



## Study of Low Density Lipoproteins to Prevent Heart Attacks

Sanna Pyysalo

**B**ad cholesterol is a condition mainly affecting those in modern industrial countries. Using the supercomputing resources offered by DEISA, the LIPOS research project has explored the structure and functions of low density lipoproteins, whose excessive accumulation in coronary arteries can lead to the formation of cholesterol plaques. Work on the project began in the autumn of 2007.

Heart attacks and strokes are two of the most typical causes of death in industrial nations today. They result from atherosclerosis, where plaques form in a coronary artery. The first stage of this complex process is the accumulation of excess low density lipoproteins (LDLs), particles also known as “bad cholesterol”, in the artery wall, which then undergo chemical changes.

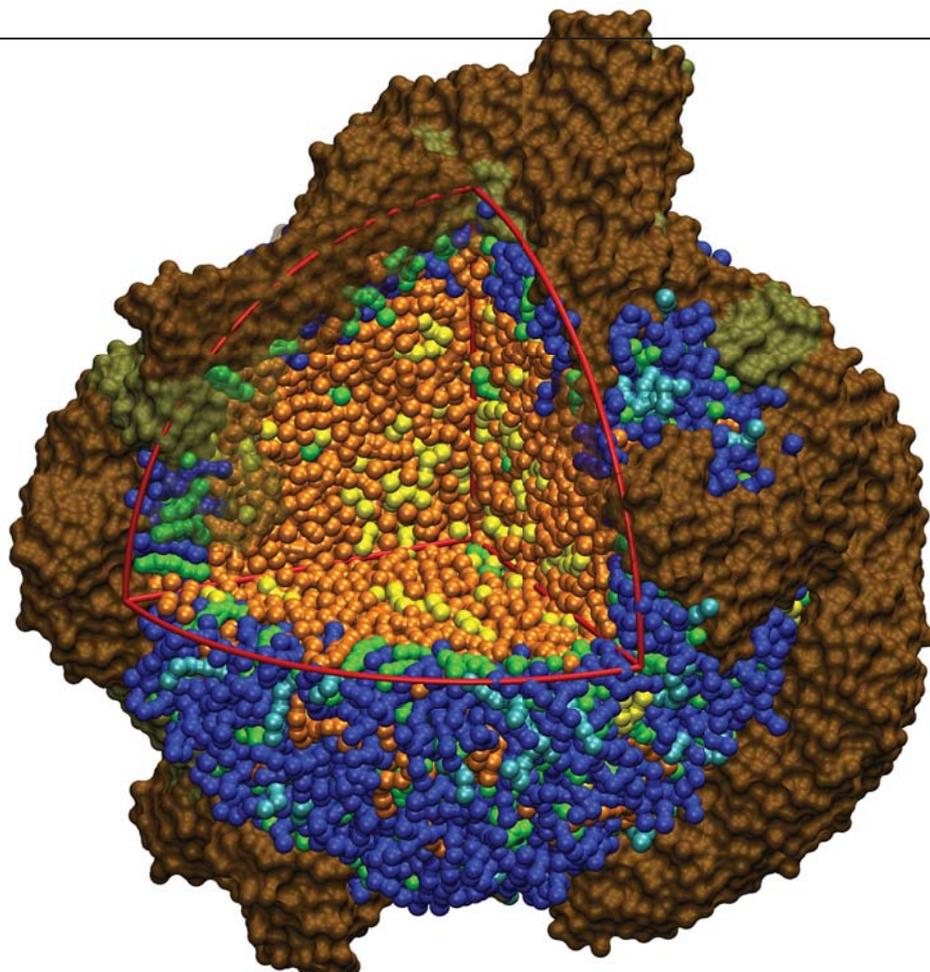
“To better understand how related diseases could be prevented, one first has to understand the structure and functions of LDL. This has been the essence of our research”, says Prof. **Ilpo Vattulainen**, the principal investigator in the LIPOS (Lipoprotein Structure and Dynamics) research project.

The work is being carried out by the Department of Physics at Tampere University of Technology in Finland, the Wihuri Research Institute in Finland, the University of Groningen in the Netherlands and the University of Western Ontario in Canada.

### Research in almost atomic detail

The objective of the research was to determine the structure of low density lipoproteins. LDL is the particle transporting cholesterol and its esters to cells, so an elevated concentration of LDL correlates to an increased risk of certain diseases, such as atherosclerosis.

“There are substantial difficulties associated with understanding how cholesterol-related diseases emerge, or even the functions of individual LDL particles. The functions of proteins depend on their structure and the structure of LDL is not well understood”, explains Vattulainen.



*Fig. 1. Equilibrated structure of a low density lipoprotein particle. A section of the particle has been cut out to make the internal structure visible. Different lipids are shown in different colors: blue and cyan for phospholipids, green for free cholesterol, orange for cholesterol esters, and yellow for triglycerides. The apoB-100 protein is shown in brown. Water and ions around the particle are not shown.*

This is largely due to their small size – only around 20 nm. Experimentally, it is particularly challenging to probe the structure of LDL and related phenomena over such small scales. However, atomistic and coarse-grained simulation techniques provide an excellent means of analysing molecular systems in almost atomic detail, hence complementing experiments.

“We paid particular attention to clarifying the role of lipids in the core particle of LDL, and their effect on the structure and dynamics of the protein sequence that surrounds it”, Vattulainen notes.

### Impressive results create new opportunities

The LIPOS research project began in the autumn of 2007, and following major surveys and background studies, the initial models for LDL particles were ready in spring 2008. Simulations using the initial models were started around May 2008 and were completed in the autumn of that year.

“The analysis is still partly in progress, but the first articles describing the main findings are already almost complete”, Vattulainen says.

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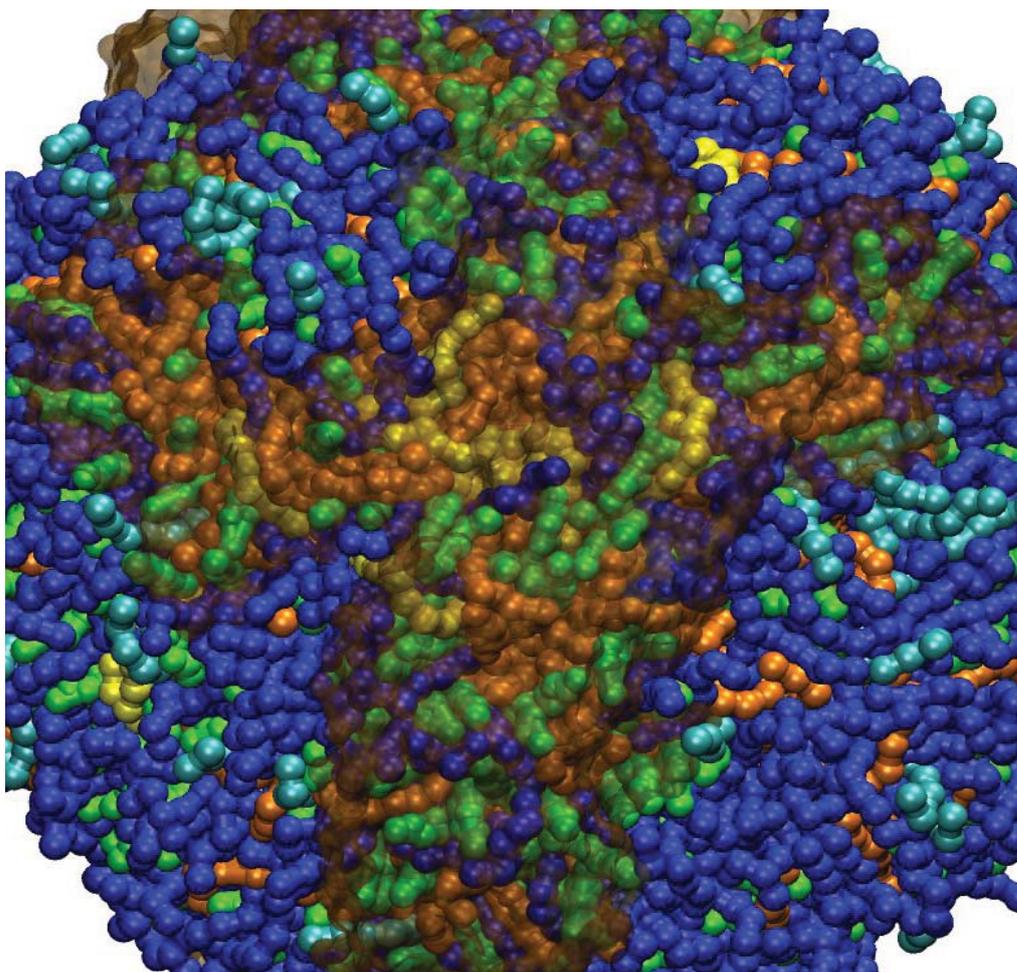


Fig. 2. ApoB-100 displaces phospholipids and makes direct contact with the cholesterol ester/triglyceride core of the LDL particle. Colors are as in Fig. 1, except that the protein is shown as transparent.

### And what were the main findings of the research?

"It provided a great deal of insight into the distribution and dynamics of lipids inside LDL, and the effects of lipids on the structure of the protein sequence wrapped around LDL. In essence, we now know the structure of native LDL in almost atomic detail", Vattulainen explains.

The research and its results also create the opportunity for further work, in order to gain greater understanding of the overall function of LDL particles.

"The results allow us to initiate an intriguing sequence of further studies, looking at how LDL particles interact, for example, with certain enzymes, oxidative agents and sugars that are involved in the chemical alterations of LDL and the consequent formation of cholesterol plaques."

### Pioneering studies with the help of DEISA

The LIPOS project has broken new ground in its field of science because the research method was truly unique.

"Previously, there have been no attempts at atomistic or coarse-grained simulations of LDL particles. In this respect, our study is pioneering as it is the first case in which LDL particles have been explored through simulations with full molecular detail", Vattulainen says.

An important factor in the success of the research project was the supercomputing resources made available through the DEISA framework.

"DEISA allowed us to carry out an extensive, state-of-the-art simulation project for a molecular entity that is biologically particularly relevant. Large-scale parallel simula-

tions for a system of this kind would not have been possible without resources of this calibre."

The benefits of DEISA were, in Vattulainen's view, obvious.

"There are only a handful of places in Europe that provide access to supercomputing resources of this size. Networking in this manner provides major added value for Europe overall", Vattulainen comments.

### Technical overview

Computations of the Lipos research project were performed at HECToR in Edinburgh, Scotland. There were 5 independent runs, which used up to 64 CPU cores each. 50 000 CPU hours were invested on the core of the production simulations.

To construct the initial models, MODELLER software was used on local computers. An open-source software package, GROMACS, was used for simulations (coded in C, parallelization via MPI).

Visualization and data analysis on local computers were done using GROMACS and VMD. GROMACS analysis tools were extended to allow flexible analysis of specific parts of the systems.

More information about the LIPOS project: [www.deisa.eu/science/deci/projects2007-2008/lipos](http://www.deisa.eu/science/deci/projects2007-2008/lipos)



Fig. 3. Prof. Ilpo Vattulainen, the principal investigator of the LIPOS research project

## Next DEISA Training Course in Amsterdam, 3-4 November 2009

DEISA is running two training courses at the SARA Computing and Network Centre, Amsterdam, in November 2009. Both courses will be based around a number of practical programming exercises.

### Introduction to the DEISA Infrastructure (3.11.2009)

The first course on Tuesday 3rd November is an Introduction to the DEISA Infrastructure. This will cover the basic aspects of the DEISA distributed supercomputer environment and the software tools that are used to access it.

No prior knowledge is assumed for this course.

### The Scalasca Performance Analysis Toolset (4.11.2009)

The second course on Wednesday 4th November will cover The Scalasca Performance Analysis Toolset.

Scalasca is an open-source, portable toolset that can be used to analyse the behaviour of parallel applications and to identify opportunities for performance optimisation. It has been specifically designed for use on large-scale HPC systems such as those in DEISA, but is also well-suited for small and medium-scale HPC platforms. Scalasca supports an incremental performance-analysis procedure that integrates runtime summaries with in-depth profiles of parallel execution. DEISA staff will be on hand to help users with the Scalasca practical exercises and to help analyse the execution of their own programs on the DEISA platforms.

The participants should already have their own parallel application that currently runs on some other HPC system.

For more detailed information and course agendas please visit the DEISA training web site:

[www.deisa.eu/usersupport/training/training-events](http://www.deisa.eu/usersupport/training/training-events)

## DEISA Mini-Symposium at ParCo 2009 “Extreme Computing in an Advanced Supercomputing Environment”

Wolfgang Gentzsch, RZG

A DEISA Mini-Symposium, “Extreme Computing in an Advanced Supercomputing Environment” was held as a part of the International Conference on Parallel Computing, ParCo 2009 ([www.ens-lyon.fr/LIP/ParCo09-3/](http://www.ens-lyon.fr/LIP/ParCo09-3/)) The conference took place at the École Normale Supérieure in Lyon, France, 1-4 September 2009. The Mini-Symposium was structured into three sessions to provide a representative overview of the application related key areas in DEISA.

The first session covered the DEISA Extreme Computing Initiative (DECI) which was launched by the DEISA Consortium in 2005, to enable a number of innovative “grand challenge” applications in all areas of science and technology. These leading, ground breaking applications submitted to DECI deal with complex, demanding and innovative simulations that would not be possible without the DEISA infrastructure, and which benefit from the exceptional resources provided by the Consortium. The DEISA applications are expected to have requirements that cannot be fulfilled by the national services alone.

Another area presented at the Mini-Symposium covered the application oriented support, a broad spectrum of advanced and integrated services for challenging applications,

such as the common global high performance file system, to greatly facilitate data management across Europe; the uniform access methods common to the entire infrastructure, such as

- the UNICORE middleware
- the DEISA Common Production Environment (DCPE)
- the European team of system operation specialists in charge of handling the different aspects of the system services operations
- and the Applications Task Force team at the service of the scientists both for user support and enabling of complex applications to utilise DEISA services efficiently.

Finally, several examples of scientific projects both from the DECI initiative and from European science communities were presented from the areas of computational fluid dynamics, material sciences, computational chemistry, plasma physics, and micro-biology.

The Mini-Symposium aimed at highlighting the scientific impact achieved so far with the DEISA infrastructure and at providing a forum for application enabling with a key role for HPC based research. And it was shown how the support model for DECI has been extended to supporting virtual scientific communities as a whole.

**DEISA at SC'09**  
14-20 November 2009, Portland

**DEISA, PRACE and EGI joint BoF session at SC'09, November 17, 2009:**

**“European HPC and Grid Infrastructures”**

BoF session web site: <http://scyourway.nacse.org/conference/view/bof159>

You will also find DEISA at the joint booth with PRACE in the exhibiton area.  
The booth number is 2973

Welcome!

