

## **“Made-to-measure bionanofactory”**

Nano-sized containers are useful for technologies in medicine and industrial processes. They can package drug molecules and deliver them to the target tissues in our body. In such clinical application, nanocontainer shells physically protect enclosed components from external enemies that could otherwise destroy them. This utility may lead to extension of drug lifetime and thus dramatic enhancement of its therapeutic effects. Nanocontainers can also direct drug contents to where they should act, for example anticancer drugs to tumors, resulting in an offset of undesired side effects. In industrial productions, nanocompartments can serve as a sort of flasks for chemical reactions. By cramming reaction components into distinct nanospaces, they can push overall production efficiency of multi-step processes, as well as reduce side products of waste disposal. Because of these prospective utilities, engineering of functional nanocompartments is currently a very hot research topic being extensively undertaken all over the world.

Nature has evolved tremendous compartmentalization systems that we want to exploit and imitate. A number of them are built by proteins, which themselves are biochemical substances constructed from a chain of 20 different building blocks called amino acids. These principal constituents can be arranged in many different ways, resulting in a wide variety of proteins with diverse shapes and functionalities. A representative protein compartment, called protein cage, is a virus shell which can package its genetic information and deliver this cargo to cells. While the infectious activity is usually not beneficial for human health, from other viewpoint, viral cages are experts in delivery of the contents to target cells. This function makes them attractive as drug carriers. Some other protein cages are specialized in production of nutrients the cells need. For example, there is a bacterial compartment that packages biological processing units to synthesize vitamin B2, boosting otherwise inefficient “manufacturing” of this compound. Analogously designed artificial nano-factories will be a novel way to obtain valuable compounds in industrial processes.

How do protein cages package their contents? This apparently simple question is not answered for many naturally existing protein cages. If we knew these biological systems more, they would become good templates for us to develop useful nanotechnologies. As such, this research will focus on the vitamin B2 producing compartment with aim to understand how the protein shells package the components and how this packaging impacts on the overall vitamin production efficiency. To achieve this goal, our team will use a cutting edge visualization technique which allows us to “look” at nano-scale objects. While it requires a special microscope, the Polish science society has set-up the most advanced instrument, one of a few in the world, here in Cracow. Our team does not want to miss this opportunity. We will be the first scientists who will look into the vitamin B2 synthesis compartment. Based on the microscopic images, this research will “tailor” the packaging system to replace the natural contents with other molecules. Our team will use a modern biotechnological method called “laboratory evolution” that mimics naturally-occurring evolutionary process, but in much shorter timescale. This new technology would allow us to put a variety of biological and chemical nanofactories in the compartment. In the future, such bionanofactories may not only feed bacteria with vitamin B2, but also become effective and eco-friendly means for producing drugs and other useful chemicals.