The machinery that enables nuclear communication

Understanding the exchange of information and molecules between nucleus and cytoplasm is one of the fundamental problems in cell biology. The molecular exchange is primarily mediated by nuclear pore complexes (NPCs), vast protein assemblies that perforate the nuclear envelope (NE). In a very simplistic view, the NPC can be viewed as a molecular sieve with a certain size limit, above which RNA and protein molecules need specific receptors in order to be transported. However, this view is based on the very limited knowledge we have about the molecular architecture of the NPC which prevented more detailed questions for many years. Over the past decade, the field has invested a significant amount of effort into understanding the NPC assembly at better and better resolution.

In our own work, we have initially focused on elucidating crystal structures of NPC components, in essence to provide building blocks for reconstructions based on electron-microscopic methods. At this point, a large portion of the architectural elements of the NPC is understood, and interesting evolutionary relationships with other modular assemblies could be established. The current task is to reconstruct meaningful assembly models for the NPC, helped by a hybrid approach that includes structural, biochemical, and genetic data.

Apart from the NPC work, we have embarked on deciphering other nucleo-cytoplasmic communication elements. LINC complexes connect nucleo- and cytoskeleton for mechanotransduction, embedded in a growing and complex network of proteins. These molecular players are involved in a staggering number of diverse human diseases, yet we are just about to begin to appreciate the underlying mechanistic details.