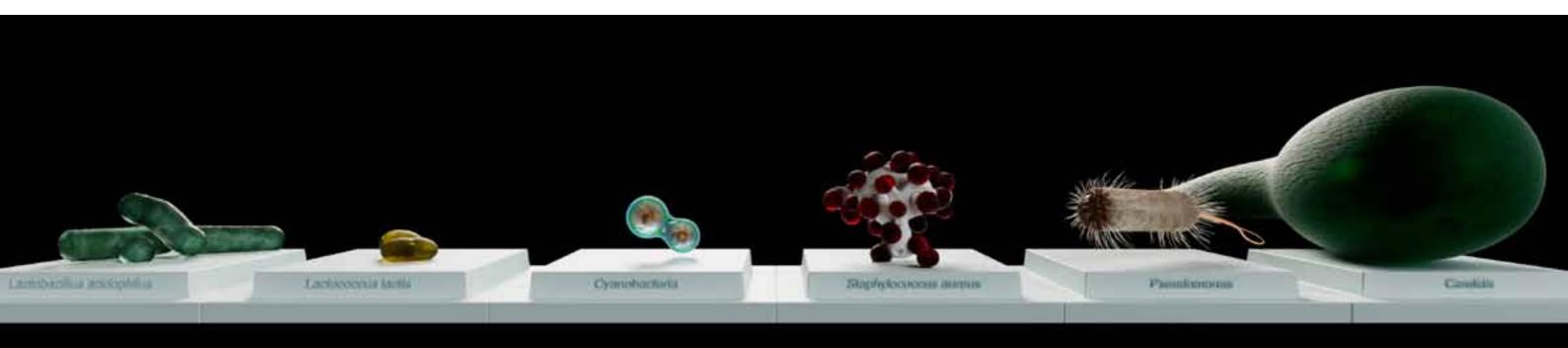
# THE SECRET RULERS OF THE WORLD



www.microbiomesupport.eu



# BIRTH OF LIFE ON EARTH

Four and a half billion years ago, the Earth was created. At that time, the planet consisted of gas and dust. Over time the Earth cooled down, a crust formed, and water accumulated. Three and a half billion years ago, the first living organism developed. How it came about is unknown. Chemical compounds grouped together and a living organism in the shape of a single living cell formed. This cell divided and single-celled organisms were formed. Small living beings like these are called microorganisms because they are so tiny that we cannot see them with the naked eye. Presumably, life originated in water, and the oldest forms of life are single-celled organisms that live in hot water near hydrothermal vents on the sea floor.

# Cyanobacteria "invented" photosynthesis

A billion years after the emergence of the first single-celled organism, the next crucial step for life on Earth occurred: cyanobacteria produced sugar and oxygen – from water and gas and with the help of sunlight. With this, photosynthesis was "invented". Cyanobacteria were now able to produce their own food. Over time the oxygen formed by the cyanobacteria accumulated in the atmosphere. This created one of the most important foundations for the further development of life: the air we breathe and on which our life depends.

# FANTASTIC

Cyanobacteria were the first producers of oxygen. They need sunlight for photosynthesis. Probably for this reason, cyanobacteria can sense light. How they manage to do so has long been a mystery. Cyanobacteria have a diameter of 3 micrometers – that means 3 millionths of a meter. No optical instruments are small enough to measure the refraction of light in the bacteria. The researchers used a trick and measured the refraction of light around the bacteria. Thus, they discovered that although the bacterium consists of only one cell, this single cell functions like an eye. The light enters through a tiny lens and activates locomotion threads located directly opposite the lens, and the bacterium can move toward the light source.

# Study

Schuergers N. et al. (2016) Cyanobacteria use micro-optics to sense light direction. https://doi.org/10.7554/eLife.12620

**CYANOBACTERIA** Cyanobacteria were and still are the most important oxygen producers on our planet. Around 2,000 different species of cyanobacteria have been classified until today

#### ARCHAEA

The so-called "primitive bacterium" and the first cell division mark the beginning of life on Earth 3.5 billion years ago.

> 300,000 years ago Homo sapiens emerged

0.5 billion years ago multicellular organisms developed, plants and animals populated land

2.5 billion years ago cyanobacteria invented photosynthesis

3.5 billion years ago single-celled organisms developed

4.5 billion years ago planet Earth formed from a cloud of dust and gas



## Microorganisms in water produce OXYGEN

Without microorganisms, there would be no life on Earth. To this day, our life depends on these organisms in water because they produce most of the oxygen.

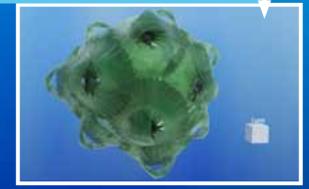
## **Algae as a RESOURCE**

Algae produce a variety of substances and are therefore researched as a sustainable raw material. They provide fats, such as the very healthy omega-3 fatty acids and are rich in minerals and vitamins. Algae multiply quickly and produce 30 times more oil than rapeseed or corn.

## **Algae - the CLEANERS**

Algae can absorb nitrogen and phosphate from wastewater. All they need is sunlight and carbon dioxide. During the purification process, the algae produce oxygen. At the same time, the algae biomass increases, and biofuel can be produced. This is a win-win-win situation.

> *Emiliania huxleyi* is an alga from the group of calcareous flagellates. The algal cell is surrounded by calcareous platelets. Certain limestone rocks, such as chalk, often contain a significant amount of calcareous flagellates. So, when we write with chalk on a blackboard, we are basically writing with algae.



### UNIQUE

Algae can also produce oil. Some algae, however, can produce n-alkanes, usually the main component of petroleum oils. A peculiar microalga called *Dicrateria rotunda* has n-alkane oil droplets in its cavities, with a chain length of 10-38, the same as petroleum. *Dicrateria rotunda* is thus the first known organism that can produce petroleum.

Study

Harada N. et al. (2021) A novel characteristic of a phytoplankton as a potential source of straight-chain alkanes . https://doi.org/10.1038/s41598-021-93204-w

# The water MICROBIOME

## Algae kept to themselves for a long time

Over the next millions of years, multicellular organisms like algae evolved. Algae have a cell nucleus to protect their genetic information. They probably combined with the cyanobacteria and were thus able to carry out photosynthesis. Algae were the only plant-like organisms on Earth for about two billion years.

# Marine ecosystem is essential for LIFE ON EARTH

70% of the Earth's surface is covered by water. Seagrasses and algae can store 20 times more carbon than forests on land. This makes them an immense factor in the fight against the climate crisis. However, if the marine habitat is further destroyed and stored carbon released, huge inputs of  $CO_2$  into the Earth's atmosphere can be expected. Life originated in the sea, and without the seas, there will be no life on Earth in the future.



#### Microorganisms consist of one or only a few cells

We call the smallest organisms microorganisms, simply because they are so small. Microorganisms include bacteria, protozoa, archaea, fungi and microalgae.

## Every organism forms a unit with its microbiome

A microbiome refers to all microorganisms that colonize a particular habitat, for example, the human skin, the leaves or the roots of a particular plant. A microbiome is a very complex and diverse community of life. The best known is the microbiome of the human gut.

# OVERWHELMING

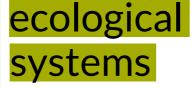
It is difficult to estimate how many different species of bacteria, fungi and algae live on our planet. However, there are so-called scaling laws that can be used to calculate species diversity. In 2016, scientists applied these scaling laws to microorganisms and calculated them: there could be 1 trillion, thus 1000 billions, microorganisms on our planet. Of these, only 10 millions have been catalogued so far, and only about 10,000 can be cultivated in the laboratory.



Locey K. J. et al. (2016) Scaling laws predict global microbial diversity. https://doi.org/10.1073/pnas.1521291113

# Biodiversity is the basis for robust

Even though we humans are technically advanced, we depend on nature and all its diversity. This diversity also includes the smallest living beings: microorganisms. The various microorganisms are everywhere: in the air, in the soil and in the water. They also populate plants, animals and humans. Every plant and animal is the habitat for millions and millions of microorganisms. Accordingly, the biodiversity of plants and animals is linked with microbial biodiversity. If a plant or animal species becomes extinct, thousands of microorganisms disappear with it – including countless yet unknown ones. There are millions of different species of microorganisms, of which only a fraction is known so far.



## **Biodiversity emerged from the simplest living things**

For three billion years, the simplest living creatures with only a few cells populated the Earth. And then, about 500 million years ago, suddenly everything happened really quickly. Within a short time, an enormous number of different species developed. Different plants and animals populated the Earth and thus formed a colourful diversity of species.

# Diversity keeps you healthy

The fundamental principle of nature is: life is diversity. The more diverse a habitat, the healthier it is. The principle of diversity also applies to manmade systems such as agriculture. For many years, humans have ignored this principle and thereby severely disturbed the balance. Monocultures, excessive livestock farming, or the use of chemicals are reasons why the diversity around us is steadily decreasing, and the planet is already facing visible consequences.



# Biodiversity describes a broad spectrum

Diversity of species includes the variety of animals, plants, and microorganisms. Genetic diversity describes the diversity within a species. Biological diversity also includes habitats, such as oceans, grasslands, and forests. All three areas are covered by the term "biodiversity".

# THE GROUND IS SWARMING WITH MICROORGANISMS

Trillions of microorganisms live together in the root zone of a plant. The sum of all microorganisms in such a community forms the microbiome. The more diverse the inhabitants are, the better for all involved parties. Because in every microbiome, diversity is the crucial factor for a functioning coexistence. All inhabitants have specific tasks to fulfil.

Fungi can form wafer-thin filaments and use them to access the most remote areas in soil that plant roots would otherwise be unable to expand into. Furthermore, fungi take up diverse nutrients and deliver them to plants. Bacteria and fungi in the soil process dead plant material and decompose substances that serve as food for other organisms. In return, the bacteria and fungi receive photosynthetic sugars from the plant.

# Cosy living communities

All plants need nitrogen as food. However, nitrogen mainly occurs in a form that cannot be absorbed directly by plants. Bacteria can modify nitrogen in a way that plants can utilize it. That is why some plants form a symbiotic relationship with the bacteria and invite them to live within their roots. You can see this particularly well in legumes. These plants form nodules, which are home to millions of so-called nodule bacteria (rhizobia) that convert nitrogen for the plant.

in roots

## Rhizobium

Legumes form a unique symbiotic relationship with bacteria. The atmospheric nitrogen is converted by the nodule bacteria (rhizobia) to ammonium and provided to the plant. This is why legumes are also grown as catch crops and for green manure in agriculture. The plants are then worked into the soil. Thereby, the essential nitrogen enters the soil and is available to the subsequently cultivated plants.

# ENORMOUS



#### EVERYONE BENEFITS FROM A HEALTHY SOIL

Plants settle where they can find what they need to survive. In agriculture, the conditions often have to be adapted because the diversity is lacking, and the soil is very strained. Fertilizers must be used to introduce nutrients into the soil, but they are often only active for a short period of time because they are washed out or become ineffective. A healthy soil life with an intact microbiome can help to save on chemical fertilizers.

Plants are important carbon suppliers for the soil. Dead plant parts are converted into soil carbon and  $CO_2$  by soil organisms. The soil organisms also die naturally. When a bacterium in the soil dies, its cell fluid is absorbed by the environment. About 10% of the dead bacterium serve as food for other microorganisms, about 50% are converted into minerals, and about 40% of the organic carbon remains in the soil. Dead bacteria and fungi make up a large portion of organic soil matter. Soil is the world's largest CO<sub>2</sub> reservoir. About 2,600 billion tons of carbon are stored in soil (twice as much as in the atmosphere).

Not all microorganisms have such a comfortable and cosy lifestyle as the nodule bacteria in the soil. Microorganisms on plant leaves have harsher living conditions. Rapid changes of sunlight, heat, cold, rain and wind are challenging for them. Therefore, they like to live in bays on the plant surface or protected by an "umbrella" on the bottom of the leaf. Bacteria, fungi, and algae settle on the leaves. They often travel with the wind over distances of hundreds of kilometres. Bacteria on leaves help a plant strengthen its immune system, protecting it from diseases. Plants with an optimal microbiome are also more resistant to stress factors such as drought and salt.

# MICROBIAL SHIELDS on a leaf

## Taste due to methylobacteria

The most common microorganisms on leaves are methylobacteria. They are also partly responsible for how fruits and vegetables taste.

Study Siegmund B. et al. (2011). Die Bedeutung von Methylobakterien für die Aromabildung von Erdbeeren. Die Ernährung, 35, 149-155



Even more bacteria than on the surface of a leaf are found inside a plant. Millions of bacteria can accumulate there, but the quantity alone does not result in any benefits. Diversity is more important than mass. After all, many of the same bacteria do not improve the microbiome. How many different microorganisms inhabit the plant is crucial. Microorganisms that fight off diseases or provide nutrients to the plant are essential.

Study 4 Shaley, O. et al. (2022)



# INNER VALUES of a plant

Commensal Pseudomonas strains facilitate protective response against pathogens in the host plant. https://doi.org/10.1038/s41559-022-01673-7

# **Microorganisms produce GAS FOR BIOGAS PLANTS**

Up to 200 different types of bacteria are found in the stomachs of cows. They digest plant-based food, thereby producing a large amount of gases. During rumination, the gases, CO<sub>2</sub> and methane, escape from the cow's mouth - up to 200 litres a day.

Although the methane gas produced by cow microorganisms cannot be captured and used as energy, biogas plants use similar microorganisms to produce gas. The microorganisms are fed plants and biowaste that they digest and produce gas in the process.

# INGENIOUS

The microorganisms in the cow can digest almost anything. Some of them even break down plastic. Until now, these bacteria have always been studied individually. Austrian scientists found that plastic degradation is improved when the entire rumen microbiome is involved.

Study Quartinello F. et al. (2021) Together Is Better: The Rumen Microbial Community as Biological Toolbox for Degradation of Synthetic Polyesters. https://doi: 10.3389/fbioe.2021.684459

A cow is much more than we can see. Because every cow is also home to trillions of bacteria that help it digest food and stay healthy. Without these bacteria, the cow could not be able to survive.

# **MICROORGANISMS DIGEST FOOD FOR COWS**

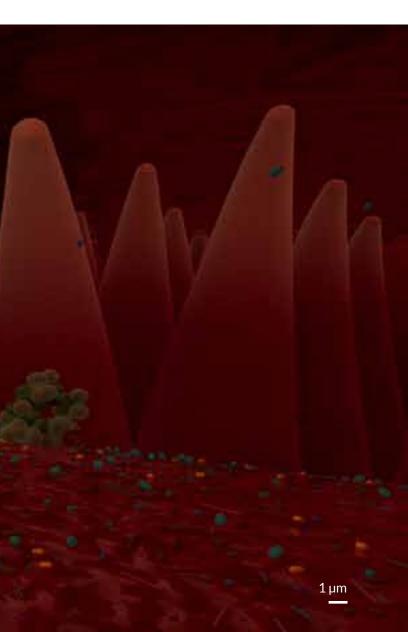
Many plants that a cow eats are indigestible to it. The task of digestion is performed by bacteria that live in symbiosis with the cow. Once a cow has swallowed a clump of plants, bacteria begin to ferment the food, producing nutritious sugars.

Anything that cannot be decomposed by the bacteria returns to the mouth, where it is vigorously salivated and then ruminated. The ruminated fine plant pulp goes into another stomach, the rumen. The resident microorganisms convert the pulp into digestible components.

A cow's tongue is full of small bumps that make it rough and simplify the process of tearing out and crushing plants. If the plant fibres in the stomach are still too large for the microorganisms, the pulp is transported back into the mouth and ruminated. The cow produces 100 to 200 litres of saliva per day.



However, microorganisms also serve as food for the cow. In addition to an average of 100 kg of grass, a cow digests up to 10 kg of microorganisms daily. Depending on which plants a cow eats, different microorganisms multiply.



# LACTIC ACID BACTERIA

Milk has been used to make dairy products for thousands of years – people were already making cheese in the Stone Age. The milk microbiome (i.e., bacteria and fungi present in milk) is crucial to cheese production. They influence the ripening and taste of raw milk cheese. Lactic acid bacteria, for example, convert lactose into lactic acid, and the milk becomes acidic. In this acidic environment, the milk protein forms lumps (called casein), giving the cheese its firm structure.

# The quality of milk also depends on microorganisms

There are numerous milk vesicles in a cow's udder. They filter protein, fat, lactose, minerals and vitamins from the blood into the milk. The components of milk differ – depending on what a cow eats and which microorganisms have colonized it.

# Lactic acid bacteria thwart harmful bacteria

The lactic acid formed by bacteria prevents harmful bacteria from multiplying – this makes food last longer. However, lactic acid bacteria are found not only in milk but also on vegetables. They are responsible for turning cabbage into sauerkraut or fresh vegetables into fermented vegetables. They also have a say when it comes to baking bread: sourdough consists of lactic acid bacteria, yeasts and flour and, in the best-case scenario, helps the bread to rise fluffy. Lactic acid bacteria are also extremely useful in the human intestine, where they prevent harmful bacteria from multiplying efficiently.

### **Pro and Pre**

Lactic acid bacteria belong to the probiotics. They are found in yoghurt, sauerkraut, kimchi and other fermented foods. We eat those foods and thus ingest the bacteria. Many of them can survive the very acidic environment in our stomach and settle in our intestines. Prebiotics, are foods that do not contain bacteria but are a favourite food for the beneficial bacteria in our gut. These include all fibres, such as those found in fruits, vegetables, legumes, and whole grains. Lactic acid bacteria and bifidobacteria love fibres and multiply when fed with them. On the other hand, sugar and too much protein support the growth of microorganisms, which are often associated with disease.

Lactic acid bacteria prefer to

mammals, but they can also be

live in the digestive tract of

# IMPRESSIVE

Casein is an excellent binding agent, it combines various substances and adheres to surfaces. For casein paints, colour pigments are added to the casein. Casein glue with very high adhesive strength is produced when casein is mixed with lime. Apparently, people have been using milk as a base for paints for thousands of years; the milk protein compounds can even be found in cave paintings. The binding power of casein was also exploited by a monk in 1531. He heated the cheese and cooled it back down. The more often he repeated this process, the firmer the mass became. He was able to shape objects with it and called the material "artificial horn". The exact recipe for artificial horn came from an alchemist named Bartholomäus Schobinger and is considered the first recipe for plastic in Germany. Around 1900, a German printer and a chemist mixed casein with various chemicals and used it to invent galalith, a casein plastic that was used to make a wide variety of objects such as buttons, handles and jewellery.

**CASEIN STRUCTURE** Casein is the protein in milk that is coagulated by the lactic acid produced by bacteria, giving it a firmer structure.

# Not only common mushrooms are edible

Yeasts are fungi that consist of only one cell. They reproduce by forming a small shoot on the mother cell. Inside, the cell nucleus is duplicated by division and transported to the shoot. The shoot separates from the mother cell and a new yeast is born. This process requires energy. The yeast gets it mainly from sugar, and while the cell converts the sugar into energy, alcohol and the gas  $CO_2$  are produced. This metabolism is known as "fermentation". The yeast *Saccharomyces cerevisiae* is our baker's and brewer's yeast. In beer production, it provides the alcohol content in the beverage. When baking with sourdough, the multiplication of the yeast ensures that small gas bubbles are created, and the dough becomes fluffy.



# Yeast consists of only one cell, but works like a sponge

Yeasts are used in clarification plants to purify wastewater. Heavy metals such as zinc, copper and cadmium adhere to the yeast and can then be chemically removed. Other microorganisms, such as bacteria and algae, also help to clean wastewater through this "biosorption" process.

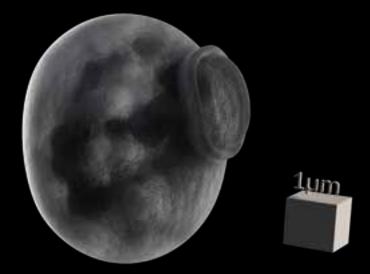
# Yeast in food production

Yeasts are found everywhere. They are in the air, in and on plants and other foods. You can make a sourdough by mixing flour and water and waiting. The yeasts multiply and the sourdough rises. However, naturally occurring yeasts cannot handle all the alcohol and baked goods production in the world. Therefore, yeasts are selectively bred and propagated and then used in food production.

# Different **yeasts** and **bacteria** support each other...

... and the result is a trendy drink: kombucha. It is a tea that has been fermented with the help of yeasts and bacteria. The special thing about kombucha is that the fermentation process is carried out by bacteria and fungi living in symbiosis. Various yeasts, such as brewer's yeast or the fission yeast *Schizosaccharomyces pombe*, lactic acid bacteria and acetic acid bacteria convert the sugar into gas (which is why kombucha is slightly fizzy) and acid. Kombucha is said to have healing effects, although there is little scientific research on it.





Saccharomyces cerevisiae Yeast actually does nothing other than multiply. During multiplication, the substances humans use are produced: alcohol and gas.

# A false fungus called SCOBY

Often the kombucha mother is called a tea fungus. This is not correct because it is not a fungus but a community of bacteria and yeasts. The technical term is SCOBY and stands for "Symbiotic Culture of Bacteria and Yeast".

Study Villarreal-Soto S. A. et al. (2018) Understanding Kombucha Tea Fermentation: A Review. https://doi.org/10.1111/1750-3841.1406

# Inside the human gut

This is what the gut of a human looks like from the inside: The villi are excavations of the small intestine; they are about one millimetre in size. Even smaller microvilli, threadlike extensions of cells, are found on the intestinal villi. The intestinal villi and microvilli enlarge the inner surface of the intestine many times, creating a huge "living room". Trillions of microorganisms such as bacteria, phages and fungi live there and do their valuable work. Together, they form the intestinal microbiome. They are protected from external influences and also receive sufficient nourishment. In return, they produce vitamins and many other valuable substances for us. A diverse intestinal microbiome supports digestion and protects against diseases.

# A big plus on the health account

What we eat counts: organic products taste good and are also rich in microorganisms that are healthy for humans. It is the diversity of microorganisms that best supports the gut and health. Researchers used to think that food microorganisms were killed by stomach acid and therefore played no role in the gut. However, it has been proven that many microorganisms enter the intestine unharmed.

Study Wassermann B, et al. (2019) An Apple a Day: Which Bacteria Do We Eat With Organic and Conventional Apples? doi: 10.3389/fmicb.2019.01629



Small intestine



#### **ASTONISHING**

With a size of 0.02-0.2 µm, bacteriophages are the smallest components of plankton. Nevertheless, bacteriophages form the numerically largest part of the plankton in our oceans: the so-called virioplankton counts 10<sup>31</sup> bacteriophages.

# Viruses as aid providers

Viruses represent unique forms. By definition, they are not living organisms because they cannot reproduce on their own. They need a host to do so. Some viruses use humans as hosts – as in the case of corona or cold viruses. Other viruses also use fungi, plants, and animals as hosts.

Some viruses exclusively attack bacteria. These viruses are called bacteriophages. For example, a bacteriophage called T4 only attacks *Escherichia coli* bacteria. T4 attaches to the bacterial surface and uses its sting to transport its DNA into the bacterium. Inside the bacterium, new viruses are reproduced using the information from the virus DNA that has been introduced. When these are ready, the bacterium bursts and up to 200 newly created viruses are released. This process is entirely harmless to humans. On the contrary, medical researchers are working on programming bacteriophages to eliminate harmful bacteria. This phage therapy can thus be used as an alternative to antibiotics against bacterial diseases.

*Escherichia coli* bacteria occur naturally in the intestines of humans and other mammals. Most of them do not cause any diseases. However, many *Escherichia coli* bacteria can cause severe infections in humans with diarrhoea, vomiting and fever. *Escherichia coli* can be easily grown in the laboratory and is therefore used as a model organism in microbiology.



# **Problems** with the microbiome

The microorganisms in the gut produce many substances. Unfortunately, not all of these substances are beneficial to us humans. Some substances can even damage our DNA and are probably involved in the onset of cancer. Extensive scientific research is still needed to discover more about the relationship between the gut microbiome and cancer. This future knowledge may make new therapies or preventive measures possible. Microbiome transplants are already being experimented with for chronic intestinal diseases.

# Microbiome and gut-brain axis

It has been known for some time that a healthy gut microbiome, formerly known as "gut flora", protects against disease. Relatively new, however, are the findings that the gut microbiome influences our brain and, thus our moods and emotions. The vagus nerve runs from the brain to our gut. This is one of the ways the gut microbiome communicates with our brain. Nevertheless, microorganisms can also produce substances that can act on neurotransmitters in the brain, such as dopamine or serotonin. Thus, the microbiome in our gut has an impact on how we feel, what we think, and what we do.

Study Yiyun C. et al. (2022) Commensal microbiota from patients with inflammatory bowel disease produce genotoxic metabolites. DOI: 10.1126/science.abm3233



Sittipo P. et al. (2022) The function of gut microbiota in immune-related neurological disorders: a review. https://doi.org/10.1186/s12974-022-02510-1

# Ruminococcus

Bacteria of the genus *Ruminococcus* in the intestine correlate with mental health. Only a few of these bacteria are found in people with a depressive illnesses.

Study Haiyin J. et al. (2015) Altered fecal microbiota composition in patients with major depressive disorder. https://doi.org/10.1016/j.bbi.2015.03.016





Which microorganisms constitute our microbiome depends strongly on our diet and lifestyle. Chronic stress and unhealthy foods disrupt the balance in our gut microbiome. Harmful bacteria can take over and affect not only our physical health, but also our mental health.

# Different microbiomes for different moods

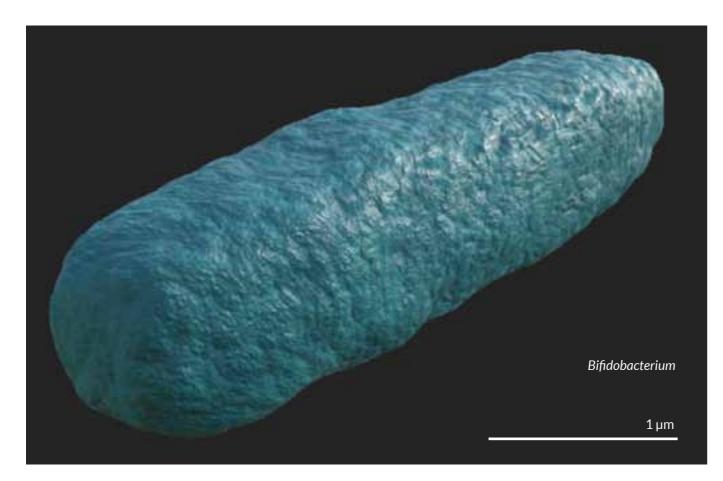
People with depression often have lower numbers of certain bacteria in their gut. These bacteria produce short-chained fatty acids and other substances. If those bacteria are not present, the person lacks these substances. It is precisely these bacteria that could be used as a kind of medicine against depression. However, this is still a vision for the future. Research on the gut-brain axis began only a few years ago, and too many questions remain unanswered. More intensive research is needed to prove temporal and causal relationships and develop treatment strategies.



Thomann A.K. et al. (2022) Depression and fatigue in active IBD from a microbiome perspective—a Bayesian approach to faecal metagenomics. https://doi.org/10.1186/s12916-022-02550-7

# **Bifidobacteria** linger in the intestinal wall

Bifidobacteria act like a blockade against hostile sieges. They literally lie around on the intestinal wall. In this way, they occupy the space and prevent harmful microorganisms from settling there. In addition, they produce an acid that inhibits the reproduction of harmful bacteria. If enough bifidobacteria are hanging around, the intestinal wall produces more immune cells, which are anti-inflammatory.



# The party is on in the gut

Estimates put the number of bacteria in the human gut at around 10 trillion. The human body consists of around 10 trillion cells. So, we are made up of the same number of bacteria as human cells. 95% of gut bacteria live in the large intestine. There are not only bacteria in the gut. Fungi, viruses, and so-called archaea also live there.

#### CANDIDA

Not all microorganisms that live in the human microbiome are harmless. *Candida* is a yeast fungus that occurs naturally in the intestine. If this fungus spreads excessively, it can lead to infections. Lactic acid bacteria, on the other hand, form a natural protective shield.

#### Microbiome as a fingerprint

The composition of the microorganisms in the gut of each person is very specific and different from that of any other person. Each microbiome is unique, like a fingerprint. The human gut microbiome is often considered an independent organ. Like other organs, it has specific tasks, for example, immune and metabolic functions. Each microorganism in the microbiome has its own DNA, which is why the microbiome is often referred to as the "second human genome".

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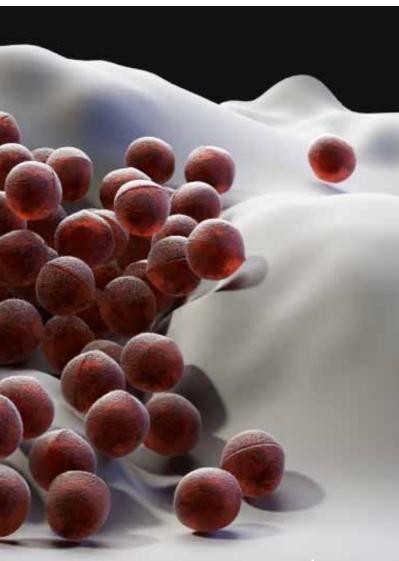
ditio

Staphylococcus

#### Fecal transplantation as a form of an "organ transplantation"

If the gut microbiome can be considered an independent organ, surely it can also be transplanted like other organs? In fact, as early as the 4th century AD in China, a "golden soup" consisting mainly of faecal matter was prescribed for food poisoning or severe diarrhoea. It seemed to restore the balance in the body – what exactly was happening was unknown to the doctors at the time. In modern medicine, faecal transplants are used in severe cases of illness. They can bring good results but must be performed with the utmost care to avoid transplanting undesirable microorganisms.





# A look into the **future**

Microorganisms are the oldest living organisms on our planet. For an incredibly long time, over billions of years, they have repeatedly adapted to new living conditions and survived. Mankind is very young compared to them and has "settled in" to this ancient world. Microorganisms were underestimated for a long time. Only now science is gaining a better understanding of the importance of microbiomes to the health of all living things. Without microbiomes, neither a blade of grass nor a cow survives. Microbiomes are also vital for humans in many ways: many inhabitants of these communities are essential, helpful and useful. Bacteria even influence the climate, but they are also affected by climate change. The fatal consequences that careless handling of biodiversity can have for humans cannot be overestimated.

# FROM THE MICROSCOPE TO DNA RESEARCH

The world of microorganisms is a cosmos of its own, with immeasurable value for all living things and their environment. However, most microorganisms have not even been discovered and researched by now. This is because they were not seen in the truest sense of the word for a long time. It was only through microscopes that science was able to take a look at them.

#### Preservation of microbiomes - a good investment for the future

Preserving the diversity of microbiomes will be crucial for establishing a sustainable bioeconomy. Innovative microbiome applications can be effective answers to the challenges of the 3rd millennium: climate change mitigation, biodiversity conservation, healthy food production and availability, bio-energy, recycling and waste management.



Many microorganisms do not survive long enough in the laboratory to be studied. A lot of groundbreaking discoveries have, therefore, only become possible through genetic research.



## Microorganisms orchestrate life on Earth

Microbiome research has increased dramatically in recent years. There is a wealth of new knowledge about microbial communities. Of course, research on the human microbiome has been particularly intense. More recently, however, it has become clear that microbiomes can help address other challenges as well. These include soil fertility, plant and animal nutrition and health, food safety and security, waste management, climate change adaptation, carbon sequestration and greenhouse gas emission reduction.

The "MicrobiomeSupport" project has brought together experts from different fields of microbiome research. These experts identified things still lacking in microbiome research: research infrastructures, data access and sharing, knowledge transfer and innovation, a suitable regulatory framework for novel products and applications and raising awareness among stakeholders and society. The formation of a standing international expert panel working on common priorities and sharing developed knowledge would help to fill these gaps efficiently.

Study Strategic Research and Innovation Agenda for future microbiome activities and applications. www.microbiomesupport.eu

# THE BIG QUESTION

Science knows quite a bit about individual microorganisms but far too little about the interactions within the microbiome, meaning between individual bacteria, fungi, and other microorganisms. How the host affects the microbiome and how microbiomes affect their host or the environment is also only partially known.

To render this, we need to be able to describe and characterize microbiomes even better. Which microorganisms live together? What work do certain microorganisms do? What substances do they produce? How do they change over time or under the influence of various external factors? In short: Who does what, where and when, and what effects does this have?

#### MAKING PREDICTIONS WITH THE MICROBIAL "CLINICAL THERMOMETER"

Only once we know exactly how microbiomes function we can make predictions. Which bacteria are healthy in food? Which microorganisms pose a risk? How do microbiomes affect food shelf life? Is my gut microbiome healthy or are some microorganisms over- or under-represented? And at what point are these changes pathological?

Knowing how certain microbiomes are composed can also help control whether they are as they should be. Biological characteristics or substances could be determined that indicate the disease or health of a microbiome. In the future, analytical systems could be developed that measure the biological characteristics of the microbiome, almost like a clinical thermometer measures temperature.





## WHAT IS not yet KNOWN

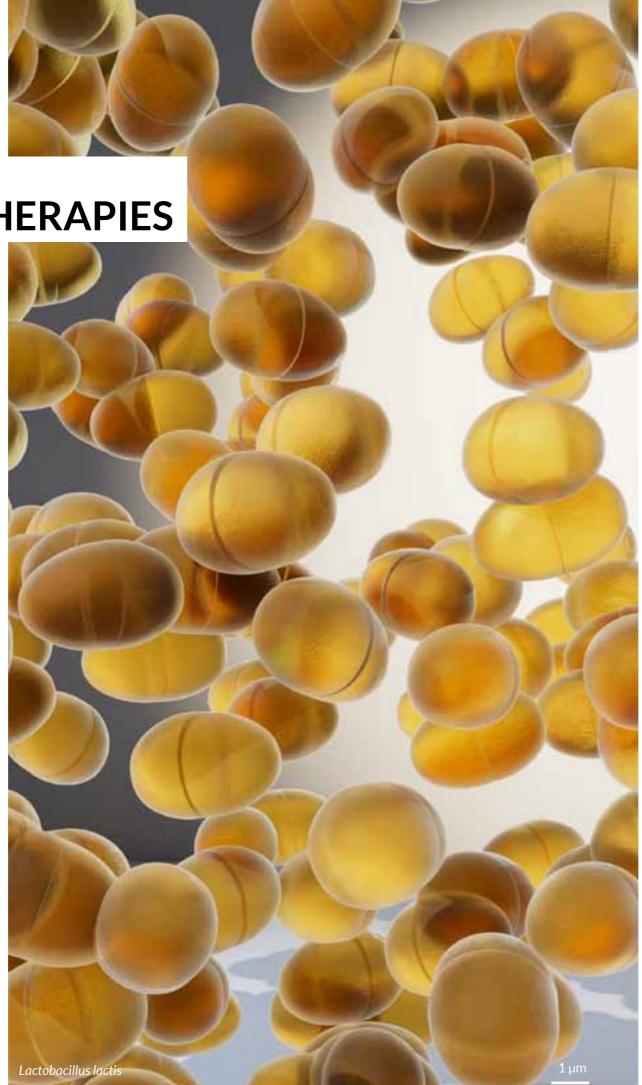
# **IN SEARCH OF NEW DRUGS AND THERAPIES**

Bacteria that cause diseases can be killed by antibiotics. Especially in animal husbandry, antibiotics are often used for prevention. However, if too many antibiotics are used, bacteria get used to them and become resistant. Antibiotic resistance is already a huge problem. Sick people and animals can no longer be treated because the drugs do not work anymore. Microbiomes may harbour new effective antibiotics or other helpful substances that could be alternatives to antibiotics. Therefore, microbiomes need to be researched to find new drugs.

Targeted attempts to change the gut microbiome also need to be based on solid scientific data. Probiotics can help restore the gut microbiome after taking antibiotics. Taking probiotics is easy and without any particular dangers. The situation is different when it comes to transplanting microbiomes: Here, special standards must be observed to ensure that health-promoting bacteria are not transplanted with disease-causing bacteria, thus endangering the health of the patient.

# THE DETECTIVE IN THE MICROBIOM

Every microbiome is like a fingerprint. If microbiome composition of a specific food product is stored in a reference database, it could be checked whether the existing microbiome is actually what it is supposed to be. Thereby, fraud could be detected. In the distant future, this would make it possible to trace the food, check certifications and detect food fraud.



balance.

More research is also needed for the development of special foods and diets as part of medical therapy. The therapeutic effect should be improved and undesirable side effects on the human microbiome must be avoided. This would be especially important for people at risk for chronic diseases and patients undergoing treatment.

The health benefits of fermented foods have been described for centuries, although many are unproven. The potential benefits are based on the presence of vital microorganisms and the fermentation-induced changes in the foods' ingredients. Foods based on microbial fermentation may positively affect the composition of the gut microbiome and support metabolism. Further research would help develop sustainable diets based on microbially fermented foods to improve human health.

Every year, 600 million people get sick from food and 420,000 die from foodborne diseases. Often, pathogens do not start multiplying until they make their way from the producer to the table at home. An early warning system that indicates dangerous changes in the microbiome already at the producer could massively reduce the risk of foodborne infections.



### **HEALTHIER FOOD FOR HEALTHIER PEOPLE**

More research is needed to gain new and deeper insights into what constitutes a healthy human microbiome and its characteristics. Disruption of the human microbiome community is associated with a variety of diseases. Impairment of the microbiome is considered one of the major factors in the dramatic increase in chronic diseases. Diet is an important instrument for shaping the microbiome. A healthy diet can thus help restore the disturbed

## **FERMENTATION AND HEALTH**

# SICK DUE TO FOOD

# **Diverse microbiomes** in AGRICULTURE and FOOD SYSTEMS

Microbiomes exist in and on humans, animals, and plants both on land and in water. Microbiomes influence soil health, plant productivity, human and animal health. Thus, they also play an important role in agriculture and food production.

The population will grow to nearly 10 billion by 2050. These people need to be fed, which requires a fair and healthy food system. Science needs to better understand microbiomes, especially in the food system. Then microbiomes can be used reasonably.

Food production is one of the systems with the largest environmental footprint. Food waste needs to be reduced. Waste and wastewater from food production could be metabolized by microorganisms and therefore be recycled as a source of energy, as fertilizer, but also as feed for animals or even as food for humans.

S 2

> This would require a better understanding of environmental microbiomes, for example soil, marine and fish microbiomes. Within those microbiomes. microorganisms useful for transformation can be discovered.

# **TRANSFORME** WASTE Aspergillı

## THE MICROBIOME IN HEALTHY AGRICULTURE

Soil is one of the most complicated ecosystems. It is an independent habitat and home to an incredible variety of living organisms that regulate and control soil fertility, nutrient cycles, and carbon sequestration. The ecological footprint of agriculture is enormous, and many soils are severely damaged by agricultural processing.

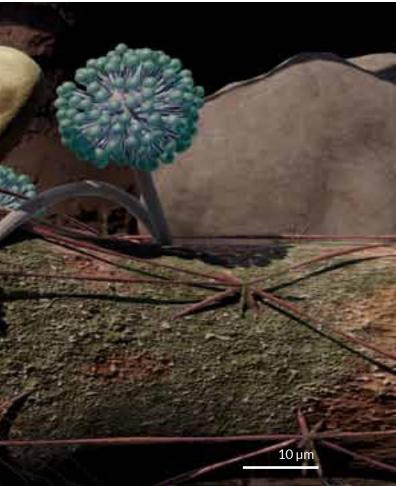
If we knew more about how microbiomes affect soil health, and therefore plant health, we could make better non-toxic pesticides and bio-fertilizers with microorganisms. Soil would be more resilient, and farmers would be less dependent on toxic pesticides and chemical fertilizers. Microbiomes could thus contribute to the transition to climate- and environment-friendly agriculture that provides consumers with safe, healthy and sustainable food.

Unravelling the complexity of the soil microbiome and better understanding the interactions within such ecosystems is essential as it can provide solutions for restoring degraded soils. However, soil microbiomes can also support carbon storage, which could contribute massively to containing the climate crisis.

## **MICROORGANISMS AND** AND ANIMAL HEALTH

How young animals are kept greatly affects the composition and functionality of their microbiomes, which impact the performance and health of adult animals as well. Healthy animals provide healthy food. Animals could also benefit from the intake of probiotics through feeds containing healthy microorganisms. How exactly? That needs to be researched.





## **CHANGING CLIMATE CHANGING MICROBIOME**

What is the impact of climate change on microbiomes in food systems? It would be important to know how microbiomes can adapt and whether they can provide the same services to our food supply under new conditions.

## THE WHOLE IS MORE THAN THE SUM OF ITS PARTS

Methods need to be established to systematically assess the impact of microbiomes on human, animal, or plant health and food safety. The evaluation of each individual bacterial strain does not reflect the properties of the entire bacterial community. For example, ecological barrier effects against chemicals, additives, or pathogens are often due to their combination rather than individual bacterial strains.

Just as microbiomes are composed of a wide variety of organisms, participants in microbiome research should be composed of a wide variety of contributors. Multidisciplinary projects involving industry, agriculture, various scientific and socioeconomic disciplines, and regulatory agencies can provide a more comprehensive picture.

## THE MICROBIOME SHOULD BE A PARLIAMENT MEMBER

There is a new player when it comes to issues such as food and chemical safety, plant and animal production, and the health of the planet and its inhabitants: the microbiome. Legislation lags behind the science. For example, there are still no explicit legal requirements to consider microbiome-related effects when examining risks and benefits within the limits of food law. As new knowledge emerges about the structure and functioning of the microbiome, it needs to be considered when evaluating legislation.

Microbiome science should advance in parallel with regulation and legislation. This would help provide the evidence needed to improve risk assessments. This, in turn, could facilitate the approval of microbiome-based innovations designed to promote human, animal, and planetary health, enhance food sustainability, productivity, safety, and nutritional quality. Open-source databases that collect information on microbiomes should be created as well. These can improve the reuse of data and mathematical models, as well as access to or sharing of information. However, these systems must ensure good data protection, sufficient storage capacity, and provide fast, user-friendly access. The databases should be free and easily accessible.

# NFORMATION FOR ALL



## COMPARING APPLES AND PEARS

Microbiome science has developed very rapidly in the last decade. Many different scientific fields are researching microbiomes. Quite often these scientific disciplines use different methods. They sort of speak different scientific languages. This makes it very difficult to compare or link findings. However, this is essential for an overall view of the performance of the microbiome.

Therefore, a uniform system and rules should be created as soon as possible, ensuring that all scientists in microbiome research follow the same or at least similar procedures: from sample collection, storage and processing to analysis and interpretation.

# **STORAGE**

Research on various microbiomes is very costly. One of the biggest technological bottlenecks at the moment is the preservation of microbiomes. How can complex microbiomes be stored so that their composition remains the same and the microorganisms continue to function? And how could we check if they are still functioning?

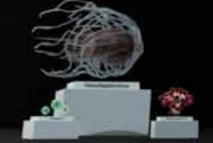
# **POOLING KNOWLEDGE**

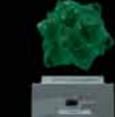
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Through microbiome research, we realize how close and comprehensive the interdependence of humans, animals, plants and microorganisms are.

Accordingly, microbiome research affects a wide variety of fields: from medicine and food systems to business and technology. It is essential that all fields concerned work closely together to advance further into the world of microbiomes.

> It is becoming increasingly evident that microorganisms rule our world. How exactly they manage to do so is still a great mystery in many cases.













#### MicrobiomeSupport

The AIT Austrian Institute of Technology led the MicrobiomeSupport project. The project was funded by the European Union's Horizon 2020 research and innovation program (grant agreement: 818116). The goal of the project was to pave the way for sustainable and circular microbiome-based food systems and the bio-economy. Twenty-nine academic and government partners from 13 European countries and 9 international partners collaborated closely to set quality standards for microbiome research and develop recommendations for a strategic research and innovation agenda in Europe and worldwide.

www.microbiomesupport.eu



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 818116.

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https://www.microbiomesupport.eu/resources/virtual-reality-movie

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\*All images are 3D illustrations.