Abstract:
Light activated channels and pumps, are well established, powerful tools for revealing the function of neuronal circuits in the new field of optogenetics. Proteins such as channelrhodopsin and halorhodopsin had a groundbreaking impact on neuroscience research because they allow for precise control of specific neuronal populations even in freely moving animals. As a biophysicist I understand that the application range of these tools is critically connected to their inherent biophysical properties. In my talk I will describe how molecular engineering created proteins with novel features which allowed us to broaden the application range of optogenetics. For instance, the speed of channelrhodopsin activation and deactivation restricts the maximum frequency for action potential generation in neurons. Accelerating channel kinetics by protein engineering resulted in the variant ChETA which enabled light induced spike generation with up to 200 Hz. In another example, I will describe the development of the chloride conducting channelrhodopsin iC++ by converting the selectivity of its ion conducting pore which ultimately allows for efficient, light-gated inhibition of neurons. The foundation for these protein designs is a fundamental understanding of their molecular mechanisms. The same principles can be applied to create a variety of new tools which will help to further elucidate the functional architecture of the brain.