oy of Finland.

Another potentially harmful bacterium, *Ruminococcus* sp. strain, was growing in the diverticles of a middle- aged woman patient. There it took advantage of the anaerobic conditions, which made the strain to grow to excessively high levels from the point of intestinal balance. This caused several metabolic problems, such as lack of cortisole in the patient's bloodstream. The problems were then fixed by finding a suitable antibiotic treatment confining the *Ruminococcus* growth and helping the other microflora to get this strain under control.

Bacteriological intestinal balance (BIB)

One important basic element in human health, and in the microbiological health of the individuals, is the Bacteriological Intestinal Balance (BIB) [28, 31, 32]. It seems possible that the incorporation of even one new strain can bring along fundamental changes in the composition of our microbiome. On the other hand, it is often difficult for a new member strain to find a permanent position in the microflora. And the better the flora is balanced and the more diverse it is, the stronger it is against any environmental changes. Consequently, the better is its metabolic cooperation with the host body system.

The BIB is an important constituent for our health and general well-being. It is based on the balance between different coliforms in the duodenum as the cornerstones [21, 33]. There the absorption of food components usually begins, after the food is introduced into the duodenum from the acidic stomach. The uptake of nutrients from the chyme in the small intestines is influenced and participated by the digestive microflora, which composes of the strains from the oro-pharyngeal tract, the gastric mucosa and the duodenal epithelia. The balance between mixed acid fermenting strains, such as *Escherichia coli*, and the more neutral substance producing members of the *Klebsiella – Enterobacter* group plays an important role in establishing the BIB [21, 33, 34] (Figure 9). Thus, the relatively small number of bacterial cells on the duodenal walls and also on the gastric membranes inoculate the chyme, which then traverses along the small intestines for about 6 -7 hours [21, 35]. The existing alimentary flora receives the microbes which enter our system with the food.

"Bacteria belonging to the genus *Klebsiella* have a dual role in human pathophysiology. Some of the strains are potent opportunistic pathogens capable of causing severe illnesses, whereas a majority of the klebsiellas belong to our normal flora, particularly in our alimentary tract."

The pathogenicity of a microbe depends not only on its infective characteristics, but also on its position in the microbial microenvironment and the defensive immune mechanisms of the human body.

Figure 9: Role of Klebsiella sp. in the human microbiome and interactome [32].

Since our microflora is in intense molecular communication with our body system, the foundations of the microbiome are in central role in our health. If the public health is to be influenced positively, one important piece should be the supporting activities of the intestinal microbiological health and the BIB. This condition of our alimentary microbiome is in a decisive role in maintaining our general and psychological health [36, 37], as well as in the protection of our body system against numerous illnesses [38, 39]. The vagus nerve serves as the signaling channel in the molecular communication between the microbiome and the regulatory mechanisms of the human body system (Figure 10). The constant stress caused by the urban lifestyle is probably one of the reasons for increased numbers of IBS/IBD in most countries. The agitation of our autonomous nerve system is provoking disturbances in the alimentary microbiome.

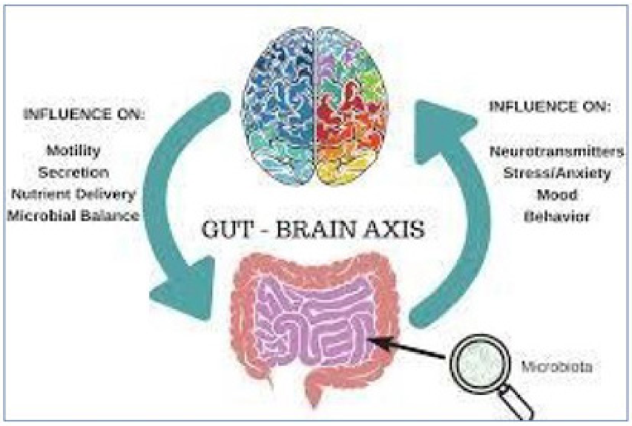

Figure 10: Molecular communication between CNS and the intestines mediated by the vagus nerve (source: fodmapeveryday.com).

In the nutritional status of human individuals, the composition and balance of our microbiome is of crucial importance. It also influences the food uptake. Therefore, for entire societies, we have to understand the role of digestive microbiota with respect to the diet and nutrition. On the other hand, if novel food sources and raw materials are developed, their microbiological dimensions need to be researched, too.

Probiotics, prebiotics and health

Microbial strains that contribute in positive way to the host health, are often called probiotics if they are deliberately used as food supplements or health promoting products. Most often these species belong to lactic acid bacteria (LAB). They are non-pathogenic, usually non-invasive, and they generally strengthen the balances in the microbiome. *Lactobacillus* and *Clostridium* are the most common bacterial genera in the digestive tract. Many members of these genera can maintain themselves in the acidic gastric areas [35].

The lactic acid bacteria seem to adapt to a balancing role in different ecosystems. Many species grow on plant surfaces, where their relatively slow-growing but stable and lactate-producing cultures prevent the overgrowth of other microbes. They have a similar role in mammals, where the new-born young individuals get protection by the presence of LAB, and by the regulation of pH in the digestion, and on the skin and epithelial surfaces. In the alimentary tract they also maintain stability as the intestinal chyme is moving them along together with the degrading food particles. In fact, they derive from the plant and animal origins of our diet, as well as from the common fermented foods. Moreover, many LAB species belong to our normal flora. In the colonic areas they produce lactic acid for the substrate of the butyric acid clostridia [40]. This organic acid is then protecting the host epithelia against serious diseases together with CO_2 bubbles, which for their part keep the intestinal content in motion by mixing it gently.

The long-term benefits of the increased use of probiotics are not fully understood, but on individual level they often improve general health and relieve the symptoms and consequences of various inflammations and infections, such as IBS/IBD (irritable bowel syndrome disease). In order to get full benefits from the LAB probiotics, they are recommended to be delivered with fibrous prebiotics. Actually, since they do not have fimbrial structures of their own for their attachment onto the gut epithelia, it is understandable that plant- derived fibers help the LAB strains in forming colonies during their passage through the gastrointestinal tract. There they seem to have a role of a moderator, as they attenuate the growth of many other intestinal bacteria thus maintaining the BIB in the intestines [41].

As like the LAB, also several members of the genus Bacillus have been used as probiotics. Some of them tend to inhibit the slow inflammatory processes caused by various Gram-negative endotoxins [42]. Similarly, many other microbial strains could be used as future preventive means against different health problems. However, it is important to get adequate understanding on their role in the microbiome, and the ways they exercise their impact on it and on our system. – In order to improve public health, we should invent and introduce novel foods which possess probiotic and prebiotic health-promoting qualities.

Our nutrition is dependent on the quality of food, on our individual metabolism, and on the strikingly important role of the micro-organisms. The intestinal microbiome is nowadays considered as an independent but interdependent organ of our body system [43, 44]. Its role in protecting our body system, as well as in seeking for balance with our neuronal, hormonal and immunological regulative systems has been increasingly well understood. Therefore, it is not the direct effect of any food component or its constituent on our anabolism and catabolism that we solely need to pay attention on. Instead it is often more important to consider the joint contribution of our microbiomic members and our own body functions to the food degradation, absorption and assimilation of various substances in our digestive tract and by other tissues.

Conclusions

Most microbial strains belong to some form of microbial community. Usually the communities are characterized by the favorable conditions for any particular strain. However, it is common that microbial community changes the conditions into favorable ones to protect its own survival and growth. Alternatively, the strains can together also downgrade any negative impacts on their joint survival. Therefore, it is typical that various strains in any community or microbial ecosystem strive for balance. Any member strain increases the genetic and biochemical net potential of the community. Thus it is advantageous for all members to keep up as much diversity as possible in any environment. Consequently, this kind of ecosystem structure is found in the alimentary microbiome, as well as in the microbial other parts of the body system. In various environments microbial communities may be confined to specific niches, or they may also form gradients which help the entire group of microbes in adapting to the changes in the conditions. Also industrial processes form such ecosystems. In order to utilize microbes for the production of energy and chemicals or food components, as well as for cleaning up the manmade changes in water or in soil, we need to understand the functions of both the microbial communities together, and the roles of different strains in them. This approach to microbiology could offer lots of means for the complementary medicine, for example in the use of probiotics and prebiotics. We have tested the concept in finding optimal treatments for patients suffering from digestive disorders or other misbalanced microbiota. Such concepts as BIB (Bacteriological Intestinal Balance) are important in defining any effects on the ecosystem by the microbial strains, nutrients or other factors. Similar settings can be observed also in the biorefinery processes, whose optimization is reflecting the search for optimal condition for some particular biochemical events in a similar fashion as it is known to happen in the alimentary tract.

Moreover, these principles are applicable also for the ecosystem engineering projects. As a matter of fact, it is the microbial community which determines the balance of any ecosystem. In order to compensate any negative changes or trends in the environment, it is worth striving to regain the microbiological balance first.

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