Chapter 29
Molecular Modelling, Dynamics, and Docking of Membrane Proteins: Still a Challenge

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ABSTRACT

Computational tools and techniques are now most popular and promising to progress the research at rapid rate. Molecular modelling studies contribute their maximum role in wide variety of disciplines especially in proteomics and drug discovery strategies. Molecular dynamics and molecular docking algorithms are now became an essential part in daily research activities of every laboratory throughout the world. These strategies are now well established and standardised to study any specific protein of interest and drug molecule. But still there exist considerable drawbacks in a special concern with membrane proteins as the presently available tools and methods cannot be applied directly to them. Modelling, dynamics and docking studies of membrane proteins need a special care and attention as several challenges are to be crossed with an intensive care to produce a reliable result. This chapter is aimed to discuss such challenges and solutions to handle membrane proteins.

INTRODUCTION

Membrane Proteins

Cell membranes are the most indispensable attributes of any living organisms that safeguard the integrity of a cell by wrapping around. It acts as a potential barrier to perform several physiological functions by offering complex molecular machineries. These multifarious functions and mechanisms of membranes are facilitated and regulated by an inimitable group of proteins called as membrane proteins which are

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of both surface and integral types (Figure 1). They play a vital role as channels for the transport of ions and molecule to meet the regular demands of biochemical functions (Cooper, 2000).

The structural and functional characterization of membrane proteins is typically a thorny task as the difficulties are associated with providing membrane environment that limits the purification and crystallization. Recent advancement in the technologies has led to the structural and functional characterization of several membrane proteins by providing their experimental structural information (Tatulian, 2000). But still it is not meeting the required demand as presently only *2%* of membrane protein structures were solved. Such demanding situations paved a spectacular way for the construction of membrane protein models through computational modelling methods (Arinaminpathy et al., 2009). There exist very narrow traditions to construct the protein models but providing an immense support to the structural biologists (Lacapère et al., 2007). Such ways even relies on the experimental data of pre-existing proteins (Ash et al., 2004). Such methods are incredibly known as homology modelling methods; nevertheless homology modelling also fails many times with membrane models as the availability of experimental data for them is very limited. Construction of such models remains as a challenge when the subject of protein is very demanding and necessitous. This chapter is going to describe how such situations will overcome. Stepwise recurrent methodologies with unequivocal and particularized algorithms can be followed where the propensities of amino acids can be utilized to construct the membrane protein models where *de novo* modelling is one of the methods comes under this technology. Even, this also never solve the problem entirely, as this idea works out well with the small proteins and still leavening the challenge unsolved as the membrane proteins usually bigger in size. This chapter will further deals, how the larger size membrane protein models are constructed. The constructed models must represent or resemble a natural conformation so as to mimic the experimental model. How it can be made? Still another chal-

Figure 1. Membrane and membrane proteins; their significant role as transporters and signal transducers