

Accepted Manuscript

Research paper

Determination of the absolute binding free energies of HIV-1 protease inhibitors using non-equilibrium molecular dynamics simulations

Son Tung Ngo, Minh Tung Nguyen, Minh Tho Nguyen

PII: S0009-2614(17)30253-1

DOI: <http://dx.doi.org/10.1016/j.cplett.2017.03.034>

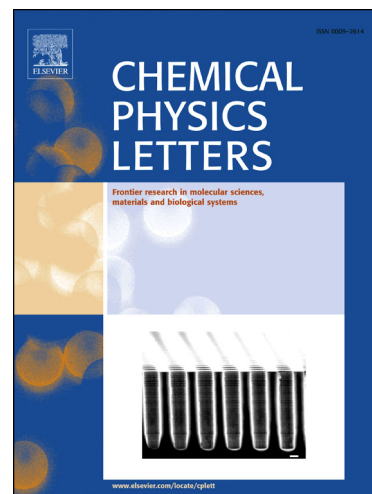
Reference: CPLETT 34634

To appear in: *Chemical Physics Letters*

Received Date: 9 January 2017

Revised Date: 9 March 2017

Accepted Date: 13 March 2017



Please cite this article as: S.T. Ngo, M.T. Nguyen, M.T. Nguyen, Determination of the absolute binding free energies of HIV-1 protease inhibitors using non-equilibrium molecular dynamics simulations, *Chemical Physics Letters* (2017), doi: <http://dx.doi.org/10.1016/j.cplett.2017.03.034>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Determination of the absolute binding free energies of HIV-1 protease inhibitors using non-equilibrium molecular dynamics simulations

Son Tung Ngo,^{ab,*} Minh Tung Nguyen,^c Minh Tho Nguyen^{abd,*}

^a*Computational Chemistry Research Group, Ton Duc Thang University, Ho Chi Minh City, Vietnam*

^b*Faculty of Applied Sciences, Ton Duc Thang University, Ho Chi Minh City, Vietnam*

^c*Binh Duong University, Thu Dau Mot City, Binh Duong Province, Vietnam*

^d*Department of Chemistry, KU Leuven, Celestijnenlaan 200F, B-3001 Leuven, Belgium.*

Abstract

The absolute binding free energy of an inhibitor to HIV-1 Protease (PR) was determined throughout evaluation of the non-bonded interaction energy difference between the two *bound* and *unbound* states of the inhibitor and surrounding molecules by the fast pulling of ligand (FPL) process using non-equilibrium molecular dynamics (NEMD) simulations. The calculated free energy difference terms help clarifying the nature of the binding. Theoretical binding affinities are in good correlation with experimental data, with $R = 0.89$. The paradigm used is able to rank two inhibitors having the maximum difference of ~ 1.5 kcal/mol in absolute binding free energies.

Keywords: Fast pulling of ligand approach; HIV-1 PR; NEMD simulations; absolute binding affinity; interaction energy; pulling work;

1. Introduction

The binding free energies between proteins and their inhibitors are of great interest in part due to their role in the understanding of biophysical problems [1]. Several methods were established to evaluate the protein-ligand binding affinity including the thermodynamic integration (TI) [2], free energy perturbation (FEP) [3],

* Corresponding author. Tel.: +84 – 8 – 37 755 035; fax: +84 – 8 – 37 755 055.

E-mail addresses: ngosontung@tdt.edu.vn (Son Tung Ngo); nguyenminhtho@tdt.edu.vn & minh.nguyen@kuleuven.be (Minh Tho Nguyen)

Download English Version:

<https://daneshyari.com/en/article/5377916>

Download Persian Version:

<https://daneshyari.com/article/5377916>

[Daneshyari.com](https://daneshyari.com)