

Toward a systems biology map of iron metabolism

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Scientists at the Wake Forest University School of Medicine, the University of Manchester in the United Kingdom, and the Virginia Bioinformatics Institute at Virginia Tech have taken the first steps toward constructing a systems biology map of iron metabolism. The team has put together a general network of chemicals and reactions important for the many steps and reactions that constitute iron metabolism.

Iron is crucial to the survival of animal cells. When iron metabolism goes wrong the consequences can be devastating. The World Health Organization estimates that approximately 2 billion people - more than 30 percent of the world's population - are afflicted by nutritional disorders that may be attributed in some way to iron deficiency.

The present study set out to provide researchers with a systems biology map of iron metabolism that would allow scientists to investigate changes in the network under different conditions.

The systems biology map was subsequently used to construct iron networks for specific types of cells that are known to be critical for iron metabolism. Mathematical approaches like the ones described in this study may prove useful in understanding the interactions between different iron-dependent species, identifying key regulatory points, simulating their response to stimuli, and understanding how these responses differ in various cell types.

Dr. Suzy Torti, professor in the Department of [Biochemistry](#) at the Wake Forest University School of Medicine, remarked: "Iron is essential to human survival. However, iron can also facilitate the formation of oxygen free radicals, which can be damaging. Because of this dual nature of iron, it is very carefully regulated at both the level of the cell and the entire body. In this study, we have taken the first steps in organizing the complex regulatory networks that control iron into a [mathematical model](#) . Over the long term, we hope this will enable a more precise understanding of how iron is controlled and how it can be manipulated for therapeutic benefit."

Pedro Mendes, professor in the School of Computer Science and Manchester Centre for Integrative Systems Biology and associate professor at the Virginia Bioinformatics Institute, remarked: "To build the systems biology map of iron metabolism described in this paper we have used the program CellDesigner to map the metabolic network in multiple types of cells. The modeling effort was facilitated by the fact that CellDesigner stores the model using the Systems Biology Markup Language." SBML is a powerful, computer-readable format for describing qualitative and quantitative models of biochemical reaction networks. It can also be used to express gene regulatory networks and other phenomena of interest in [systems biology](#). SBML is designed to enable the exchange of biochemical network models between different software packages. It therefore allows for the sharing and publishing of models in a form other researchers can use in various software environments. For example, SBML is also understood by biochemical modeling software such as COPASI and networks generated in CellDesigner can therefore be simulated or analyzed by this software package.

Dr. Valerie Hower, who was a postdoctoral researcher at the Virginia Bioinformatics Institute and the Wake Forest University School of Medicine at the time of the research, and who is currently working in the

Department of Mathematics at Georgia Tech, remarked: "We were able to construct an iron metabolic network that comprised 151 different chemical species and 107 reactions and transport steps. We believe we are the first to use the CellDesigner program to map one metabolic network in multiple types of cells."

Vladimir Shulaev, associate professor at VBI and the Department of Horticulture, Virginia Tech, commented: "This collaboration is a good example of a project that benefits from a transdisciplinary approach to the study of molecular biosystems. We have been working with our partners at the Wake Forest University School of Medicine on several biomedical projects over the past few years and our scientific approach is delivering a solid platform for further discoveries. We have built a team of researchers with expertise in biology, mathematics, biochemical modeling, and metabolism that works closely with clinical scientists who understand the first-hand impact of iron metabolism on health. This work is helping us to build a comprehensive system-wide understanding of iron metabolism and its clinical ramifications."

VBI and Virginia Tech Mathematics Professor Reinhard Laubenbacher added: "We hope to use the iron metabolic networks as a starting point to identify changes that take place in healthy and diseased tissues. The addition of kinetic information to our structural network should permit the simulation of iron metabolism in different tissues as well as under conditions of health and disease. This should provide us with a much needed tool to look at the impact of such changes on the systems level network."

More information: Valerie Hower, Pedro Mendes, Frank M. Torti, Reinhard Laubenbacher, Steven Akman, Vladimir Shulaev and Suzy V. Torti (2009) A general map of [iron metabolism](#) and tissue-specific subnetworks. *Molecular BioSystems* 5: 422-443.

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