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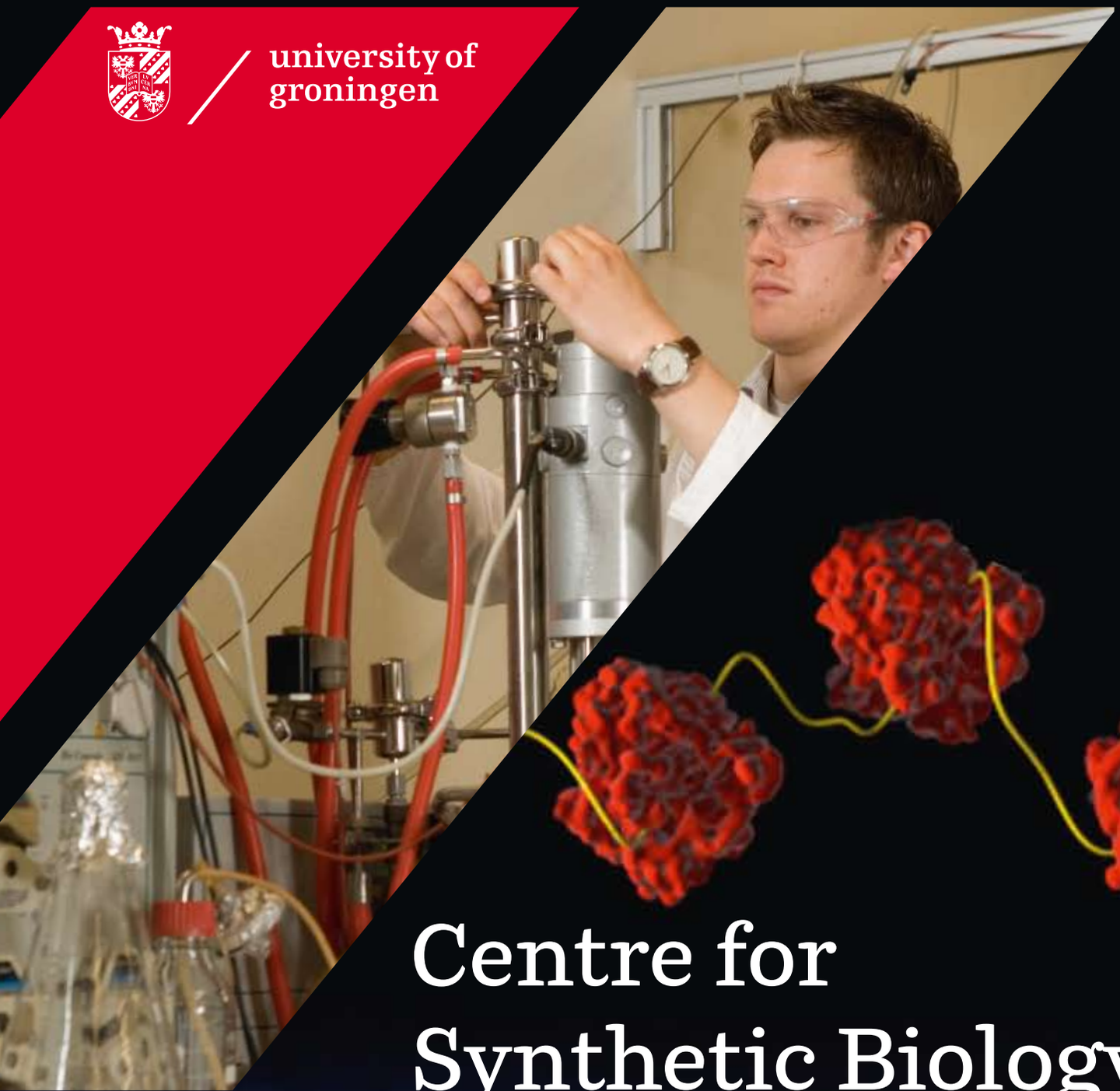
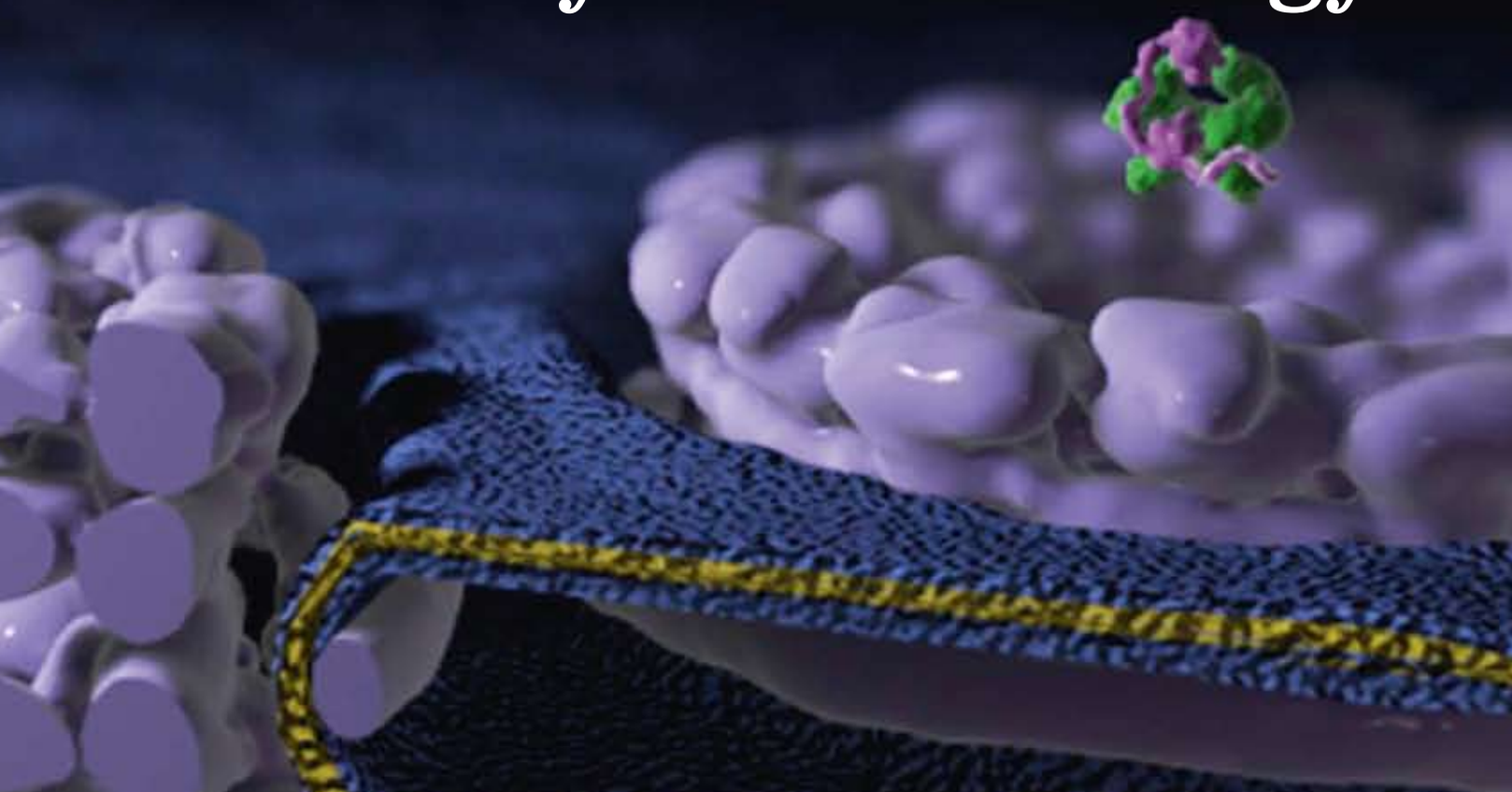


Centre for Synthetic Biology



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Preface

The Groningen Centre for Synthetic Biology (CSB) was established to foster research expertise in the emerging field of synthetic biology. It incorporates advanced knowledge in molecular biology, bioinformatics, molecular chemistry, physics and engineering. It uses this to create new biological functions and biohybrid materials. Engineering principles are applied to (re)design and build bio-inspired devices, ranging from diagnostic sensors to sophisticated drug delivery systems and cell-based chemical conversion factories.

The Centre was founded in 2008 and has its roots in collaborative research between groups within the Groningen Biomolecular Sciences and Biotechnology Institute, the Stratingh Institute for Chemistry and the Zernike Institute for Advanced Materials. Researchers from these three institutes form the core of the centre.

Professor Bert Poolman
Program Director

Contents

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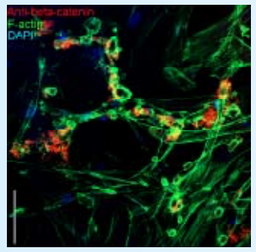
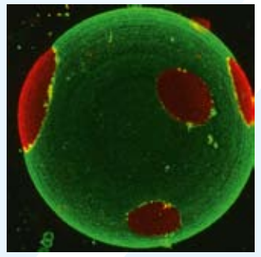
Introduction

Synthetic Biology is a rapidly emerging discipline at the interface between biological, chemical, physical and engineering sciences. It focuses on foundational research as well as on applications. The ultimate aim is to revolutionize the (ab initio) design of cellular systems or novel functionalities within these systems and of bio-inspired devices.

Examples are:

› The (re)design and engineering of microorganisms for synthesis of new drugs, chemicals and fuels;
› The design and construction of novel bio-inspired sensing, signal transduction and transport devices.





Molecular Biology, incl. Biochemistry
('molecular analysis')

Systems Biology
('integrated analysis')

Chemical Biology
('chemical tools')

Synthetic Biology
('systems design & fabrication')

Biological & molecular knowledge and understanding
Tools for analysis of complex biological systems

(Bio)physical Chemistry
(Bio)physics
('computational & physical tools')

(Bio)Catalysis
Chemical Engineering
Polymer Chemistry
Synthetic Organic Chemistry
('molecular design & synthesis')

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DNA synthesis in the laboratory.

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Mission

The Centre for Synthetic Biology (CSB) will integrate and expand its research programs to further develop expertise in the rapidly emerging field of synthetic biology. The Centre incorporates advanced knowledge in molecular biology, bioinformatics, molecular chemistry, physics and engineering. The aim is to evoke a paradigm shift in biological research, that is, a transition from discovery- to design-based research, and harness this change to create new functions and materials. Engineering principles are applied to (re)design and build bio-inspired devices, ranging from diagnostic sensors and sophisticated drug delivery systems to cell-based chemical conversion factories. The CSB will train the next generation of students to become 'biological engineers', communicate synthetic biology to the general public and establish an innovation network with industrial partners.

Separation and analysis of tiny amounts of molecules by nano-flow liquid chromatography and mass spectrometry.

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Research

The research within the Centre for Synthetic Biology includes the design and construction of ***cellular*** and ***biohybrid*** systems.

Cellular systems

Cell-based engineering involves the production of bioactive molecules such as antibiotics and bioactive peptides and proteins, using fungi and bacteria as cell factories. There are major efforts in biotransformation of synthetic compounds, and in engineering of biological membranes to improve the robustness of cells. Unique expertise is available and toolboxes have been developed for the in vivo production and quality control of proteins in bacteria.

Biohybrid systems

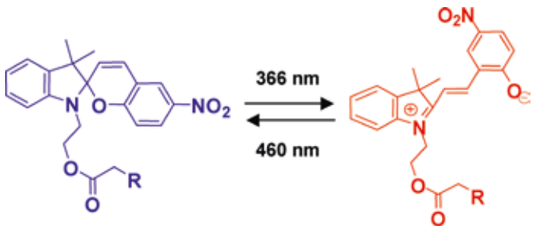
The design and synthesis of novel bio-inspired catalysts, sensing devices and vesicular systems has its roots in the Zernike Institute. There is major expertise in biomimetics and biocatalysis, which is crucial to develop future (auto-)catalytic kinetically-driven processes and key to sustain the synthesis of complex molecular systems. Interfacing between biomolecules and surfaces is another important topic. The physical analysis of bio-inspired systems includes state-of-the-art microscopic and spectroscopic methods, as well as expertise to characterize charge transport.

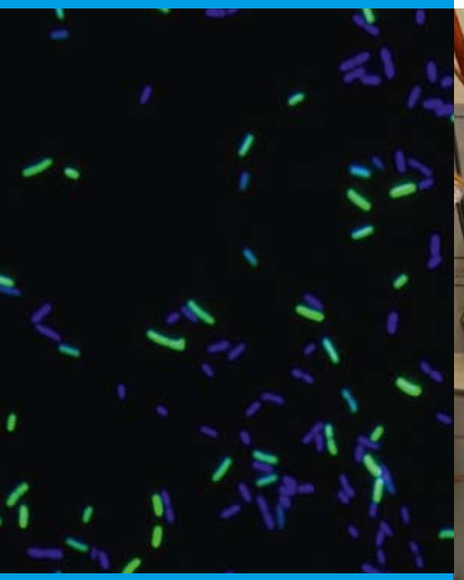
Synthetic switch, engineered in membrane-reconstituted channel protein, allows opening and closing of the pore for controlled release of cargo in response to light. The light-induced charge separation in the synthetic switch is shown on the right of the channel structure. In live cells, the channel protein gates in response to membrane tension and protects cells against hypoosmotic stress.

Transport factor divides protein synthesis between mother and daughter cells. A new biological mechanism was discovered, which ensures that proteins are synthesized exactly where they are needed in a cell. The mechanism takes effect when cells divide, a process that is asymmetrical in yeast.

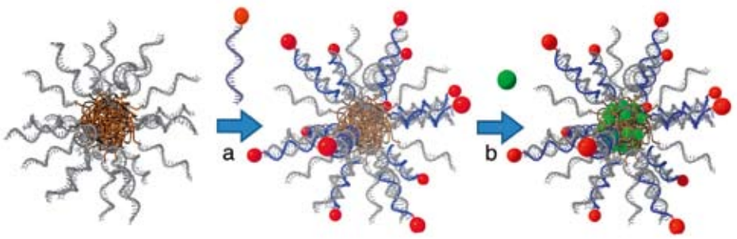
Research focus

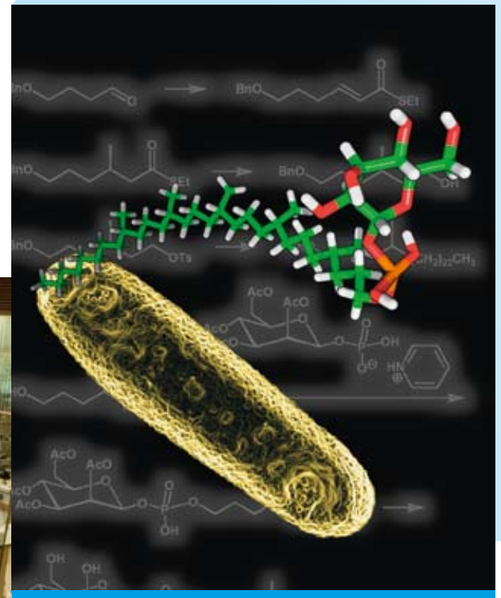
- Biosensors
- Bistability in cells and microbial communities
- Biotransformations based on hydrophobic compounds
- Biohybrid drug delivery systems
- DNA replication
- Engineering for protein production
- Engineering of channel proteins
- Mechanisms of molecule transport
- Membrane engineering in bacteria and yeast
- Molecular motors
- Synthesis of biohybrid materials
- Synthesis of novel antibiotics and bioactive peptides and proteins





Single-stranded amphiphilic DNA block copolymers self-assemble into spherical micelles. When equipped with targeting units (a) and after incorporation of hydrophobic anticancer drugs (b), the nanocontainers are efficiently taken up by cancerous cells which are then killed by the toxic payload.





The cell wall of *Mycobacterium tuberculosis* has a very complex structure which is responsible for both virulence and persistence of the associated disease. By chemical synthesis of native glycolipids, and analogues of them, the physical and immunological properties of the mycobacterial cell wall are mimicked.

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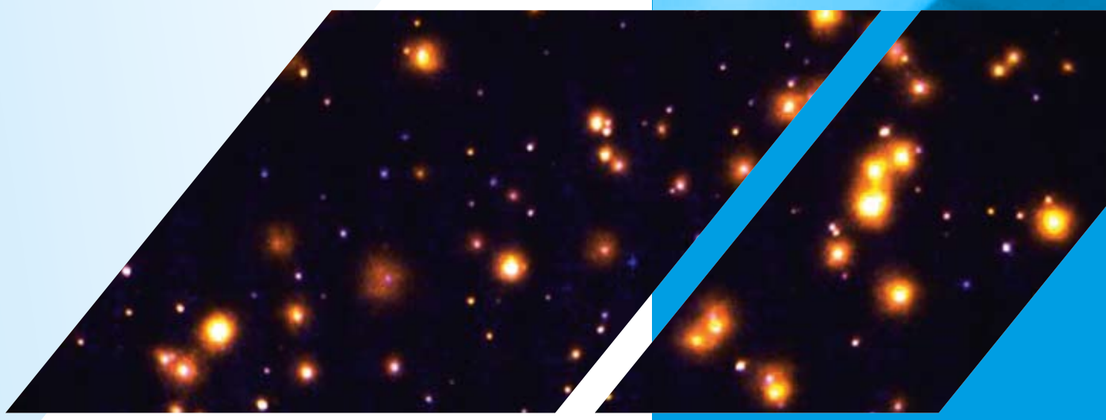
New research directions

Microbial Cell Engineering
Experimental and modelling efforts will be pursued with the long-term goal of attaining a system understanding of cell metabolism. Important knowledge will be obtained at the single-cell level in order to understand how metabolism is involved in cellular decision making. The resulting quantitative understanding and mathematical models ultimately provide a solid basis for forward-engineering of biological systems.

Molecular Biophysics
Single-molecule optical methods will be developed and applied to probe the dynamics and structure of supramolecular protein assemblies. The orchestration of the various enzymatic activities in complex molecular systems such as the DNA-replication fork and the mechanistic principles underlying membrane fusion will be studied at the single-molecule level. This research is crucial for the unraveling of intricate biomolecular processes and will contribute to the development of hybrid devices based on biomolecules or synthesized as mimics.

Synthesis of Complex Systems
The bottom–up synthesis approach requires major efforts to adapt and re-engineer biomacromolecules, using the tools of synthetic chemistry and biochemistry. It will also be crucial for the construction of complex systems with novel functions. Synthetic engineering of nucleic acids, proteins and cell membrane components will be pursued with the aim to create cellular mimics and to develop ex vivo nanostructured materials and devices with functions controllable at the molecular level.



Fluorescence microscopy image of individual influenza viral particles fusing with a synthetic, planar target membrane. Different colors correspond to the fluorophores that are embedded in the particles to track various fusion intermediates. The yellow diffuse clouds represent particles after fusing, the discrete pinpoints are virus particles docked to the surface that have not fused yet.

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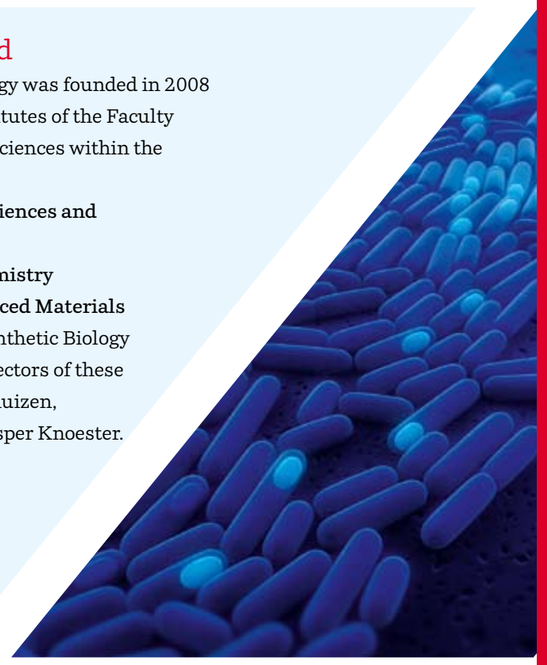
Organization and contact

Organization & Board

The Centre for Synthetic Biology was founded in 2008 by three leading research institutes of the Faculty of Mathematics and Natural Sciences within the University of Groningen:

- **Groningen Biomolecular Sciences and Biotechnology Institute**
- **Stratingh Institute for Chemistry**
- **Zernike Institute for Advanced Materials**

The board of the Centre for Synthetic Biology is formed by the Scientific Directors of these institutes: Prof. Lubbert Dijkhuizen, Prof. Ben Feringa and Prof. Jasper Knoester.



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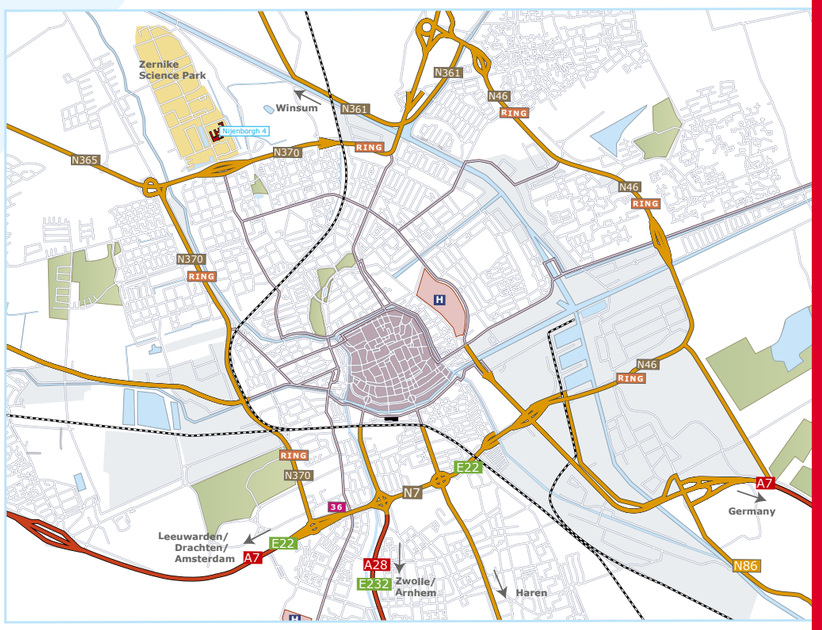
How to reach us

By car

The Zernike complex is situated very close to the northern ring road of Groningen as seen on the map to the right.
For detailed instructions on how to get there please refer to our website **www.rug.nl/centreforsyntheticbiology.**



By public transport

If you arrive by plane at Amsterdam Airport Schiphol, you can take a direct train from the airport to Groningen Central station, which takes about 2 hours and 30 minutes.
At Groningen Central station you can take a taxi: Ask the driver to take you to the Zernike complex, Nijenborgh 4. Buses No.11 and 15 also connect the Groningen Central Station to the Zernike complex.

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Colophon

This is a publication of the Centre for Synthetic Biology, University of Groningen, Faculty of Mathematics and Natural Sciences.

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