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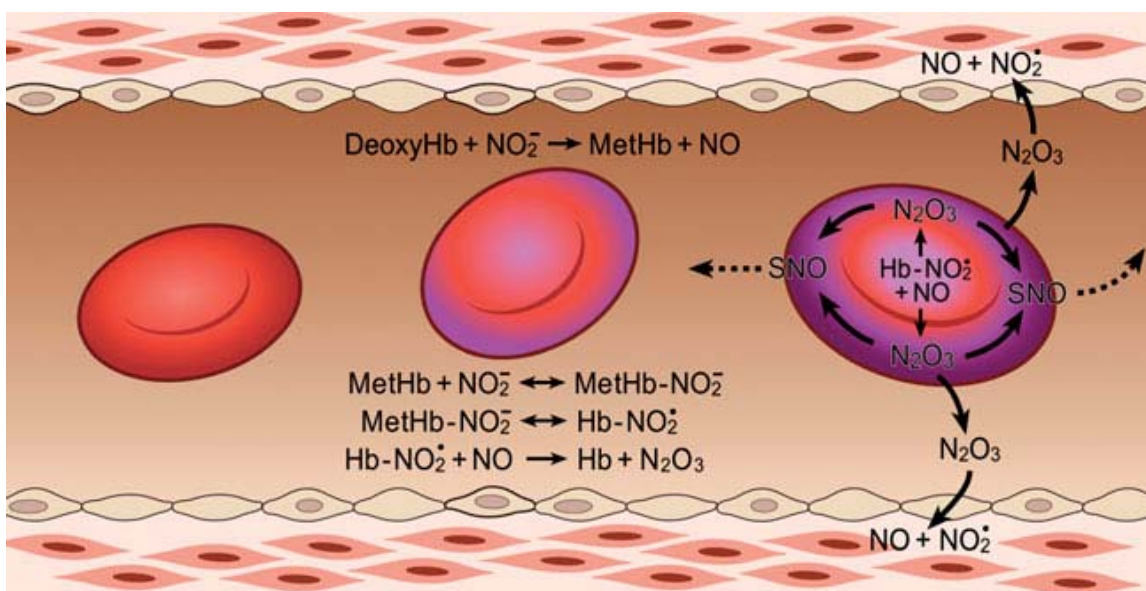
Tromsø chemists help crack a major biomedical puzzle: how does nitrite control blood pressure?

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It has long been known that nitrite, a ubiquitous anion present in blood, plays a key role in blood pressure regulation (vasodilation). But exactly how this happens has remained unclear. Now, working with biomedical researchers at the NIH and Wake Forest University in the USA (Professors Daniel Kim-Shapiro and Mark Gladwin), members of the Center for Theoretical and Computational Chemistry at the University of Tromsø (Professor Abhik Ghosh and visiting researcher Dr. Jeanet Conradie) have helped crack the puzzle. The research appeared in *Nature Chemical Biology* on November 4, 2007. The puzzle in question consists of the following:

Since NO is the ultimate agent for blood vessel dilation, nitrite must somehow be converted to NO in the course of the process. Indeed, nitrite does react with the deoxy (oxygen-free ferrous) form of hemoglobin to generate NO. The problem is that the hemoglobin resides inside the red blood cells and before NO can diffuse out of the red cells to reach the blood vessel walls, it will be recaptured by hemoglobin to form a very stable NO complex. How then does the vasodilation occur?

It turns out (as shown in the figure) that nitrite reacts with the ferric form of hemoglobin in the red cells to generate a highly reactive (“ferric-nitrite”) intermediate, which in turn reacts with NO to generate N_2O_3 . It's the latter species that diffuses out of the red cells, dissociating to NO and NO_2 along the way and this is how nitrite-derived NO reaches the blood vessel walls to accomplish the vasodilation.



Ghosh and Conradie's contribution consisted of characterizing the crucial ferric-nitrite intermediate using the University of Tromsø's excellent supercomputer facilities. Experimentally, this intermediate is a most elusive species so it proved critical to use computer modeling to gain an understanding of its properties.

It was a lot of fun working with our American colleagues, the medical doctors who really led the project. A lot of different kinds of thinking – from cardiovascular research to theoretical chemistry – led to the cracking of this age-old puzzle; it was all exhilarating. Although it's early days, we remain optimistic that this discovery will lead to new medicines in the cardiovascular field.