Continuum descriptions of membranes and their interaction with proteins: towards chemically accurate models

David Argudo, Neville P. Bethel, Frank V. Marcoline, Michael Grabe

PII: S0005-2736(16)30033-5
DOI: doi: 10.1016/j.bbamem.2016.02.003
Reference: BBAMEM 82128

To appear in: *BBA - Biomembranes*

Received date: 19 December 2015
Revised date: 30 January 2016
Accepted date: 1 February 2016

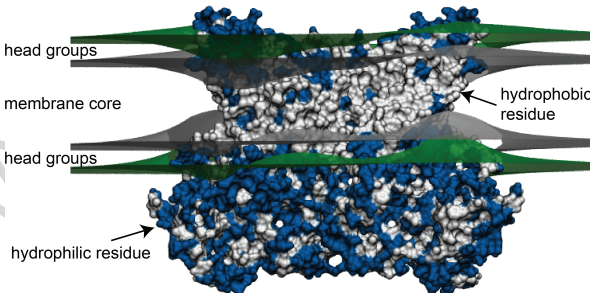
Please cite this article as: David Argudo, Neville P. Bethel, Frank V. Marcoline, Michael Grabe, Continuum descriptions of membranes and their interaction with proteins: towards chemically accurate models, *BBA - Biomembranes* (2016), doi: 10.1016/j.bbamem.2016.02.003

Continuum descriptions of membranes and their interaction with proteins: towards chemically accurate models

David Argudo*, Neville P. Bethel*, Frank V. Marcoline, Michael Grabe**

Cardiovascular Research Institute, Department of Pharmaceutical Chemistry, University of California San Francisco, San Francisco, CA 94158

Abstract



Biological membranes deform in response to resident proteins leading to a coupling between membrane shape and protein localization. Additionally, the membrane influences the function of membrane proteins. Here we review contributions to this field from continuum elastic membrane models focusing on the class of models that couple the protein to the membrane. While it has been argued that continuum models cannot reproduce the distortions observed in fully-atomistic molecular dynamics simulations, we suggest that this failure can be overcome by using chemically accurate representations of the protein. We outline our recent advances along these lines with our hybrid continuum-atomistic model, and we show the model is in excellent agreement with fully-atomistic simulations of the nhTMEM16 lipid scramblase. We believe that the speed and accuracy of continuum-atomistic methodologies will make it possible to simulate large scale, slow biological processes, such as membrane morphological changes, that are currently beyond the scope of other computational approaches.

Highlights

- The evolution of continuum elastic models of the membrane is briefly outlined.
- Membrane elastic models need to incorporate protein's chemistry and geometry.
- A fast and accurate hybrid continuum-atomistic model is proposed.
- Hybrid model reveals extreme bending of the membrane in the presence of nhTMEM16.

Keywords: A. biological membrane, B. bilayer, C. electrostatics, D. transmembrane protein, E. hydrophobic mismatch

1. Introduction

Biological membranes are crowded with transmembrane proteins and peripherally associated proteins that carry out a host of tasks ranging from ion and small molecule transport to cell motility. The distribution of proteins is

*Authors contributed equally
**Corresponding author
Email address: michael.grabe@ucsf.edu (Michael Grabe)
[1]Phone: 415-502-2874