Freeze: Scientists film protein in action

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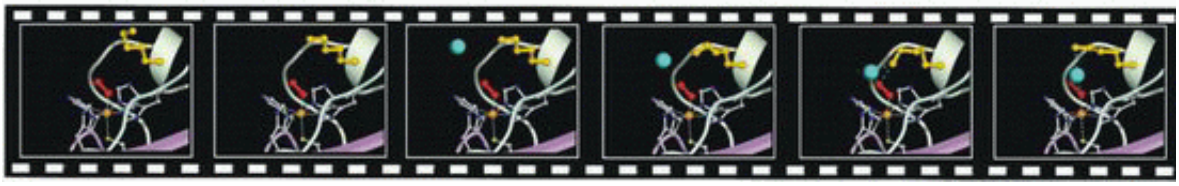

The film shows how the lysine amino acid (yellow part of the protein) grabs a water molecule (in blue) and imports it into the enzyme to perform the catalytic reaction on the superoxide (in red). Credits: Gergely Katona.

It is difficult to find similarities between Grenoble and Hollywood or between the researchers at the ESRF and the Institut de Biologie Structural (IBS) and world-known filmmakers. However, scientists from these institutes based in Grenoble (France) have managed to produce a movie. The actors are not celebrities but a protein whose role is to eliminate toxic molecules. They filmed this protein in action by freezing it at several states. They publish their results this week in *Science*.

Most of the research done on proteins is based on their study in a resting state and their study in movement is extremely limited due to technological limitations. Today, a French team has made a movie of an enzyme (a protein that catalyses chemical reactions) found in bacteria.

“The achievement of this research is two-fold: on one hand there is the technological success of filming an enzyme in action and on the other hand there are the results that contribute to the knowledge of how this

enzyme works", explains Dominique Bourgeois, corresponding author for the paper.

The enzyme filmed in action is called "superoxide reductase", its role is to eliminate a toxic molecule called "superoxide radical". In order to survive, all living organisms have to fight oxidative stress, produced by outflows of the oxygen metabolism. In humans, about 2% of the oxygen used to breathe is transformed into this toxic "superoxide radical" molecule, instead of water. This production is increased in people affected by neurodegenerative diseases such as Alzheimer. A high amount of these molecules worsen these illnesses, so scientists are looking for drugs to eliminate them.

The enzyme studied by the team acts uniquely in bacteria and its counterpart in humans is more complex. Synthesizing an enzyme like the one studied through biomimetics is an exciting possibility for developing future drugs.

In order to produce the film, the team used the ESRF-IBS "Cryobench" laboratory to freeze the protein in three different states while the reaction took place. In order to make sure that they "trapped" the right intermediate states, the researchers used the technique of Raman spectroscopy. This technique provided them with strong evidence that the states were the appropriate ones by showing them the chemical bonds in each stage of the reaction. Once they had identified the right states, they studied the sample with synchrotron X-rays. "We expect this new methodology to be of use for many researchers in the field", Bourgeois explains.

Filming certain proteins while reactions occur has been possible at the European Synchrotron Radiation Facility for some years. However, until today, experiments were restricted to proteins that can be excited by light and are very resistant in crystalline form.

Reference: Katona et al., "Raman-Assisted Crystallography Reveals End-On Peroxide Intermediates in a Nonheme Iron Enzyme", *Science*, 20 April 2007.

Source: European Synchrotron Radiation Facility