Computer-assisted protein enginerring of glycoside hydrolases with BINDSCAN

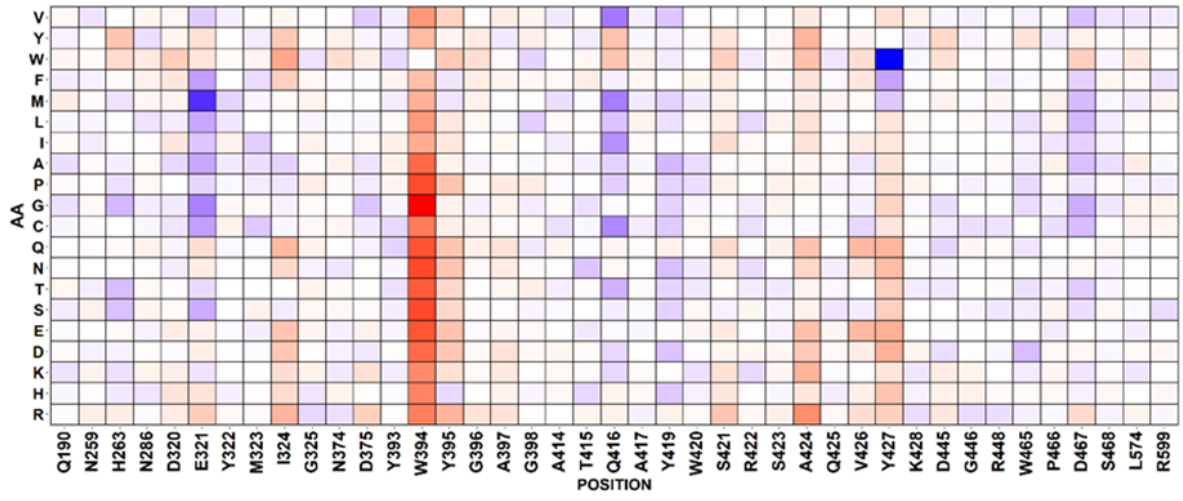
Xevi BIARNÉS [1], Aitor VEGA [1], Antoni PLANAS [1]

[1] Institut Química de Sarrià, Universitat Ramon Llull. Barcelona, SPAIN

xevi.biarnes@iqs.url.edu

BINDSCAN is an in-house computational protocol aimed at assisting in the design of biocatalysts. It simulates and predicts mutational effects on a protein-substrate complex with the objective of modulating different enzymatic properties such as substrate specificity, enzymatic reactivity or stability in the context of biocatalysis. BINDSCAN can be used for either enhancing protein's performance or to redesign its function towards novel substrate specificities. It is especially useful when it is necessary to expand the range of chemical structures on which a specific enzyme is bioactive. The protocol is composed of three separate modules: 1) generation of the enzyme mutant library, 2) modelling the 3D structure of the protein-substrate complex and 3) evaluation of specificity and reactivity metrics. Mutational effects on the target property can then be analyzed with different selection criteria and graphical representations

BINDSCAN has been applied to different CAZYmes in our group including glucosidases, fucosidases, hexosaminidases, xylosidases and transglycosidases among others [1, 2]. Here we will present the recent advances incorporated to the protocol and its validation against massive experimental data on the hydrolytic activity of mutants of Spodoptera frugiperda β-glucosidase (O61594, GH1) [3]. Results showed that BINDSCAN can effectively be used for the identification of mutation sites to redesign enzymatic activity. Statistical analysis comparing experimental data with BINDSCAN results using different metrics will be presented and the method sensitivity and specificity discussed.



BINDSCAN example heatmap. Color-intensive spots are to be considered for experimental protein design

Bibliographic references:

[1] B. Bissaro et al. (2015), ACS Catalysis (5), 4598–4611
[2] M. Castejón-vilatersana et al. (2021), Int. J. Mol. Sci., (22), 1–15
[3] F.K. Tamaki et al. (2016), PLoS One (11), e0167978