

VEGA ZZ: a versatile toolkit for drug design and protein modelling

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In the last years, the computer hardware and software were significantly improved in terms of performance and friendliness of use. This trend is especially evident in the personal computer market, where the users require complex applications (e.g. productivity software, Web navigation, games, etc.) needing high computational power and exceptional graphic performances. Using a common PC, it's now possible to do what once needed an expensive graphic workstation. However, the computational chemistry was born in the Unix workstation age and thus some important molecular modelling packages are still command-line based and, in some cases, require an Unix-like operating system.

Starting from this ground, some years ago, the VEGA ZZ^{1,2} project started with a view to create an easy-to-use molecular modelling software with a complete 3D graphic interface. It was specially developed to teach the students spending few time to explain the software functionalities and the operating system use. Indeed, VEGA ZZ was created to run on student-friendly Windows-based PCs and to do the most common molecular modelling operations in fast and easy way.

As time goes by, VEGA ZZ became a more complete software, changing from a teaching tool to a complete molecular modelling suite for researcher, even preserving the starting philosophy. Today, VEGA ZZ can be successfully used to solve many computational chemistry problems about drug design, ligand optimization, homology modelling of proteins, and calculation of QSAR molecular descriptors.

As an informative example of the fertile potentialities of VEGA ZZ program, some successful applications on the metabolism prediction will be presented. Because metabolic problems lead to too many failures during clinical trials, much effort is devoted to *in silico* models to predict metabolic stability and metabolites. In these studies, VEGA ZZ can afford a significant contribution as in the prediction of the hydrolytic activity of the carboxylesterase 1 and 2. The obtained results emphasize some crucial properties of the catalytic cavity of these enzyme, confirming that hCES1 prefers substrates with small alcohol groups and large hydrophobic acyl moieties, whereas hCES2 better accommodates substrates with with large alcohol groups and small acyl moieties. Finally, the docking results confirm the relevance of hydrophobic interactions, which seem to govern the hCES1 recognition and allows a robust prediction of hCES1 catalytic activity.

¹ A. Pedretti, L. Villa, G. Vistoli, "VEGA: A versatile program to convert, handle and visualize molecular structure on Windows-based PCs", J. Mol. Graph., Vol. 21, 47-49 (2002).

² A. Pedretti, L. Villa, G. Vistoli, "VEGA - An open platform to develop chemo-bio-informatics applications, using plug-in architecture and script programming", J.C.A.M.D., Vol. 18, 167-173 (2004).