Analysis of Binding Energies between Luciferin and Luciferase Adsorbed on Si Surface by Docking Simulations

Katsuhiko Nishiyama ^{a,*}, Takanobu Watanabe ^b,
Tadatsugu Hoshino ^c, Iwao Ohdomari ^b

^a*Tsuruoka National College of Technology, 104 Sawada, Inooka, Tsuruoka City,
Yamagata 997-8511, Japan*

^b*Waseda University, 3-4-1 Ohkubo, Shinjuku-ku, Tokyo 169-8555, Japan*

^c*Chiba University, 1-33 Yayoi-cho, Inage-ku, Chiba 263-8522, Japan*

Abstract

The binding energies between luciferin and luciferase adsorbed on a Si surface were estimated by docking simulations. These binding energies were more stable on a hydrophilic Si surface than on a hydrophobic Si surface, but their difference was small. Luciferase adsorbed more strongly on the hydrophobic Si surface than on the hydrophilic Si surface. The luciferase active site was not covered by the Si surface in this adsorption state. The hydrophobic surface would be suitable for the immobilization of luciferase both from the viewpoints of the binding of luciferin to luciferase and the adsorption of luciferase to the Si surface.

Key words: luciferase, Si surface, nanostructure, docking simulations, biomedical application, protein chip

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1 Introduction

The inactivation of enzymes immobilized on solid surfaces is a severe problem for biomedical applications, such as biosensors and bioreactors, because the sensitivity of biosensors and the reaction efficiency of bioreactors are depend on enzymatic activity intensity[1,2]. Certain reports have indicated that enzymes are linked on solid surfaces via organic molecules in order to avoid inactivation[3,4]. These methods are feasible if these organic molecules do not inhibit enzymatic activities. Current Si-process technology enabled us to fabricate a nanostructure array on a Si surface[5,6]. The delicate control of surface conditions, such as hydrophobic or hydrophilic properties, is also available owing to the recent progress of wet treatment technology for Si. Therefore, a Si surface with a nanofabricated and wet-treated array may be compatible with many types of enzyme. The purposes of our study are to clarify the inactivation mechanism of an enzyme on an artificial surface and to determine surface conditions suitable for immobilization. In our previous study, we analyzed the interactions between luciferase and a Si surface by molecular dynamics (MD) simulation[7]. Results showed that the adsorption-induced changes in the structure of luciferase are larger on the hydrophobic Si surface than on the hydrophilic Si surface. In this study, we analyzed the binding energies between luciferin, the substrate for luciferase, and luciferase adsorbed on the Si surface by docking simulations (Fig. 1). Here, we report the binding energies between luciferin and luciferase adsorbed on the Si surface and surface conditions suitable for the immobilization of luciferase.

* Corresponding author. phone number +81-235-25-9076, fax number +81-235-24-1840

Email address: `nisiyama@asagi.waseda.jp` (Katsuhiko Nishiyama).

Fig. 1. Binding between luciferin and luciferase adsorbed on Si surface.

2 Methods

The docking simulations between luciferin and luciferase were performed using AutoDock3.0[8]. AutoDock3.0 is a suite of programs, making it possible to predict how ligands bind to macromolecules. The Lamarckian genetic algorithm (LGA) was used as a search engine. The step sizes of 0.1 nm for translation and 50 degrees for rotation were chosen. For each of the 100 independent runs, 10000 LGA operations were generated on a single population of 50 individuals. Operator weights for crossover, mutation, and elitism were set to be 0.80, 0.02, and 1, respectively. The Solis and Wets algorithm was used as a local search method in the LGA and the contraction and expansion factors were set to be 0.5 and 2.0, respectively. The structural data for luciferase was derived from our previous MD simulation results[7]. The structural data for luciferin was created on the basis of Hartree-Fock molecular orbital calculations using the program package Gaussian 98[9]. The binding states between luciferin and luciferase were explored within the luciferase active site (residues 218, 246, 247, 251, 315, 341, 342, 343, 347, 348, 351, and 529). Figure 2 shows the luciferase active site.

Fig. 2. Luciferase active site (highlighted).

3 Results and Discussion

We performed the docking simulations of luciferin to luciferase_{isolated} (luciferase isolated in water), to luciferase_{hydrophobic} (luciferase adsorbed on a hydrophobic Si surface), and to luciferase_{hydrophilic} (luciferase adsorbed on a hydrophilic Si surface). Figure 3 shows the binding energies of luciferin to luciferase_{isolated}, to luciferase_{hydrophobic}, and to luciferase_{hydrophilic}.

Fig. 3. Binding energies of luciferin to luciferase when isolated (a), adsorbed on hydrophobic surface (b), and adsorbed on hydrophilic surface (c).

The time averages of the binding energies were -9.71 kcal/mol for luciferase_{isolated}, -8.41 kcal/mol for luciferase_{hydrophobic}, and -8.62 kcal/mol for luciferase_{hydrophilic}. The time standard deviations of the binding energies were 0.73 kcal/mol for luciferase_{isolated}, 0.80 kcal/mol for luciferase_{hydrophobic}, and 0.90 kcal/mol for luciferase_{hydrophilic}. Figure 4 shows the Gaussian distributions of these binding

energies.

Fig. 4. Gaussian distributions of binding energies of luciferin to luciferase when isolated (a), adsorbed on hydrophobic surface (b), and adsorbed on hydrophilic surface (c).

These results show that the binding energies of luciferin are more stable for luciferase_{isolated} than for luciferase adsorbed on the Si surface. These results also show that the binding energies of luciferin are more stable for luciferase_{hydrophilic} than for luciferase_{hydrophobic}, but their difference is small. Enzymatic activity should be modified by the deformation of an enzyme active site. Luciferase adsorbed more strongly on the hydrophobic Si surface than on the hydrophilic Si surface[7]. In these adsorption states, a luciferase surface area with a relatively high hydrophobicity contacted the Si surface, and the luciferase active site was not covered by the Si surface[7]. Therefore, the hydrophobic surface would be suitable for the immobilization of luciferase. In a future study, we will perform the docking simulations between luciferin and luciferase adsorbed on the nanofabricated Si surfaces.

4 Conclusions

The binding energies between luciferin and luciferase were more stable on a hydrophilic Si surface than on a hydrophobic Si surface, but their difference was small. Enzymatic activity should be modified by the deformation of an enzyme active site. Luciferase adsorbed more strongly on the hydrophobic Si surface than on the hydrophilic Si surface. The luciferase active site was not covered by the Si surface in this adsorption state. The hydrophobic surface would be suitable for the immobilization of luciferase both from the viewpoints of the binding of luciferin to luciferase and the adsorption of luciferase to the Si surface.

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* Graphical Abstract (synopsis)

The binding energies between luciferin and luciferase adsorbed on a Si surface were estimated by docking simulations.