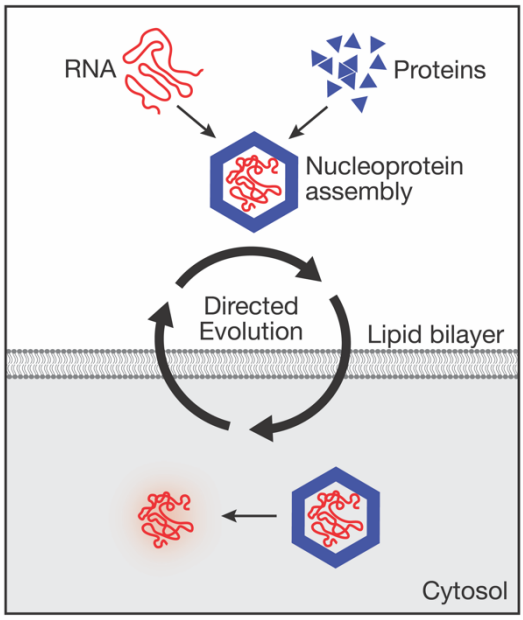
PhD positions available
@ Laboratory of Biomolecular Engineering and Nanomedicine

Gene therapy is a promising approach for preventing or treating disease by replacing or inactivating mutated genes, or by introducing new genes that support the body in its fight against illness. For gene therapy to be effective, nucleic acids need to be packaged and delivered safely and efficiently across the plasma membrane to their intracellular target site. The problem is that the plasma membrane has evolved over billions of years to be highly selectively permeable; charged biomacromolecules, such as ribonucleic acid (RNA), do not pass this barrier in their native state. Formulated as lipid nanoparticles, the mRNA COVID-19 vaccines have been immensely successful and administered to entire countries' populations. Yet it is estimated that only 1–2% of the injected mRNA dose reaches its target site and is translated into a protein antigen.

Viruses are experts at delivering genes into cells. The simplest examples of these infectious particles consist of just two components: a genome and many copies of a capsid protein that assemble into a protective shell around the genome. Although some engineered viruses have been approved for gene delivery, the two main roadblocks preventing them from becoming broadly useful are related to gene size and adverse immunogenic reactions. To address these limitations, the field of viral vector-mediated gene delivery is dominated by top-down approaches that characterize existing viruses, their mechanisms of entry, and aim to repurpose them for delivery.

The Laboratory of Biomolecular Engineering and Nanomedicine (LIBN) will approach the delivery problem from a different angle. **Our aim is to take a bottom-up approach and engineer minimal RNA nanocarriers inspired by how viral nucleic acid-protein assemblies transport their genomes into cells** and **harness this knowledge for delivery.** In the short term, we will use the previously evolved, non-viral nucleocapsid NC-4[1], which exhibits a striking $T = 4$ structure with 240 subunits and small pores, and repurpose it for RNA delivery. Methods will rely heavily on **protein design and engineering, directed evolution combined with high-throughput sequencing, cryo-electron microscopy, and mammalian cell culture assays**. PhD positions are available in three areas: (1) RNA packaging, (2) nanocarrier targeting, and (3) RNA release & translation.



Candidates need to be motivated to learn new skills, capable of leading their own project, and able to communicate in a diverse and interdisciplinary environment. They must be fluent in English with a degree in chemistry, biochemistry, or a related subject.

To apply for a position, please send a short letter of motivation, a CV, and the names of at least two references to Angela Steinauer (angela.steinauer@epfl.ch) with the email subject "LIBN PhD application" and submit the application to the EPFL doctoral program in Chemistry and Chemical Engineering (https://www.epfl.ch/education/phd/edch-chemistry-and-chemical-engineering). The positions are available immediately (as early as March 1, 2023).

(1) Tetter, S.; Terasaka, N.; Steinauer, A.; Bingham, R. J.; Clark, S.; Scott, A. J. P.; Patel, N.; Leibundgut, M.; Wroblewski, E.; Ban, N.; Stockley, P. G.; Twarock, R.; Hilvert, D. Evolution of a Virus-like Architecture and Packaging Mechanism in a Repurposed Bacterial Protein. *Science* **2021**, *372* (6547), 1220–1224.