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Nano-impacts: A new perspective on enzymes

Enzymes are an integral part of all living organisms and play a central role in a wide range of biological processes. The latter, among many, include most biological metabolism as for instance the digestion of food in mammals or photosynthesis in plants, and the reproduction of genetic information in all cell division. Broad knowledge on the role and functionality of different enzymes is hence crucially required to gain a deep understanding of processes in our bodies and related diseases.

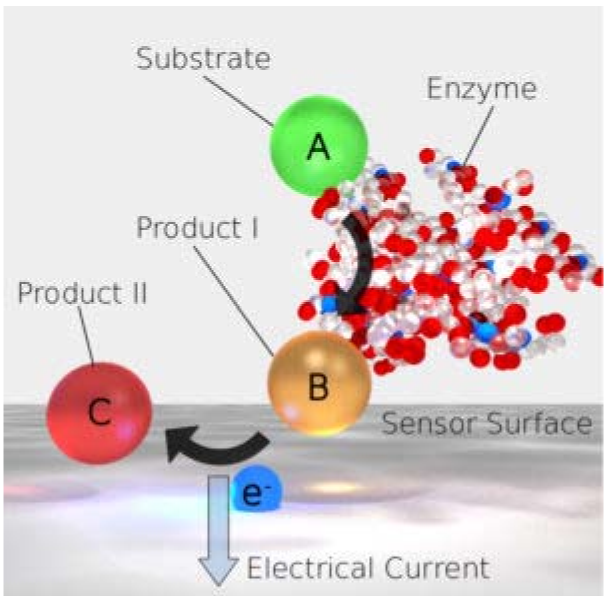

Fig. 1. Illustration of one possible detection mechanism. The enzyme moves freely in liquid while continuously catalysing substrate molecules A into product molecules B. If the enzyme is located close to the electrified sensor surface, electrons may `jump' from product molecules B into the sensor surface transforming B into another product C. The electron transfer is observed in the electrical sensor current and may provide insight into the nature of the enzyme.

Though found in highly diverse functions, most generally speaking, all enzymes fulfil a similar role acting as a catalyst to a specific biological process. Depending on their immediate environment, the reaction of one or multiple `substrate' materials to one or multiple `products' is facilitated. By this means, chemical reactions can be moderated and regulated to best suit certain biological functions.

Due to their utmost importance to biology, significant effort has been made to investigate enzymes and a broad range of measurement techniques has been developed. Among these, methods enabling the characterisation of *individual* enzymes (rather than huge ensembles) in their natural surrounding are of particular interest when it comes to understanding the exact function of a specific enzyme. In this regard one of the latest additions to the range of promising scientific tools is the nano-impact technique, which has only been explored in single enzyme detection since last year.

Though exact detection mechanisms and whether single enzyme detection has already been achieved through the above method are at least in part controversially discussed, the general experimental set-up that various scientific groups employ is almost identical: A small metallic surface is electrified and set in contact with a liquid containing an enzyme and its substrate. If then, randomly, an enzyme diffuses past the surface, electrons may `jump' between the electrode and the enzyme or its product, which may be observed in a change in the electrode current. Such changes may be specific to the passing enzyme and its reaction and hence provide the desired insight in the individual enzyme functionality and momentary activity. As an example, one possible reaction mechanism is depicted in Figure 1.

In spite of the simplicity of the nano-impact method, nevertheless there are challenges that particularly arise in the detection of single enzymes. As shown in the figure, the only quantity that can be measured during an experiment is the electrical current at the sensor surface, while in a standard experiment neither the enzyme nor the substrate or the product can be visually tracked. The experimentalist is hence solely left with a, due to the random enzyme movement highly stochastic, signal which reflects the actual enzymatic process in a complex fashion. Consequently, the analysis of data is not straightforward but detailed theoretical knowledge is required to extract useful information. This issue was addressed in a recent publication by Lin *et al.* in *Chemical Science* in which the authors provide a comprehensive theoretical analysis and direct guidance to experimentalists for a reaction mechanism similar to the mechanism shown in the figure.

Recent theoretical advances in the above and other studies are in our view a major step forward towards the exploitation of nano-impacts to full extent and we remain looking forward to see combined theoretical and experimental work being published to unambiguously demonstrate the electrochemical detection and characterisation of a single enzyme.

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Publication

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