Molecular Dynamics Simulation to design an Enzyme-based Nanobiosensor using Atomic Force Microscopy to detect Glyphosate herbicide

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INTRODUCTION

The functionalization of atomic force microscopy (AFM) tips with biomolecule is capable of measuring the force of interaction between this biomolecule with the analyte on a substrate, acting thus as a nanobiossensor[1]. The potential of mean force (PMF) method is a practical method that can be used to analyze the intermolecular interactions in protein-ligand systems. In this study PMF calculations were performed for determination of the absolute binding free energies for (EPSPs, Shikimate-3-phosphate)-Glyphosate system (figure 1) in order to mimic the interaction between the AFM tip functionalized with the EPSP enzyme and glyphosate.

METHODS

Calculations were performed with the software program GROMACS 4.6[2] using the NPT ensemble (1 bar and 298K) for 4ns in vacuum. The PMF calculations were carried out using Sterred Molecular Dynamics (SMD) applying to the distance constraints between the GPJ and active site of EPSPs(S3P) a force constant of 367 $kJ.mol^{-1}.nm^{-1}$, with a constant velocity of 0.001 $nm.ps^{-1}$.

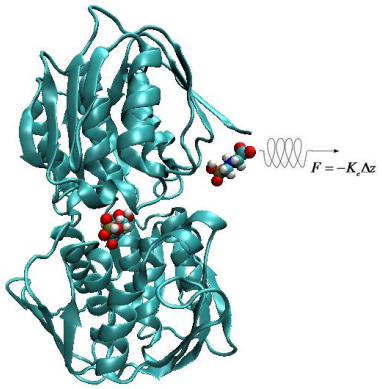

Figure 1: Possible unbinding pathway of glyphosate from the EPSPs active site.

RESULTS AND DISCUSSION

The figure 2 shows the force-extension profiles of the interaction between GPJ and active site EPSPs with the presence of S3P substrate. It is observed that the maximum of force necessary required to remove the herbicide from active site occurs around 2500 $KJ.mol^{-1}.nm^{-1}$ around 500 ps, from the start of the simulation, which can be attributed to the moment of rupture of the main interactions between residues of enzyme and S3P with the GPJ.

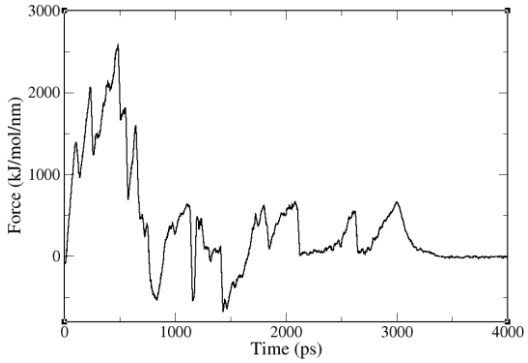

Figure 2: SMD force-extension profiles between GPJ and active site EPSPs-(S3P).

CONCLUSIONS

Obtaining the force of interaction between the GPJ herbicide and the active site of EPSPs-S3P will provide comparative information of the sensitivity of this new biosensor.

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