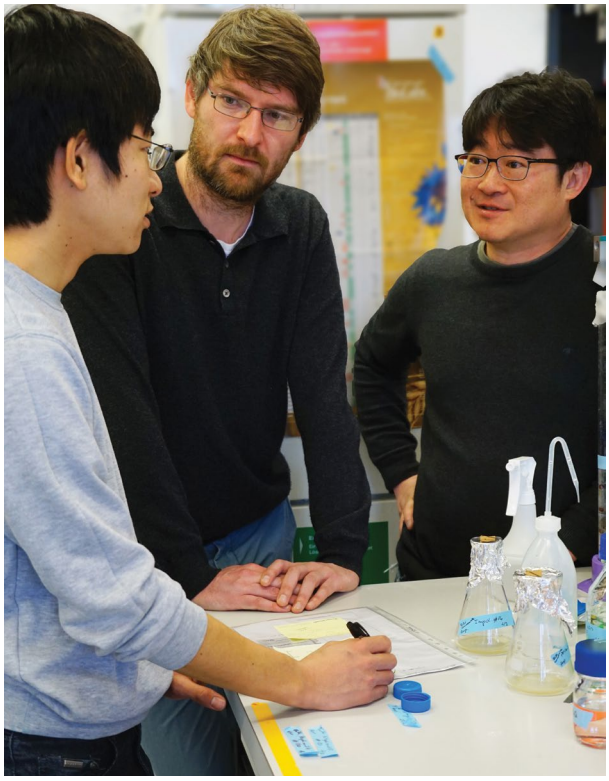
Use of Findings for Applications

SNI scientists focus on nanopores

Argovia Professor Roderick Lim and his team study natural and artificial nanopores. On one hand, they aim to understand in detail how nuclear pore complexes control the selective exchange of molecules between the nucleus and cytoplasm in living cells. On the other hand, the Lim team uses this fundamental knowledge as a source of inspiration to create "smart" bio-synthetic nanopores with potential technological applications.



Biological machines that sort molecules

The nuclei of higher organisms are separated from the surrounding cytoplasm by a biomembrane. This membrane has tiny nanoscale holes known as nuclear pores that facilitate the exchange of molecules between the nucleus and cytoplasm. For water and small metabolites, this exchange is driven by diffusion. However, large molecules cannot automatically bypass the nuclear pores, which are protected by a molecular filter consisting of barrier-forming proteins known as FG Nups (phenylalanine-glycine nucleoporins). In fact, only specific molecules can selectively transport through the FG Nup barrier. Nonetheless, an understanding of how the FG Nups work remains a "holy grail" in the field given that they have never been seen inside NPCs. Therefore, it remains a mystery whether they are arranged in a static manner or fluctuate dynamically in time.

Captured on film for the first time

Argovia Professor Roderick Lim has been investigating this nanoscopic transport process for some years. Now, using a high-speed atomic force microscope, his team has become the first to watch natural nuclear pore complexes at work in situ. Yusuke Sakiyama, a doctoral student in Roderick Lim's laboratory at the SNI PhD School, has recorded these observations as movies. Their findings have been submitted for publication and are anticipated to contribute to a better understanding of the transport processes through the nuclear pores.

Creating artificial nanopores that mimic biology

Ludovit Zweifel, another doctoral student (and ex-Nano student) in the Lim team creates artificial nanopores from glass capillaries that mimic nuclear pores. In collaboration with Ivan Shorubalko at the Swiss Federal Laboratories for Materials Science and Technology (EMPA, Dübendorf), Zweifel uses scanning transmission ion microscopy to determine the geometry of these glass nanopores. Applying this accurate analytical method, Roderick Lim and his colleagues could optimize the fabrication process of the nanocapillaries. They produced capillaries with several tip geometries and opening angles and analyzed the transport processes of single molecules depending on theses different parameters.

Sensing single molecules using electrical currents

The scientists use these glass capillaries as nanopores to detect single molecules. They place an electrical potential across two small salt-solution-containing reservoirs connected via a glass capillary. This establishes a steady stream of ions through the nanopore. If DNA or proteins are added to one of the reservoirs, these partially block the nanopore, which leads to a decrease of the ionic current. Based on the duration and amplitude of the current changes, researchers get important information about size and charge of the respective molecules. Importantly, this is anticipated to significantly improve single molecule biosensors and DNA sequencing.

Nanopores for molecular engineered systems

In living cells, different biochemical processes run in parallel. This is only possible because each cell is separated in different compartments by membranes. Various research programs aim at developing nanotechnological systems with membrane-bound machines based on nature as example. In this respect, the Lim team is contributing to the efforts of the National Center for Competence in Research "Molecular Systems Engineering" by designing nanoporous synthetic vesicles (proteoliposomes) that function as "artificial nuclei". Specifically, their goal is to import, compartmentalize and accumulate specific macromolecular modules against concentration gradients.