



## POLYRES project: Curvy membranes make proteins attractive!

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When proteins bind to cell membranes and, in doing so, bend them, they can attract each other indirectly due to the membrane deformations they cause. With enough proteins available this may lead to a membrane invagination. Using large-scale computer simulations we have for the first time verified this physical model for the initial steps of vesiculation in cells.

The cells of our body are highly complex biochemical factories in which thousands of substances are created, processed and decomposed. To control this metabolism, all eukaryotic cells (such with a cell nucleus) possess various distinct organelles that are responsible for specialized tasks: Our genome is stored and read in the nucleus, proteins and lipids are synthesized in the endoplasmic reticulum, and the Golgi apparatus takes for instance the task of sorting proteins.

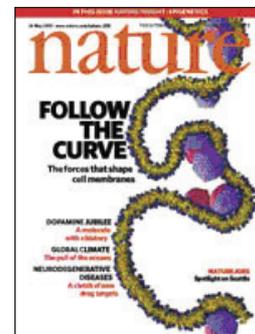
All these organelles are formed by lipid membranes. These are flexible double layers of lipid molecules, only five nanometers thin, which also make up the exterior envelope of each cell. In order to enable transport of material between the organelles - as well as into and out of the cell - they can change their shape. Particularly important is a process

called "vesiculation" (see Fig. 1), during which a membrane bud forms that is later cut off the membrane. Proteins enclosed in the interior of such a "vesicle" can be transported to a different location inside the cell without getting mixed up along the way with other substances. How exactly all this happens is an important question in cell biology that is currently being studied with great intensity.

Since such membrane deformations cost energy, the cell drives them using special proteins. Today we know in many cases their identity. Yet, how they actually create a vesicle is much less understood. We have now used computer simulations to provide evidence for a physical mechanism that can lead to vesiculation. Remarkably, it is not necessary that the involved proteins interact with each other, for instance by mutual specific binding. Rather, proteins influence each other indirectly by the deformation of the lipid membrane which they cause by adhering to it.

To create curved membrane structures, each protein has to bend the membrane a little bit. This local curvature spreads around a protein like a little "halo". When two proteins approach, the overlap of their halos may lead to an indirect interaction. One may think of the attraction between two balls lying on a tense rubber membrane. Usually this picture serves as an illustration of Einstein's theory of gravity by space-time curvature. And indeed these two seemingly different phenomena are formally closely related and can be described by similar mathematics.

Since almost two decades physicists have been on the track of membrane mediated interactions, yet the phenomenon remained confusing: on the one hand experiments documented attractions between membrane-bound objects. On the other hand all available theories indicated repulsion - at least if the membrane is curved uniformly. Since neither experiment nor theory are free of potential artifacts, the existence of curvature-mediated protein attractions



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remained elusive. Nevertheless, cell biologists started to be interested in the effect, as it provided a clear physical model of vesicle creation - provided it worked! The simulations performed in our group show that under suitable conditions (e.g. a minimum curvature imprint of each protein) the mechanism indeed leads to an attraction, and with enough proteins available to cooperative vesicle formation. For very strong curvatures the force can even be "measured" directly in the simulation (see Fig. 2).

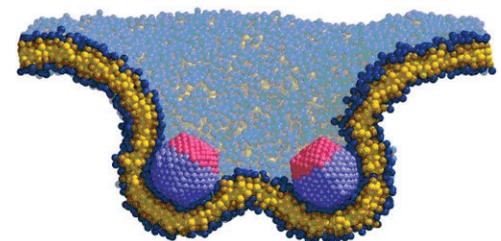


Figure 2: Cross-section of a membrane that is curved by two symmetrically adhering particles. In such a simulation the force between the particles can be "measured".

The creation of transport vesicles is not just of fundamental importance for all life processes in cells, such as signal transduction or transport of nutrients. The involved mechanisms should also be at work in many other shape-determining tasks of membrane organelles. They furthermore play a role in the interaction of cell membranes with other objects, such as viruses or drugs. Since all this happens on sub-optical scales (about 100 nanometer), the experimental investigation of such events is a great challenge. Suitable computer simulations therefore support and complement available experimental techniques quite considerably.

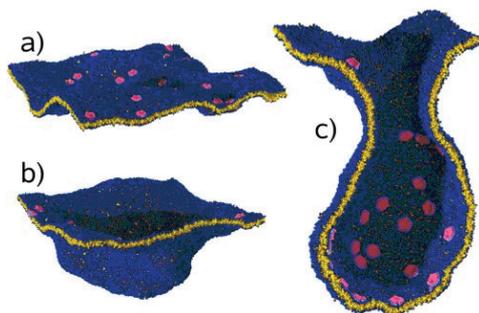


Figure 1: Vesiculation, as seen in a model simulation: a) pro-teins (red) adhere on a membrane (blue/yellow) and locally bend it; b) this triggers a growing invagination. In c) a cross-section through an almost complete vesicle is shown.

# Direct numerical simulation of a supersonic jet and its acoustic field

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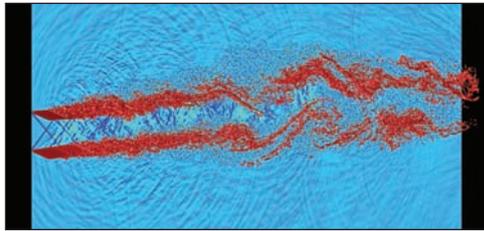


Figure 1: vorticity (iso-surface, red) and dilatation (plane, blue)

Shock-induced noise is generated by supersonic jets which are not perfectly expanded. This means that their nozzle exit pressure is above or below the ambient pressure. The flow adapts to the ambient pressure by a series of oblique shocks, compression and expansion waves. These interact with the shear layers, producing shock-induced or shock-associated noise. To this end direct numerical simulation was performed to study the physical processes responsible, many of which have not yet been clearly identified. The main challenge was to simultaneously resolve the small-scale nonlinear turbulent structures and at the same time the large-scale, small amplitude acoustic waves they produce.

In this project, the method of direct numerical simulation was used to compute a three-dimensional supersonic rectangular jet that is not perfectly expanded, as it is found at the nozzle exit of jet engines for aircraft. Numerical methods of high order of accuracy were chosen for the direct solution of the compressible Navier-Stokes equations. This gave us the possibility to compute the sound field, that was generated by the supersonic jets, directly.

## Physical situation

Consider a supersonic jet, e.g. at the exit of a jet engine, in the over- or under-expanded case. A regular pattern of compression and expansion waves will be found within the supersonic part of the jet flow. A compression wave incident on the sonic line will be reflected as an expansion wave, and vice versa. At the location of interaction between the compression wave and the turbulent mixing layer, acoustic waves are generated. This shock-induced noise also plays an important role in what is called jet screech. This phenomenon manifests itself by a strong and sharp peak in the sound pressure level spectrum, corresponding to a tonal noise at high amplitude

(up to 160 dB), which may cause damage to parts that are near the nozzle due to the high dynamic loads. Screech is induced by shock-induced acoustic waves travelling upstream and forcing the "young" shear-layer at the nozzle exit. At this point Kelvin-Helmholtz instabilities are growing to vortices, transported downstream and interacting with the shock tips which are emanating noise again and closing a feedback loop.

## Methodology

The compressible Navier-Stokes equations were solved, based on a characteristic-type formulation on an orthogonal grid (approx. 300 million grid points) stretched in both the stream-wise and the transverse directions. Along the span-wise direction, periodicity and statistical homogeneity were assumed.

To capture the sound generation and propagation processes, spatial discretization was done using a finite difference compact scheme of sixth order and a spectral like method in the periodic direction. The code is parallelized using the Message Passing Interface (MPI). For the current setup 1020 CPU's were used on a SGI-Altix 4700 with Itanium2 Madison 9M processors. Approx. 12 TB of data were written to disk and 0.5 TB of main memory were used.

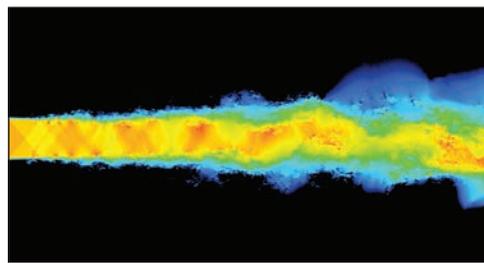


Figure 2: absolute velocity ( $|u|$ )

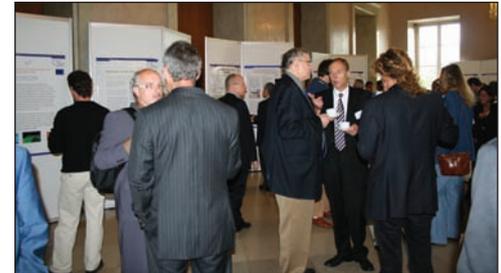
## Results

In fig. 1 an iso-surface of the vorticity ( $|\text{rot}(u)|$ ) is shown in a three-dimensional sketch with a plane of the dilatation field ( $\text{div}(u)$ ). A dominant noise source seems to be close to the nozzle exit (between the first and second shock-cell). The absolute velocity is presented in fig. 2 which visualizes the persisting shock-cell structure in the jet core.

## Acknowledgment

We thank the DEISA Consortium (co-funded by the EU, FP6 project 508830), for support within the DEISA Extreme Computing Initiative.

# Towards Petascale Computing in Europe



Petascale computing was the theme of the third annual DEISA Symposium, in the Bavarian Academy of Sciences and Humanities, Munich, on 21–22 May. The symposium focused on perspectives for petascale computing in Europe, looking at the initiatives and strategies being deployed to enhance the outreach of high performance computing in Europe. At the event existing HPC focused infrastructures, DEISA in Europe, NAREGI in Japan and Teragrid in the US were presented. Technology trends for petascale computing were discussed at the symposium and there were various scientific cases for petascale computing in Europe discussed, too.

In his speech Mário Campolargo, Head of Unit "GÉANT and e-Infrastructures" at the European Commission, discussed the e-Infrastructure area in the EU's 7th framework programme and the way towards a European Supercomputing Infrastructure. DEISA's role in the new cycle of e-Infrastructures in FP7 is to provide concrete support to the deployment of a European HPC eco-system, including new European petaflop machines.

Presentations of the Symposium are available at [http://www.deisa.org/news\\_events/deisa\\_events/munich\\_symposium.php](http://www.deisa.org/news_events/deisa_events/munich_symposium.php)

## 5th DEISA Training

29 - 31 October '07, Bologna, Italy

- Global description and introduction to the usage of the DEISA infrastructure
- UNICORE and DESHL client
- Hands on Session
- Special topic to be defined
- Use Cases

The registration will open in September.