|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Table S1**: Proximity of isoflurane to residues within each site. | | | | | | | |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |
| **Extracellular Site** | | |  |  |  | **Cavity Site** | |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |
| **Residue** | **a** | **b** | **c** | **d** |  | **Residue** | **a** | **b** | **c** | **d** |
| **E172** | 95 | 82 | 82 | 86 |  | **T220** | 97 | 93 | 77 | 82 |
| **L179** | 98 | 97 | 84 | 87 |  | **F227** | 79 | 73 | 84 | 71 |
| **L182** | 100 | 100 | 100 | 93 |  |  |  |  |  |  |
| **Q186** | 100 | 100 | 100 | 92 |  | **Fenestration Site** | |  |  |  |
| **W193** | 20 | 35 | 36 | 33 |  |  |  |  |  |  |
| **A194** | 92 | 100 | 100 | 100 |  | **Residue** | **a** | **b** | **c** | **d** |
| **M198** | 92 | 100 | 100 | 100 |  | **F185** | 55 | 17 | 55 | 84 |
| **R199** | 94 | 99 | 100 | 94 |  | **V188** | 61 | 35 | 55 | 90 |
| **F202** | 94 | 100 | 100 | 100 |  | **T189** | 65 | 40 | 56 | 91 |
|  |  |  |  |  |  | **L190** | 75 | 74 | 60 | 67 |
| **Linker Site** | |  |  |  |  | **L217** | 92 | 87 | 31 | 88 |
|  |  |  |  |  |  | **T220** | 54 | 62 | 46 | 77 |
| **Residue** | **a** | **b** | **c** | **d** |  | **I223** | 87 | 78 | 85 | 98 |
| **L133** | 1 | 0 | 89 | 100 |  | **F224** | 100 | 98 | 93 | 94 |
| **A136** | 0 | 0 | 73 | 100 |  | **L226** | 72 | 4 | 43 | 91 |
| **L137** | 11 | 0 | 87 | 99 |  |  |  |  |  |  |
| **I147** | 100 | 0 | 5 | 88 |  | **Key:** | <10% occupancy | | |  |
| **N225** | 100 | 0 | 0 | 90 |  |  | 40-80% occupancy | | |  |
| **N234** | 1 | 0 | 89 | 93 |  |  | > 80% occupancy | | |  |
|  |  |  |  |  |  |  |  |  |  |  |
| Numbers shown here are the percent of frames in which isoflurane was within 5A of each residue listed, color coding sorts residues by non-interacting (red), possibly interacting (orange) and likely-interacting (green) based on persistence of isoflurane proximity (see key). To estimate the persistence of isoflurane proximity to residues that make up each site, we selected residues that were within 5A of the protein during *any* frame and then asked whether they were within 5A for *each* frame over the last 250 ns of trajectory. This was done separately for each subunit (a-d) to account for asymmetry. | | | | | | | | | | |