Press Release, February 14, 2020

dr. christiane menzfeld

phone: +49 89 8578-2824
menzfeld@biochem.mpg.de
www.biochem.mpg.de/news
@MPI_Biochem

Genetically reproductive material from the laboratory

Max Planck researchers have for the first time developed a genome the size of a minimal cell that can copy itself.

The field of synthetic biology does not only observe and describe processes of life but also mimics them. A key characteristic of life is the ability to ability for replication, which means the maintenance of a chemical system. Scientists at the Max Planck Institute of Biochemistry in Martinsried generated a system, which is able to regenerate parts of its own DNA and protein building blocks. The results have now been published in *Nature Communications.*

In the field of synthetic biology, researchers investigate so-called “bottom-up” processes, which means the generation of life mimicking systems from inanimate building blocks. One of the most fundamental characteristics of all living organism is the ability to conserve and reproduce itself as distinct entities. However, the artificial “bottom-up” approach to create a system, which is able to replicate itself, is a great experimental challenge. For the first time, scientists have succeeded in overcoming this hurdle and synthesizing such a system.

A biological machine produces its own building blocks

Hannes Mutschler, head of the research group "Biomimetic Systems" at the MPI for Biochemistry, and his team are dedicated to imitate the replication of genomes and protein synthesis with a “bottom-up” approach. Both processes are fundamental for the self-preservation and reproduction of biological systems. The researchers now succeeded in producing an *in vitro* system, in which both processes could take place simultaneously. "Our system is able to regenerate a significant proportion of its molecular components itself," explains Mutschler. In order to start this process, the researchers needed a construction manual as well as various molecular "machines" and nutrients. Translated into biological terms, this means the construction manual is DNA, which contains the information to produce proteins. Proteins are often referred to as "molecular machines" because they often act as catalysts, which accelerate biochemical reactions in organisms.

The basic building blocks of DNA are the so-called nucleotides. Proteins are made of amino acids.

Modular structure of the construction manual

Specifically, the researchers have optimized an *in vitro* expression system that synthesizes proteins based on a DNA blueprint. Due to several improvements, the *in vitro* expression system is now able to synthesize proteins, known as DNA polymerases, very efficiently. These DNA polymerases then replicate the DNA using nucleotides. Kai Libicher, first author of the study, explains: "Unlike previous studies, our system is able to read and copy comparatively long DNA genomes." The scientists assembled the artificial genomes from up to 11 ring-shaped pieces of DNA. This modular structure enables them to insert or remove certain DNA segments easily. The largest modular genome reproduced by the researchers in the study consists of more than 116,000 base pairs, reaching the genome length of very simply cells.

Regeneration of proteins

Apart from encoding polymerases that are important for DNA replication, the artificial genome contains blueprints for further proteins, such as 30 translation factors originating from the bacterium *Escherischia coli*. Translation factors are important for the translation of the DNA blueprint into the respective proteins. Thus, they are essential for self-replicating systems, which imitate biochemical processes. In order to show that the new *in vitro* expression system is not only able to reproduce DNA, but is also able to produce its own translation factors, the researchers used mass spectrometry. With this analytic method, they determined the amount of proteins produced by the system. Surprisingly, some of the translation factors were even present in larger quantities after the reaction than added before. According to the researchers, this is an important step towards a continuously self-replicating system that mimics biological processes.

In the future, the scientists want to extend the artificial genome with additional DNA segments. In cooperation with colleagues from the research network MaxSynBio, they want produce an enveloped system that is able to remain viable by adding nutrients and disposing of waste products. Such a minimal cell could then be used, for example, in biotechnology as a tailor-made production machine for natural substances or as a platform for building even more complex life-like systems.

Original Publication:

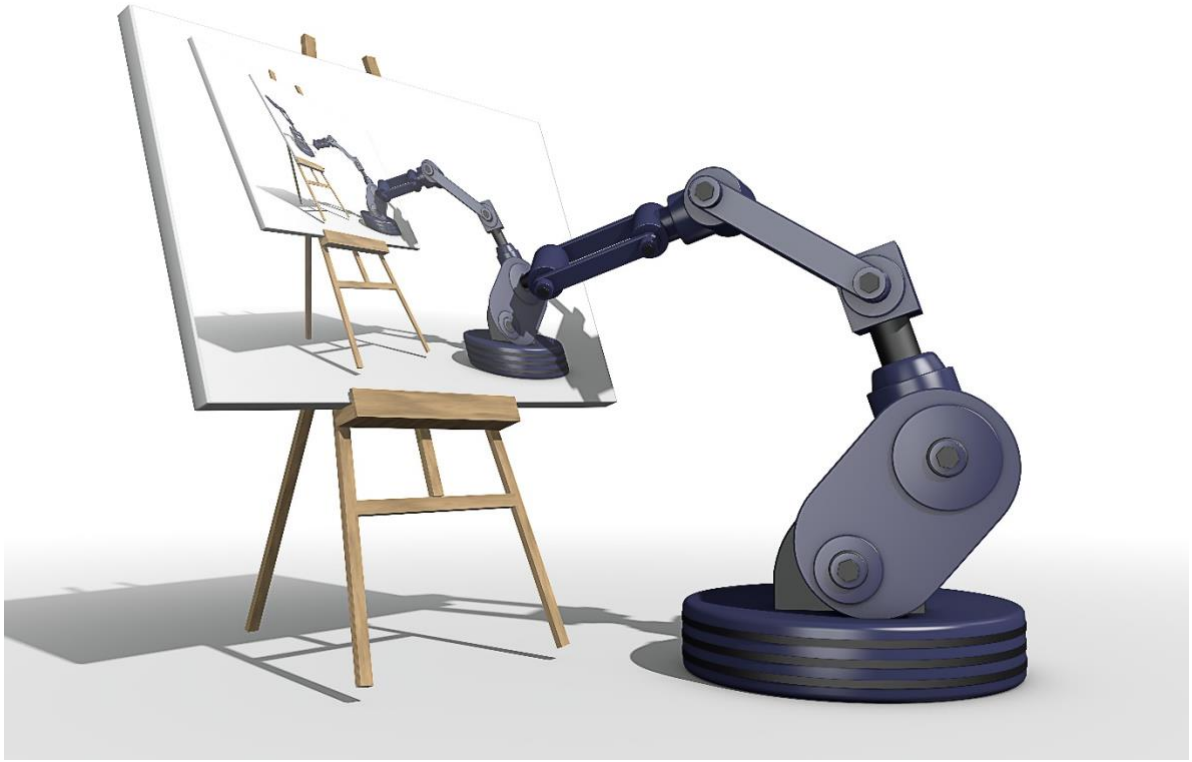
Kai Libicher, Renate Hornberger, Michael Heymann & Hannes Mutschler:
In vitro self-replication and multicistronic expression of large synthetic genomes
Nature Communications, February 2020
DOI: 10.1038/s41467-020-14694-2

About Hannes Mutschler

Hannes Mutschler conducted his doctoral research at the MPI for Medical Research in Heidelberg and received his PhD from the Heidelberg University. Supported by a FEBS Long-Term-Fellowship, he worked as a postdoctoral researcher at the MRC Laboratory of Molecular Biology (UK) before he joined the MPI of Biochemistry as an independent MaxSynBio Junior Research Group Leader for “Biomimetic Systems”.

About the Max Planck Institute of Biochemistry

The Max Planck Institute of Biochemistry (MPIB) belongs to the Max Planck Society, an independent, non-profit research organization dedicated to top level basic research. As one of the largest Institutes of the Max Planck Society, 850 employees from 45 nations work here in the field of life sciences. In currently eight departments and about 25 research groups, the scientists contribute to the newest findings in the areas of biochemistry, cell biology, structural biology, biophysics and molecular science. The MPIB in Munich-Martinsried is part of the local life-science-campus where two Max Planck Institutes, a Helmholtz Center, the Gene-Center, several bio-medical faculties of two Munich universities and several biotech-companies are located in close proximity. http://www.biochem.mpg.de



Caption:
Scientists built a biological machine *in vitro*, which is capable of replicating itself.
Illustration: ©emieldelange by adobestock

Contact:

Dr. Hannes Mutschler
Biomimetic Systems
Max-Planck-Institut für Biochemie
Am Klopferspitz 18
82152 Martinsried

E-Mail: mutschler@biochem.mpg.de
www.biochem.mpg.de/mutschler

Dr. Christiane Menzfeld
Öffentlichkeitsarbeit
Max-Planck-Institut für Biochemie
Am Klopferspitz 18
82152 Martinsried
Tel. +49 89 8578-2824
E-Mail: pr@biochem.mpg.de
www.biochem.mpg.de