

Free-binding energies and molecular interactions of yessotoxin in the voltage-gated sodium channel Na_v1.5: an *in silico* approach



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INTRODUCTION

Several marine dinoflagellates produce unique secondary metabolites with intriguing biological activities. Yessotoxin (YTX) and analogs are produced by three species of marine dinoflagellates, with potent ion-channel activity. This study aimed to evaluate the affinity of YTX for the Na_v1.5 channel, using *in silico* modelling tools.

MATERIALS AND METHODS

Primary channel structure

UniProt
Q14524
Homo sapiens

Sequence search

Swiss model
<https://swissmodel.expasy.org/>

Homology modeling

Alignment Selection Coverage

Basic and theoretical structure

Molecular Docking

Blind docking

AutoDockTools
Triplicates

126 x 126 x 126 Å
Binding free energy

Conformations

Data analysis
AutoDock Tools 1.5.6

Interactions

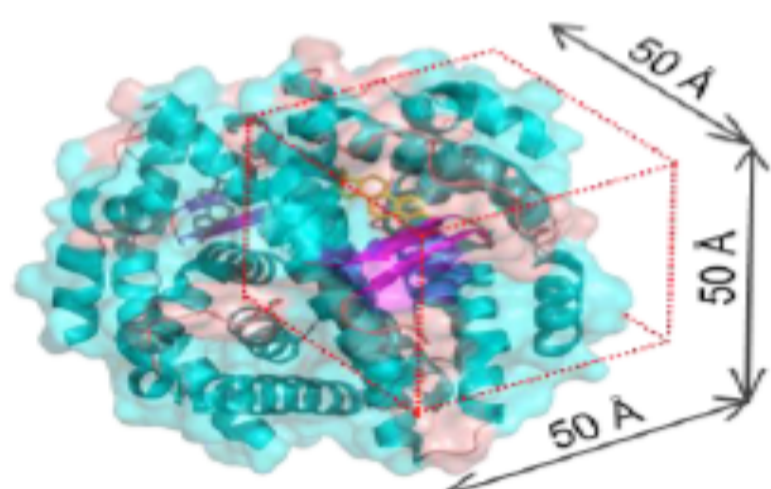
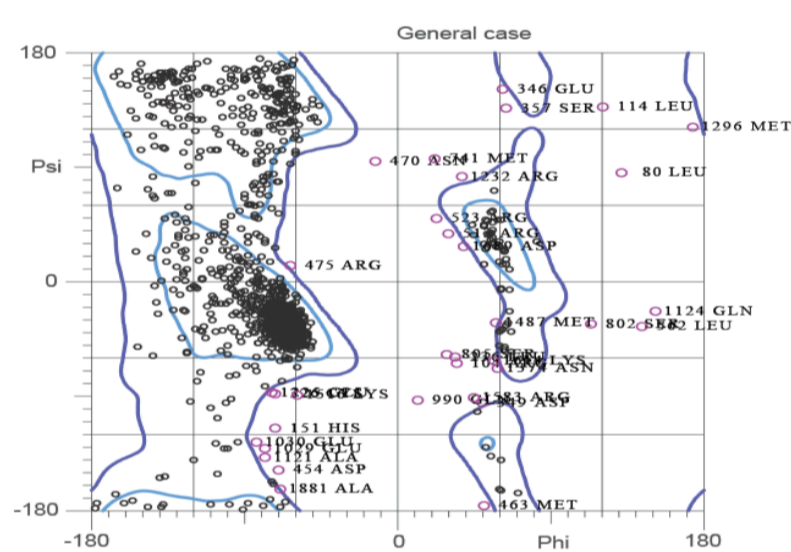


Characterization & validation

Model refinement

Structural validation

Functional validation



Region 1

Region 2

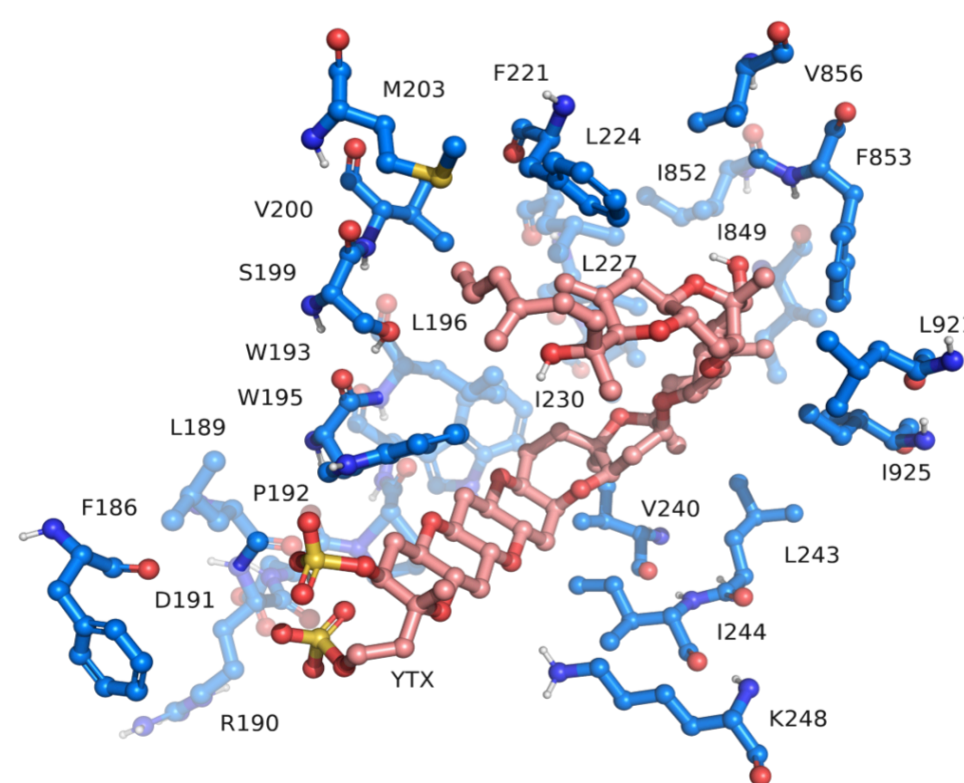
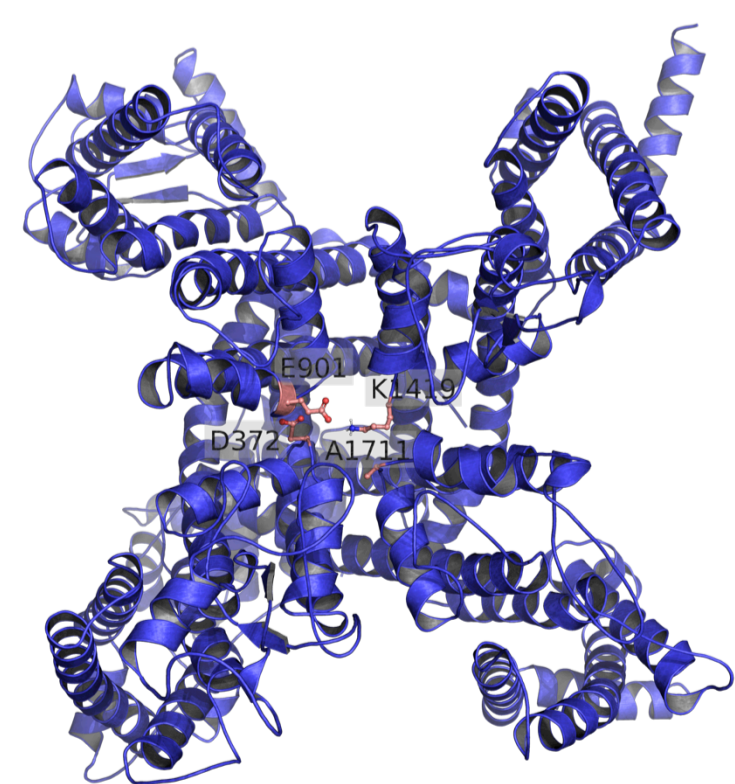
Region 5

Region 3

Region 4

RESULTS

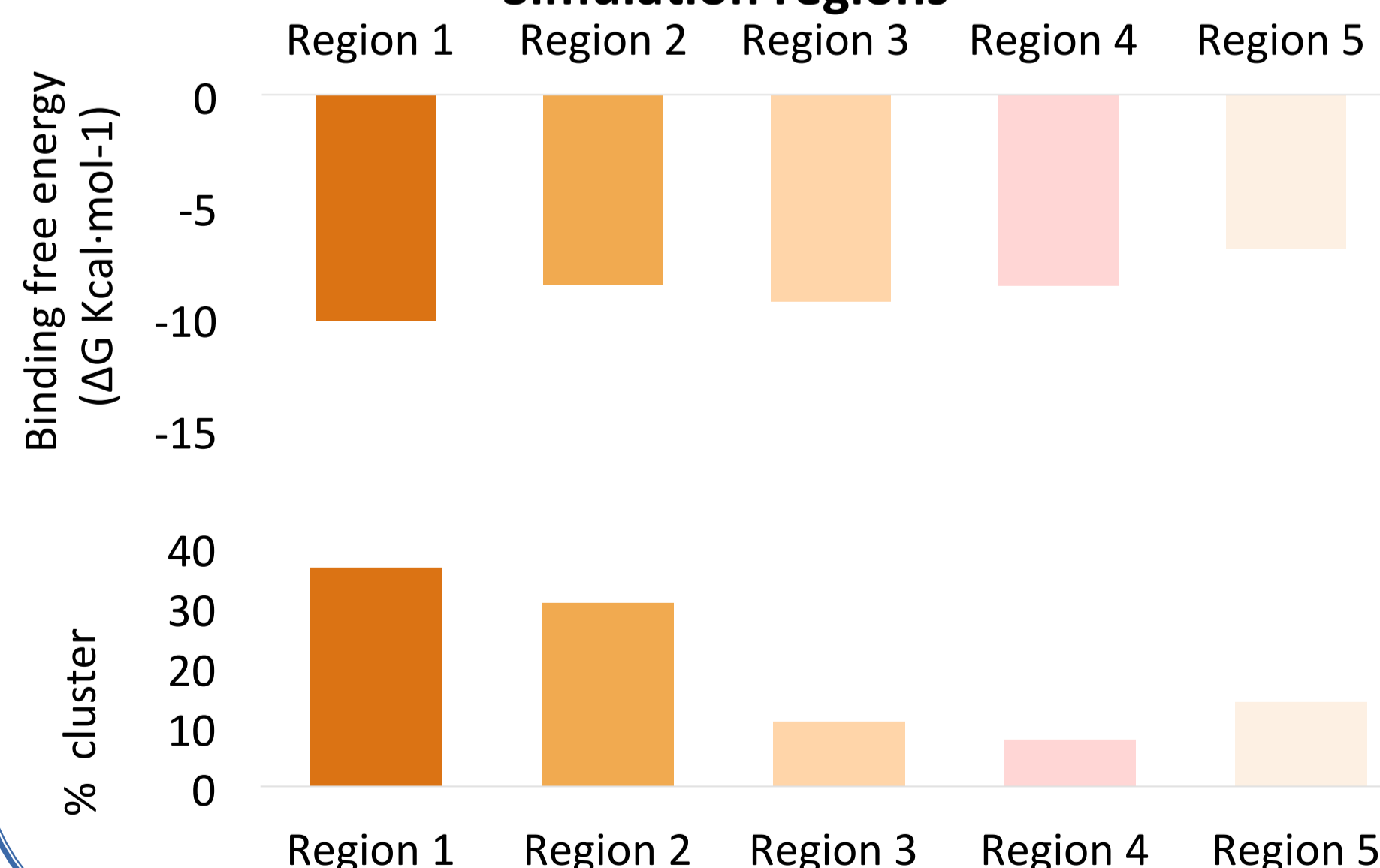
Average $\Delta G = -10.3 \text{ Kcal mol}^{-1}$



Interaction of YTX in DI and DII of Na_v1.5. YTX (pink) and different amino acids (blue)

Significant interactions and low binding free energies (ΔG), between -6.79 and $-10.32 \text{ Kcal mol}^{-1}$ for YTX in the Na_v1.5 protein model. Certain amino acid residues in Domains I and II were reached, indicating that this toxin is a potential Na_v1.5 modulator.

Simulation regions



This study constitutes the first approach to *in silico* exploration of polyketide-derived dinoflagellate toxins in pursuit of evaluating their therapeutic potential.

Thanks to:



What's next? To understand the effects of YTX on the voltage-gated sodium channel different studies are needed, i.e. electrophysiology and molecular dynamics analyses