Pore dynamics and conductance of RyR1 transmembrane domain

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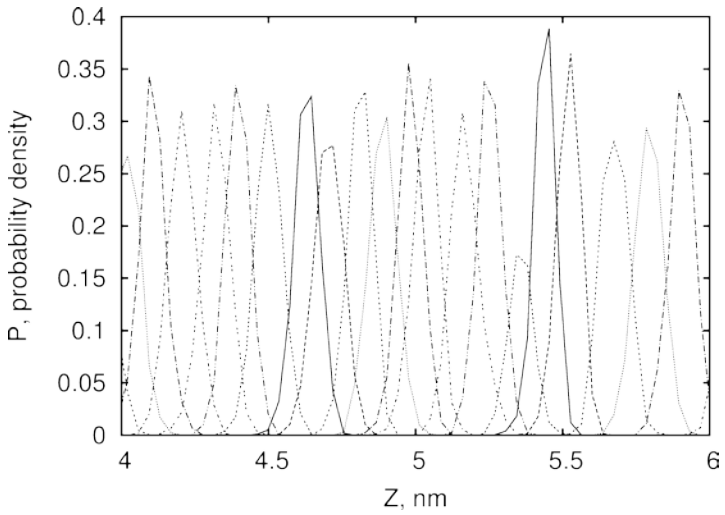
Supporting Materials



Supporting Figure 1. WHAM histograms for ion position sampled within selectivity filter region. Each peak corresponds to the average position of a probe ion obtained in an independent umbrella sampling simulation. Probe ion spacing is 0.1 nm, mean square magnitude of position fluctuations is 0.005 nm^2. Probe positions were sampled every 0.3 ps in the course of 1.5 ns simulations. WHAM analysis was performed using tools provided by the GROMACS suite.

Restraints applied during simulation

; residue indexes correspond to .

; restraints.itp

[distance_restraints]
; ai aj type index type' low up1 up2 fac

; S4-S5 bend

; M4839/O -> L4843/N

1766 1804 1 2 1 0.34 0.60 0.90 2.0

; T4840/O -> L4844/N

1780 1823 1 3 1 0.60 0.62 0.90 2.0

; V4841/O -> A4845/N

1796 1842 1 4 1 0.60 0.62 0.90 2.0

; G4842/O -> V4846/N

1803 1852 1 5 1 0.34 0.60 0.90 2.0

; S6 bend

; L4928/O -> I4932/N

3189 3238 1 6 1 0.43 0.52 0.90 2.0

; L4929/O -> Q4933/N

3208 3257 1 7 1 0.28 0.35 0.60 2.0

; A4930/O -> G4934/N

3218 3274 1 8 1 0.41 0.50 0.90 2.0

; I4931/O -> L4935/N

3237 3281 1 9 1 0.55 0.65 0.90 2.0

; I4932/O -> I4936/N

3256 3300 1 10 1 0.37 0.45 0.90 2.0

Simulation parameters

; RyR1.mdp

```
title= NPT compression and equilibration for RyR-POPC

; Run parameters
; BD ; md = leap-frog integrator
integrator                = md

;3 * 6000000 = 18000 ps
nsteps          = 6000000

; Time step 3 fs
dt                        = 0.003

; Output control
nstxout         = 10000
nstxtcout                 = 1000
nstvout         = 0
nstenergy                 = 100
nstlog          = 100

continuation    = no

; Bond parameters
constraint_algorithm = lincs
constraints               = all-bonds
lincs_iter                = 1
lincs_order               = 4

; Neighborsearching
ns_type         = grid
nstlist         = 20
rlist                     = 1.2
rcoulomb                  = 1.2
rvdw                      = 1.2
cutoff-scheme   = Verlet

; Electrostatics
coulombtype               = PME
pme_order                 = 4
fourierspacing  = 0.144

; Temperature coupling is on
bd_fric         = 0
ld_seed         = -1
tcoupl          = V-rescale

; three coupling groups - more accurate
tc-grps         = Protein POPC Water_and_ions
tau_t           = 0.1     0.1       0.1
; reference temperature, one for each group, in K
ref_t           = 300     300       300

; Pressure coupling
pcoupl          = berendsen
; only along x-y
pcoupltype                = semiisotropic
tau_p           = 5.0
ref_p           = 1.0 1.0
compressibility = 4.5e-5 4.5e-5

; Periodic boundary conditions: 3-D PBC
pbc             = xyz

; Dispersion correction, account for cut-off vdW scheme
```

```
DispCorr        = EnerPres

; Velocity generation
; assign velocities from Maxwell distribution
gen_vel         = yes
gen_temp        = 300
gen_seed        = -1

; COM motion removal
; These options remove motion of the protein/bilayer relative to the solvent/ions
nstcomm                 = 100
comm-mode       = Linear
comm-grps       = Protein_POPC Water_and_ions

; Compressed XTC output: only protein and ions
xtc_grps= Protein-H Ion

; distance restraints
disre           = simple
disre_fc = 480
disre_tau       = 0

; PMF calculation, umbrella sampling
pull                    = umbrella
; pull probe ion relative to the protein center of mass
pull_geometry   = position
; pull only along Z axis
pull_dim                = N N Y
; write distance every 0.3 ps
pull_nstxout    = 100
; write force every 0.3 ps
pull_nstfout    = 100
; pull 3 group (of 3 ions)
pull_ngroups    = 3
; reference group is the protein
pull_group0             = Protein
; name of the probe ion group in the index file
pull_group1             = Ion1
; 240 kJ/mole/nm^2 is ~ 1 kT / A (for harmonic umbrella potential)
pull_k1         = 960
; do not add the COM distance of the starting conformation to pull_init
pull_start              = no
; start at configuration defined distance from protein COM, the full range will be from -3.5 to 2.5
pull_init1              = 0.0 0.0 -1.4
; no drag
pull_rate1              = 0
; pull along Z axis
pull_vec1               = -1.0 -1.0 -1.0
; O atom in GLY172, near the protein COM
pull_pbcatom0   = 2647
```