Atomistic Models of General Anesthetics for use in *In Silico* Biological Studies

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Table S1: Summary of Recent Molecular Dynamics Simulations Utilizing Anesthetics

Summary	Anesthetic	Force Field	Parameter Reference
Interaction of Propofol with an apoferritin dimer[1]	Propofol	CHARMM	—
Parameterization of Isoflurane and free energy of binding to apoferritin[2]	Isoflurane	CHARMM	—
Interaction of Halothane with $\alpha 4\beta 2$ nAChR model[3]	Halothane	CHARMM	[4]
Flooding of GLIC with Isoflurane[5]	Isoflurane	CHARMM	[2]
Dynamics of GLIC with bound Isoflurane[6]	Isoflurane	CHARMM	[2]
Free energy of Propofol binding to GLIC[7]	Propofol	CHARMM	—
Effect of Propofol Stoichiometry on GLIC dynamics[8]	Propofol	CHARMM	—
Testing the effects of Propofol on GLIC mutants[9]	Propofol	CHARMM	[8]
Flooding of voltage-gated Na^+ channel, NaChBac, with Isoflurane[10]	Isoflurane	CHARMM	[2]
Free energy of binding to GLIC and GLIC mutants[11]	Desflurane Halothane	GROMOS	—
Flooding of Na^+ channel, NaChBac, with Sevoflurane[12]	Sevoflurane	CHARMM	—

A literature search for articles published within the last 5 years was conducted in PubMed using the keywords "desflurane", "isoflurane", "sevoflurane", "propofol", "anesthesia", and "anesthetic" in conjunction with "molecular dynamics". Here, the title of the article is presented along with the anesthetic used and force field. Those entries with "—" in "Parameter Reference" signify that the parameters used in the paper were developed in the same study.

Table S2: Comparison of Computed Physicochemical Properties Employing Previously Parameterized Models and Those Developed in this Study.

Anesthetic		Dipole (D)	Density (g/mL)	ΔH_{vap} (kcal/mol)
Isoflurane[a]	Previous	1.38 (-44.5%)	1.53±0.01 (2.7%)	8.48±0.03 (11.43%)
	Present	2.91 (17.8%)	1.48±0.02 (-0.7%)	8.03±0.01 (5.5%)
Propofol[b]	Previous	2.02 (26.3%)	0.93±0.01 (9.7%)	15.82±0.02[c]
	Present	1.92 (20%)	0.98±0.01 (-4.8%)	16.27±0.05

Calculated values for dipole moment, density and heat of vaporization are presented for both the previously parameterized model (Previous) and the currently developed models (Present) with the percent error from experimental values shown in parenthesis. The geometry optimized molecule with the optimized charge distribution was utilized to calculate the dipole moment. Again, it should be noted that the values for the *in silico* models should be 10-20% higher than experimental measurements to reproduce condensed phase properties. The density and heat of vaporization are presented mean±S.D. calculated across five replicates.

a. Calculated physicochemical properties are done using the parameters from Hénin, *et al.*[2]

b. Calculated physicochemical properties are done using the parameters from LeBard, *et al.*[7]

c. Due to the high boiling point of propofol (529K), the heat of vaporization varies widely as discussed in the Results section.

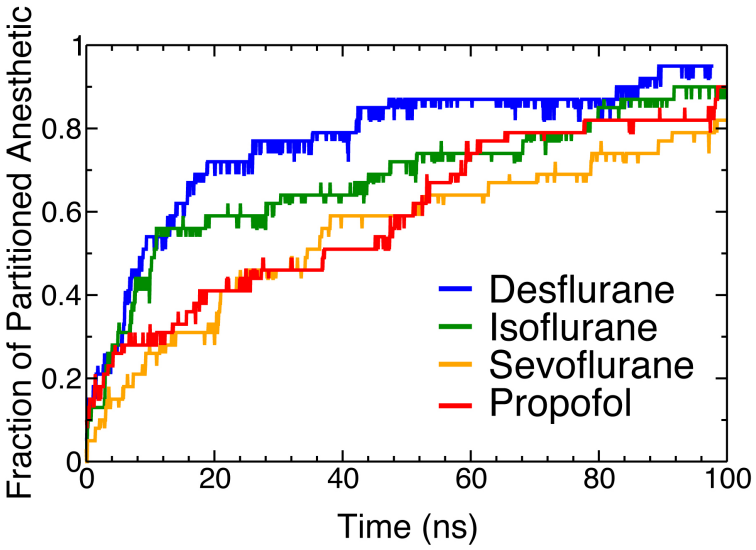

Figure S1: Plot of the fraction of desflurane (blue), isoflurane (green), sevoflurane (orange), and propofol (red) partitioned into the POPC membrane as a function of time.

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