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Monomeric proteins are the preferential substrates of the peroxisomal protein import machinery

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Peroxisomal matrix proteins are synthetized on cytosolic ribosomes and targeted to the peroxisomal membrane by the shuttling receptor PEX5. At the peroxisomal membrane, the PEX5-cargo complex gets inserted into the docking/translocation machinery with the concomitant release of the cargo protein into the peroxisomal matrix. It is widely accepted that peroxisomes have, unlike other organelles, the remarkable capacity to import already oligomerized proteins. However, it remains unknown whether or not these are the most frequent and preferred clients of the protein import machinery. In this work, we provide data suggesting that 1) PEX5 binds newly synthesized acyl-CoA oxidase 1 (ACOX1) and urate oxidase (UOX), inhibiting their oligomerization; 2) ACOX1 and UOX are much better imported in their oligomeric forms than after oligomerization; and 3) an ACOX1 lacking the peroxisomal targeting information can be piggybacked to peroxisomes with a PTS1 containing ACOX1 *in vivo*, but this process is very inefficient. These data support a model in which many of the protein translocation events occurring at the peroxisomal DTM involve monomeric cargoes.

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Mechanistic basis for site-specific functions of focal adhesion kinase

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Focal adhesion kinase (FAK) controls adhesion-dependent cell motility, survival, and proliferation, and plays a major role in development and cancer. Interestingly, FAK has different functions in different cellular compartments. For example at focal adhesions, FAK regulates integrin signalling in a kinase-dependent manner, whereas in the nucleus it exerts kinase-independent anti-apoptotic effects. We have combined SAXS with data from x-ray crystallography, NMR, bioinformatics, biochemical and functional analyses, to provide first structural insights into full-length FAK. Through specifically affecting the structural dynamics of FAK, we show that low-probability conformational transitions are of biological importance. Collectively, our data show how the dynamics and allosteric interplay between ligands and FAK's several domains controls site-specific activity of FAK. Our results reveal how FAK detects the coincidence of multiple signals to generate an environment-specific outcome.

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MD simulation of dynamics and transport in 5-HT3 receptor

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The 5-HT3 receptor is a member of cation selective ligand-gated ion channels. It plays an important role in functioning of central and peripheral nervous systems. There are currently no high resolution structures of the 5-HT3 receptor in open state, but crystal structure of 5HT-3 in complex with stabilizing nanobodies, as well as crystal structures of closely related proteins are available.

In this work molecular dynamics simulations of transmembrane domain of mouse serotonin 5HT-3 receptor was used to study dynamics and ion permeation. Transmembrane part of the receptor (X-ray structure PDB 4PIR) was used to set up the calculations. The structure was prepared in dimyristoyl-phosphatidylcholine lipid bilayer with TIP4P water model. GROMACS software was used for MD simulations. Position restraints were used on extracellular amino-acid residues of the ion channel. RMSD data after 15 ns of MD calculations indicates stability of the system. Minimum pore diameter remained at around 3,5 Å. Umbrella sampling method was used to estimate the potential of mean force for Na+ ions along the protein pore. All simulations were performed using "Arian Kuzmin" supercomputer center of NEFU, the work was supported by the Ministry of Education and Science of Russian Federation.

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Molecular and computational analysis of temperature compensation of the *Neurospora* circadian clock

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Circadian clocks are molecular oscillators that drive rhythms in gene expression, physiology and behaviour that ultimately allow organisms to anticipate and exploit predictable daily changes in their environment. A hallmark of circadian clocks is their ability to maintain a constant period in a range of temperatures. In the filamentous fungus *Neurospora crassa*, the circadian clock imparts rhythmicity on asexual spore development (conidiation) and both the circadian oscillator and its output are temperature compensated between 18°C and 32°C. Temperature compensation of circadian systems is thought to be encoded within the core circadian oscillator itself, but the underlying molecular mechanisms are not well understood. We have highlighted previously that in poikilothermic organisms such as *Neurospora,* temperature compensation must also occur downstream of the oscillator if a stable phase relationship with the environment is to be achieved, and identified the *Neurospora* blue-light photoreceptor VIVID (VVD) as important for this process. To gain further insight into how VVD exerts control on temperature compensation of the phase of circadian outputs we have performed next-generation sequencing of RNA from both wild type and *vvd* knockout cultures grown at different temperatures. This has allowed us to examine the effect VVD has on gene expression, relating to conidiation genes as well as the wider transcriptome. Using a dynamic model of the circadian clock, we present data that explore how temperature compensation functions within the