# EVOLUTION OF GLYCOSIDE HYDROLASES AND THEIR ELECTROSTATIC PROPERTIES

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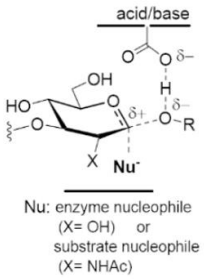
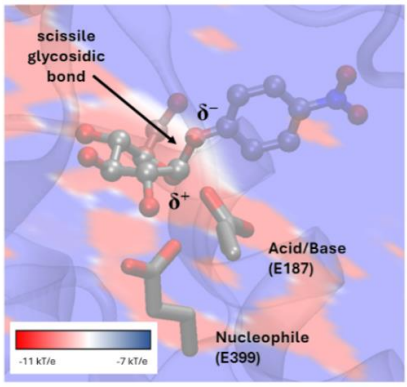
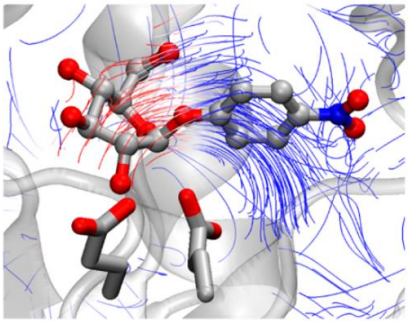
The high catalytic efficiency of enzymes is attained, in part, by their capacity to stabilize electrostatically the transition state of the chemical reaction. In glycoside hydrolases, the oxocarbenium ion-like nature of the transition state has been well characterized both experimentally and computationally [1]. However, limited attention has been paid to how this oxocarbenium-ion gets stabilized by glycoside hydrolases. Here we will present how the structure of this large family of enzymes has evolved to generate an electrostatic potential gradient at the active site complementary to the charge separation that is formed along the scissile glycosidic bond during the catalytic reaction [2]. These electrostatic properties have never been analysed before from the perspective of the glycoside hydrolase enzyme. We will show how such electrostatic potential gradient at the active site is an evolutionary constrained feature present across all clans of the glycoside hydrolases families. We have translated this property into an easy to compute metric that can be used to guide protein engineering. We will present examples of how this metric is able to predict mutation sites aimed at modulating the hydrolytic activity of glycosidases, for example, for the development of efficient transglycosidases [2].



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**References:**
1. M. A. B. Morais, A. Nin-Hill, C. Rovira, *Curr. Opin. Chem. Biol.* **2023**, *74*, 102282.
2. A. Vega, A. Planas, X. Biarnés, *FEBS J.* **2025**, *Early View*, doi:10.1111/febs.70121