Abstract

The survival strategy of bacteria depends on its capability to adapt and respond to the ever-changing environmental conditions. This specific skill of bacteria to respond to chemicals is called chemotaxis and is possible by the run and tumble motion as guided by the rotational direction of the bacterial flagella. The bacterial flagellar motor consists of rotor and stator. Bacterial flagella can rotate either in counterclockwise (CCW) or clockwise (CW) direction, which is governed by the conformational states of the motor (i.e., rotor and stator) proteins located at the base of flagella.

This dissertation focuses on the construction of protomer unit of the flagellar switch complex. The asymmetry between 26 copies of FliG and 34 copies of FliM has also been attempted to solve using the developed protomer unit. The switch complex assembly fulfilling the experimentally available geometric constraints has been built to understand the molecular mechanism behind the bacterial flagellar switching. The diameter of our assembled switch complex rotor ring corroborates with Morimoto and Minamino(Biomolecules (2014) **4**, pp 217-234). Our arrangement of protomer units across the flagellar cross-section finds a closer resemblance with the conformational spread model. Normal mode analysis results helped us to propose the mechanism of flagellar switching.

Next, we propose a computational framework by combining two orthogonal approaches (namely, sequence-based and structure-based) to identify critical residues responsible for protein interactions. Our proposed technique has been successfully tested on the phosphate sink mechanism of CheV in *Bacillus subtilis* (*B. subtilis*), suggesting that the phosphate sink property of CheV is being affected by single point mutations in the critical residues of wild-type CheV. The novelty of our advanced method lies in the identification of Ala41, which being apart from the phosphate binding site can significantly reduce the binding affinity from 9.2 for wild-type to -16.9. We designed stable mutants of the CheC-CheD complex in *B. subtilis* which will function similar to the wild-type CheC-CheD complex, in order to understand the CheC-CheD system in the adaptation mechanism.

Finally, we propose an advanced machine learning based phosphorylation site prediction method to identify protein phosphorylation sites using amino acid specific features as input. Our proposed computational approach implements a lightGBM algorithm using evolutionary, structural, sequence environment, and amino acid specific features to predict phosphorylation sites. Our approach proved to be much better than existing machine learning and deep learning based methods. Our method is useful in identifying phosphorylation sites of chemotaxis proteins, and hence, will assist to further explore molecular mechanism for bacterial chemotaxis.

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