Barth Lab PhD project

Expanding the universe of protein functions for synthetic biology and biomedicine

Our lab is developing and applying hybrid AI-based computational/experimental approaches for engineering classes of proteins with novel functions for cell engineering, synthetic biology and therapeutic applications. Through our bottom up design approach, we also strive to better understand the molecular and physical principles that underlie the emergence, evolution and robustness of the complex functions encoded by proteins and their associated networks.

We are part of RosettaCommons (https://rosettacommons.org/), a collaborative network of academic laboratories that develop the software platform Rosetta and AI-based approaches for macromolecular modeling and design. Ultimately, we aim to develop a versatile tool for designing novel potent, selective therapeutic molecules, synthetic proteins, receptor biosensors, networks and pathways for reprogramming cellular functions. We are also affiliated to the Ludwig Institute for Cancer Research in Lausanne.

Projects in the lab are often multidisciplinary and involve the development of novel methods (e.g. Feng, *Nat Chem Biol* 2016; *Nat Chem Biol* 2017; Paradis, *Nat Comm* 2022; Dumas, *biorxiv* 2023) and their application involving experimental studies (e.g. Young, *PNAS* 2018; Chen, *Nat Chem Biol* 2020*;* Yin, *Nature* 2020; Keri et al., *biorxiv* 2023; Jefferson, *Nat Comm* 2023). Projects involving external collaborations with other research groups around the world or internal collaborations between computational biologists, physicists and experimentalists in the lab are frequent. We also actively translate our findings to the clinic in collaboration with physicians (e.g. Dr. Arber, Coukos from the Ludwig Institute for Cancer Research). Specific research topics include: 1. The design of protein biosensors, mechanosensors and signaling receptors for reprogramming cell (e.g. CAR T cell) functions and enhance cell-based therapies; 2. The design of highly selective and potent protein and peptide-based therapeutics towards challenging targets such as GPCRs or ion channels; 3. The study, prediction and design of protein dynamics and allostery using AI and classic computational approaches; 4. The development of novel AI-based algorithms for modeling & design of protein structures, interactions and motions.

Dry lab candidates should have strong programming skills in python/C/C++ and expertise in the development of deep learning methods. Knowledge in protein biophysics, chemistry, structural biology, bioinformatics, computational biomolecular modeling including molecular dynamics simulations is a plus. Candidates more oriented towards the wet lab should have strong skills in molecular and cell biology including experience in protein biochemistry, biophysics, mammalian cell culture, microscopy, and structural biology. Hybrid computational / experimental projects are also possible.