Toxins In Motion:
Computational Exploration of Snake Venom Protein Mechanisms

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Snakebite envenoming is the most serious neglected tropical disease, causing 81-138 thousand deaths annually [1]. The venom's lethality results, in part, from the action of several highly toxic enzymes secreted in the venom. This talk will focus on some of the most relevant enzymatic toxins and explain how computational chemistry helps understand their mechanism of action [1].

We will analyse the results of rigorous computer simulations of viper enzymatic toxins through molecular dynamics and quantum-mechanical methods. The toxins are simulated in their realistic physiological matrices. In particular, we will analyse their chemical catalytic mechanisms and interaction with vital biological targets, such as the cell membrane [2-4], hyaluronic acid, collagen IV, and coagulation factors [2-5]. We will further propose a molecular mechanism of toxicity of C-terminal peptides derived from snake venom phospholipase A2-like proteins [6].

Finally, we will discuss the possibility and strategies for inhibiting these toxins with small molecules, including making the inhibitors more universal. By providing a microscopic view of the catalytic processes underlying toxicity, computational chemistry highlights the destructive precision of venom enzymes and the opportunities they offer to understand advanced principles of catalysis and specificity.

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