

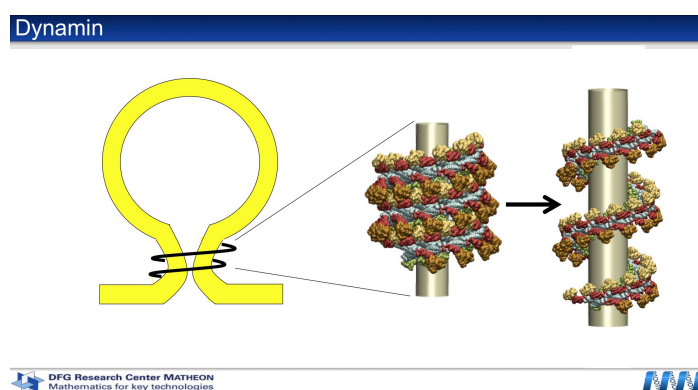
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## Pressemitteilung

### The pathway into the cell

#### MATHEON mathematicians are helping to unravel molecular processes

“Imagine an inflated balloon attached to a pump, but much, much smaller. By pinching off the neck of the balloon with a noose, it is detached from the pump and is able to move about freely.” The description is an approximation of one of the molecular processes looked at by mathematician Dr. Frank Noe as part of MATHEON’s ‘A19, Modelling and Optimisation of Functional Molecules’ project. Specifically, the molecular structure and mechanism of Dynamin.



Dynamin is a protein and the ‘noose’ which detaches the balloon from the pump. The vesicle (the scientific name for the balloon) has to be detached to allow it to perform its role as a vesicle for transporting messenger substances and nutrients into the cell.

Substances which need to be transported into the cell first accumulate in a vesicle formed by invagination from the surface of the cell. The dynamin molecule then attaches to the neck of the vesicle and forms a spiral around it. It then severs the neck of the vesicle. The vesicle is now free to transport nutrients into the cell.

Whilst scientists have long known about the process, the molecular details of how dynamin works were until now unknown. A group of researchers at the Max Delbrück Center for Molecular Medicine (MDC) in Berlin has now managed to obtain snapshots of the detailed molecular structure and, with the help of mathematical research carried out by Frank Noe and his team at MATHEON, been able to breathe life into these static structures.

“Without mathematical methods, it would not have been possible to simulate the processes which occur when the neck of the vesicle is severed,” explains the mathematician. Simulating this molecular process is extremely difficult. “A simulation encompasses 250,000 particles and each iteration of the calculation takes around 1 second, even on a mainframe. To directly simulate this process, we would have to perform millions of iterations. That would take decades – scission within the cell takes just milliseconds.” With the help of mathematical methods developed at MATHEON, it was possible to divide the scission process up into many smaller, more manageable simulations.

In the case of dynamin, this allowed the precise mechanism of action to be visualised in individual steps. It turns out that the molecule operates via a specific pathway. “We were able to identify three primary states of the molecule,” explains the mathematician, describing the process as follows, “Initially, dynamin molecules attach to the neck of the vesicle individually, before linking up to form between one and a half and two tight turns around the neck of the vesicle. This structure then expands like a spring and rotates in on itself. The result is that the semi-fluid material making up the neck of the vesicle is more or less ripped apart. “

Understanding this process is important for medical science, as it represents a point of attack for fighting poisons and disease. “Many neurotoxins, for example, act at this point, thereby blocking nerve function,” explains Frank Noe. Degenerative neurological diseases such as Parkinson’s also affect the uptake of vesicles by nerve cells. “If we can obtain a better understanding of the mechanism of dynamin, we may be able to find new approaches to early diagnosis or treatments,” says Dr. Noe.

Collaboration between doctors, structural biologists and mathematicians in this area is set to continue. “The mathematical research being carried out within the MATHEON project will continue to make an important contribution to producing further useful insights,” explains Frank Noe.

The study has been published in the journal ‘Nature’, issue 477, page 556. Further information on the study can be found at

<http://www.nature.com/nature/journal/v477/n7366/full/nature10369.html>

and

[www.biocomputing-](http://www.biocomputing-berlin.de/biocomputing/en/projects/matheon_project_a19_modelling_and_optimization_of_functional_molecules)

[berlin.de/biocomputing/en/projects/matheon\\_project\\_a19\\_modelling\\_and\\_optimization\\_of\\_functional\\_molecules](http://www.biocomputing-berlin.de/biocomputing/en/projects/matheon_project_a19_modelling_and_optimization_of_functional_molecules)

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