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 dimer¹       | Propofol   | CHARMM      | —                   |
| Parameterization of Isoflurane and free energy of binding to apoferritin² | Isoflurane | CHARMM      | —                   |
| Interaction of Halothane with α4β2 nAChR model³         | Halothane  | CHARMM      | ¹                   |
| Flooding of GLIC with Isoflurane⁴                        | Isoflurane | CHARMM      | ²                   |
| Dynamics of GLIC with bound Isoflurane⁵                  | Isoflurane | CHARMM      | ²                   |
| Free energy of Propofol binding to GLIC⁶                 | Propofol   | CHARMM      | —                   |
| Effect of Propofol Stoichiometry on GLIC dynamics⁷       | Propofol   | CHARMM      | —                   |
| Testing the effects of Propofol on GLIC mutants⁸         | Propofol   | CHARMM      | ⁸                   |
| Flooding of voltage-gated Na⁺ channel, NaChBac, with Isoflurane¹⁰ | Isoflurane | CHARMM      | ²                   |
| Free energy of binding to GLIC and GLIC mutants¹¹        | Desflurane | GROMOS      | —                   |
| Flooding of Na⁺ channel, NaChBac, with Sevoflurane¹²     | 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.
| Anesthetic   | Previous | Present  | Density (g/mL) | ∆H_vap (kcal/mol) |
|-------------|----------|----------|----------------|------------------|
| Isoflurane^a| 1.38 (-44.5%) | 2.91 (17.8%) | 1.53±0.01 (2.7%) | 8.48±0.03 (11.43%) |
| Propofol^b  | 2.02 (26.3%) | 1.92 (20%)   | 0.93±0.01 (9.7%) | 15.82±0.02^c      |

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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