

## Functional Movements of the GABA type A Receptor

Csilla Várnai<sup>1,2</sup>  
Babraham Institute  
Cambridge CB22 3AT, U.K.

B.W.J. Irwin<sup>2</sup>, M.C. Payne  
Theory of Condensed Matter Group, Cavendish Laboratory  
Department of Physics, University of Cambridge  
Cambridge CB3 0HE, U.K.

Gábor Csányi  
Department of Engineering, University of Cambridge  
Cambridge CB2 1PZ, U.K.

P.-L. Chau<sup>3</sup>  
Bioinformatique Structurale, Institut Pasteur  
CNRS URA 3528, CB3I CNRS USR 3756, 75724 Paris, France

June 9, 2020

<sup>1</sup>present address: Centre for Computational Biology, University of Birmingham, Birmingham B15 2TT U.K.

<sup>2</sup>These two authors contributed equally

<sup>3</sup>corresponding author, email: pc104@pasteur.fr

## **S1 Supplementary Material**

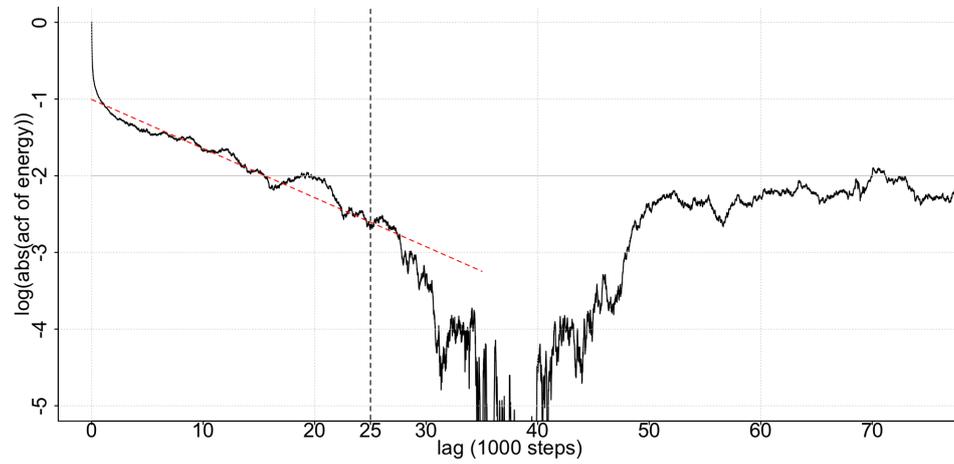


Figure S1: Diagram showing the log of the absolute value of the auto-correlation function of the energy of the system against the lag between the energies sampled. Equilibration is complete where the graph crossed a given  $y$ -value that is no higher than the background. In this case, it is 25000.

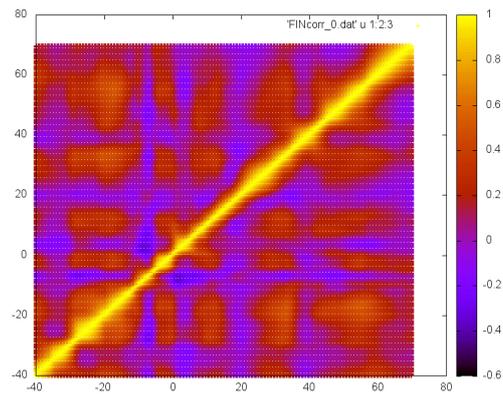


Figure S2: Movement correlation matrix of the system at step = 0.

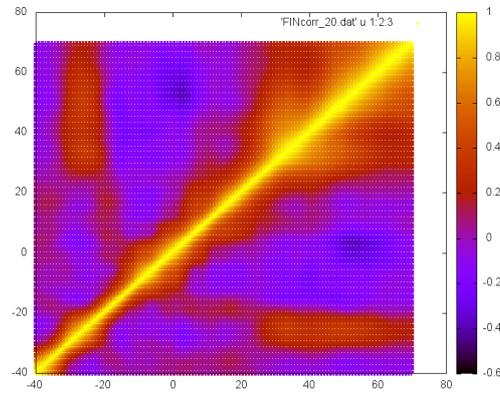


Figure S3: Movement correlation matrix of the system at step = 20000.

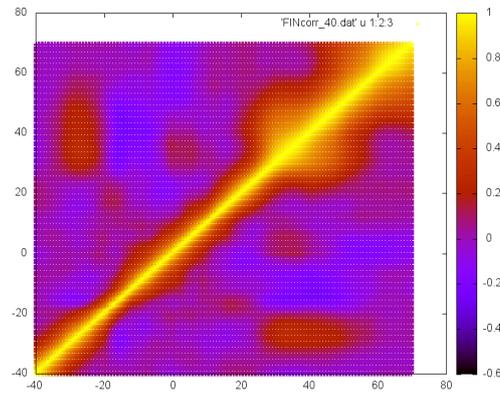


Figure S4: Movement correlation matrix of the system at step = 40000.

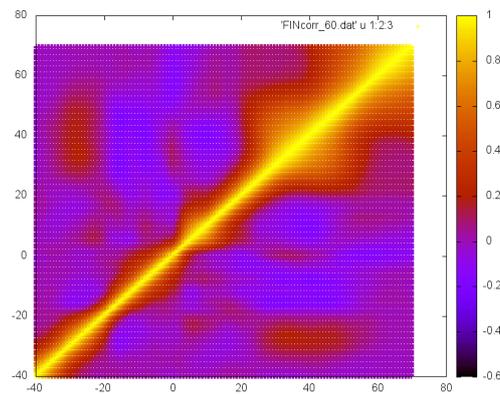


Figure S5: Movement correlation matrix of the system at step = 60000.

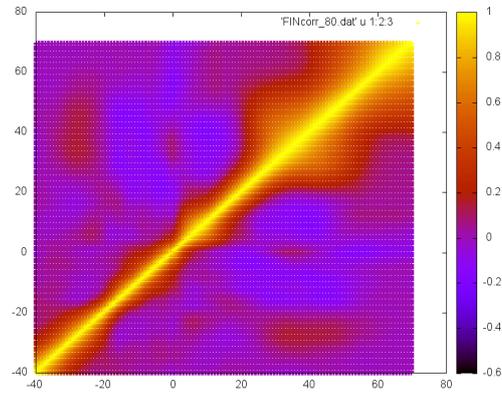


Figure S6: Movement correlation matrix of the system at step = 80000.

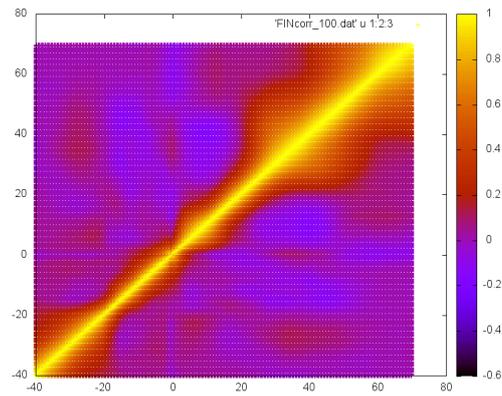


Figure S7: Movement correlation matrix of the system at step = 100000.

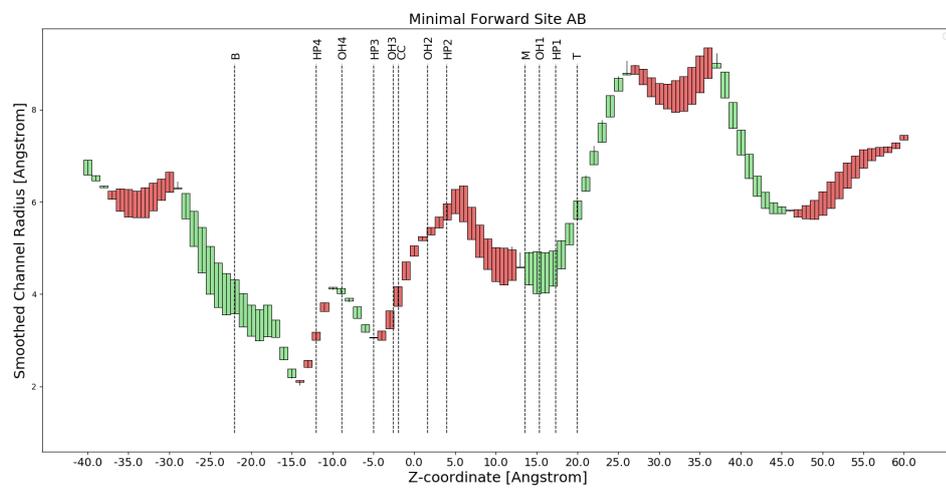


Figure S8: Diagram showing the effect of GABA binding to the AB site. This is the binding site where the  $\beta 2$ -subunit is adjacent to the  $\gamma 2$ -subunit. Forward vectors are applied to Phe 92 and Arg 94 from the  $\alpha 1$ -subunit and Tyr 181 and Tyr 229 from the  $\beta 2$ -subunit. Sometimes as the applied forces went from 0 to 1, the direction changed with an extremum around 0.5; this is shown by the stick parts that overshoot the bars.

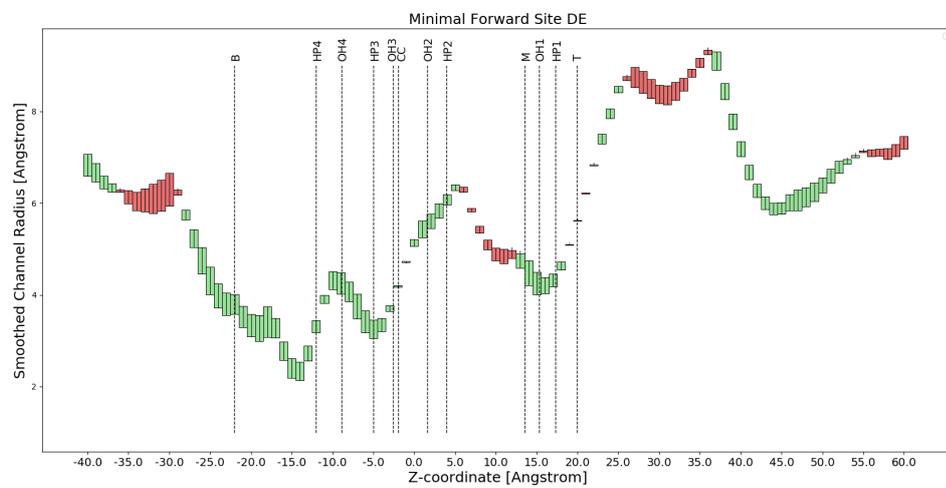


Figure S9: Diagram showing the effect of GABA binding to the DE site. This is the binding site where the  $\alpha$ 1-subunit is adjacent to the  $\gamma$ 2-subunit. Forward vectors are applied to Phe 92 and Arg 94 from the  $\alpha$ 1-subunit and Tyr 181 and Tyr 229 from the  $\beta$ 2-subunit. Sometimes as the applied forces went from 0 to 1, the direction changed with an extremum around 0.5; this is shown by the stick parts that overshoot the bars.

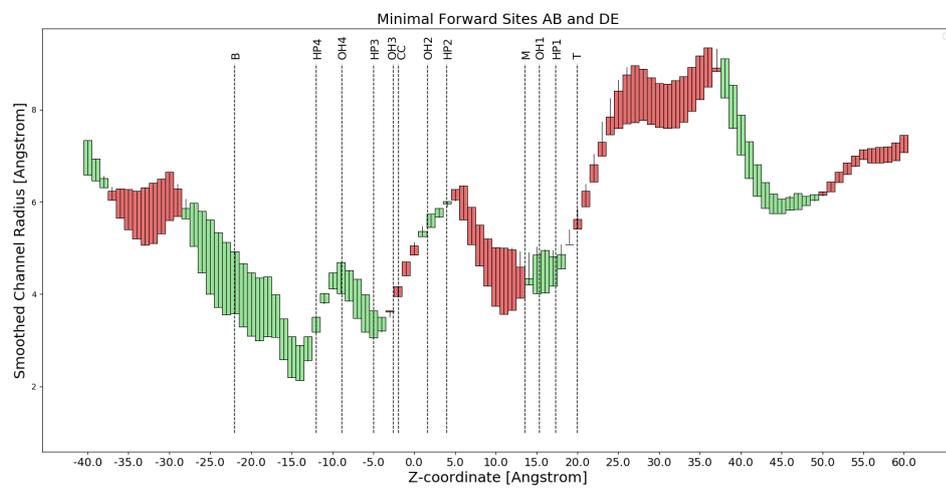


Figure S10: Diagram showing the effect of two GABA molecules binding to both the AB and DE sites. Forward vectors are applied to Phe92 and Arg94 from the  $\alpha$ 1-subunit and Tyr181 and Tyr229 from the  $\beta$ 2-subunit. Sometimes as the applied forces went from 0 to 1, the direction changed with an extremum around 0.5; this is shown by the stick parts that overshoot the bars.

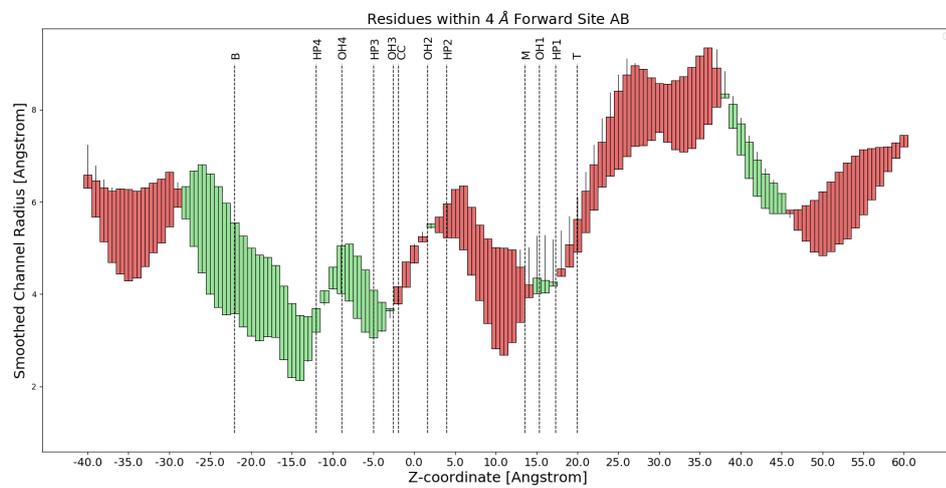


Figure S11: Diagram showing the effect of GABA binding to the AB site. This is the binding site where the  $\beta 2$ -subunit is adjacent to the  $\gamma 2$ -subunit. Forward vectors are applied to only those amino acids within 4 Å of the bound GABA. Sometimes as the applied forces went from 0 to 1, the direction changed with an extremum around 0.5; this is shown by the stick parts that overshoot the bars.

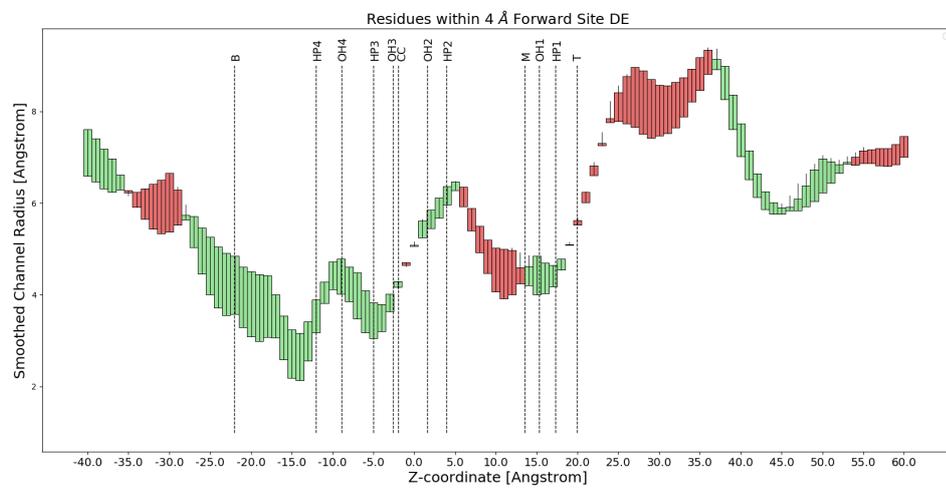


Figure S12: Diagram showing the effect of GABA binding to the DE site. This is the binding site where the  $\alpha$ 1-subunit is adjacent to the  $\gamma$ 2-subunit. Forward vectors are applied to only those amino acids within 4 Å of the bound GABA. Sometimes as the applied forces went from 0 to 1, the direction changed with an extremum around 0.5; this is shown by the stick parts that overshoot the bars.

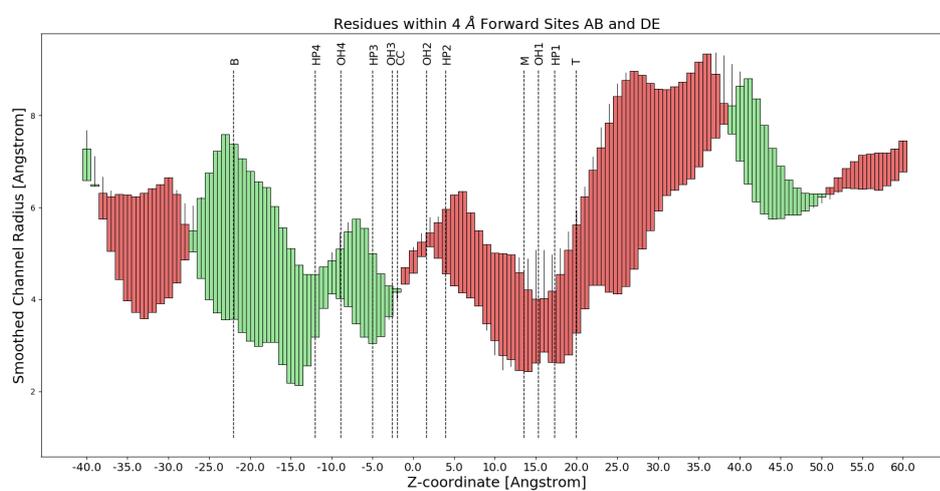


Figure S13: Diagram showing the effect of two GABA molecules binding to both the AB and DE sites. Forward vectors are applied to only those amino acids within 4 Å of the bound GABA. Sometimes as the applied forces went from 0 to 1, the direction changed with an extremum around 0.5; this is shown by the stick parts that overshoot the bars.

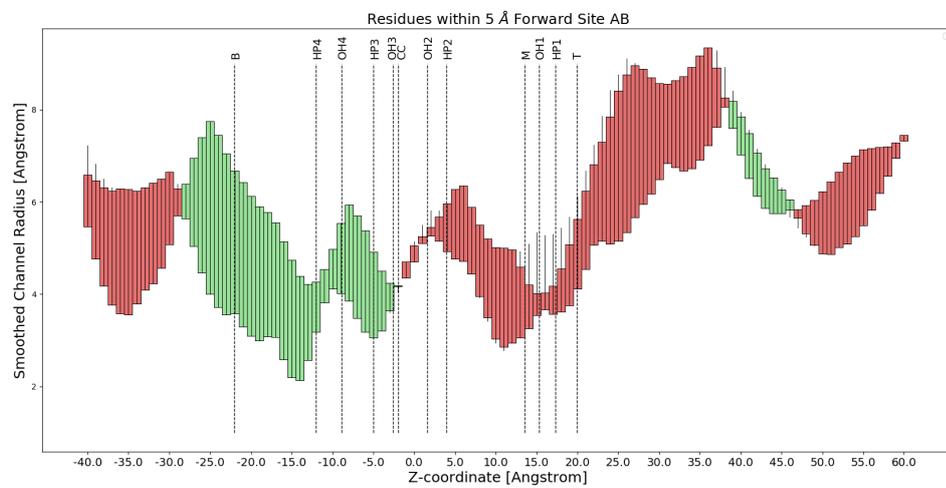


Figure S14: Diagram showing the effect of GABA binding to the AB site. This is the binding site where the  $\beta 2$ -subunit is adjacent to the  $\gamma 2$ -subunit. Forward vectors are applied to only those amino acids within 5 Å of the bound GABA. Sometimes as the applied forces went from 0 to 1, the direction changed with an extremum around 0.5; this is shown by the stick parts that overshoot the bars.

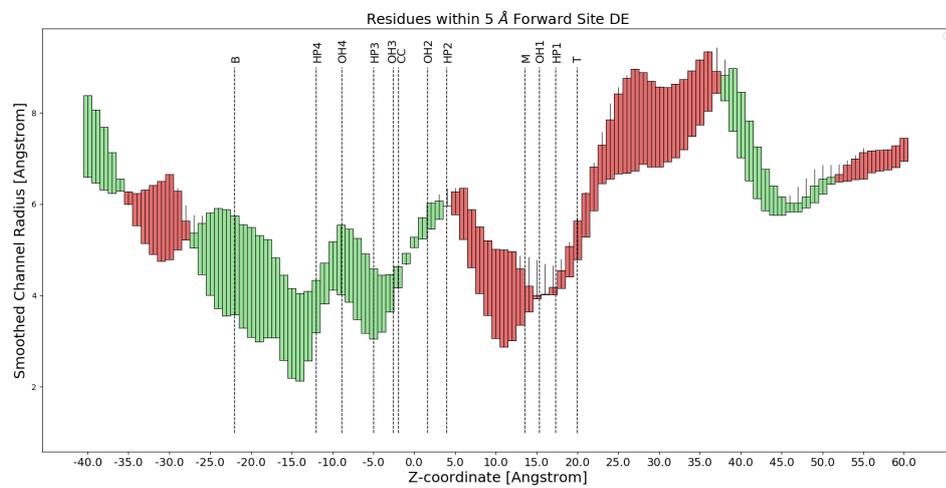


Figure S15: Diagram showing the effect of GABA binding to the DE site. This is the binding site where the  $\alpha$ 1-subunit is adjacent to the  $\gamma$ 2-subunit. Forward vectors are applied to only those amino acids within 5 Å of the bound GABA. Sometimes as the applied forces went from 0 to 1, the direction changed with an extremum around 0.5; this is shown by the stick parts that overshoot the bars.

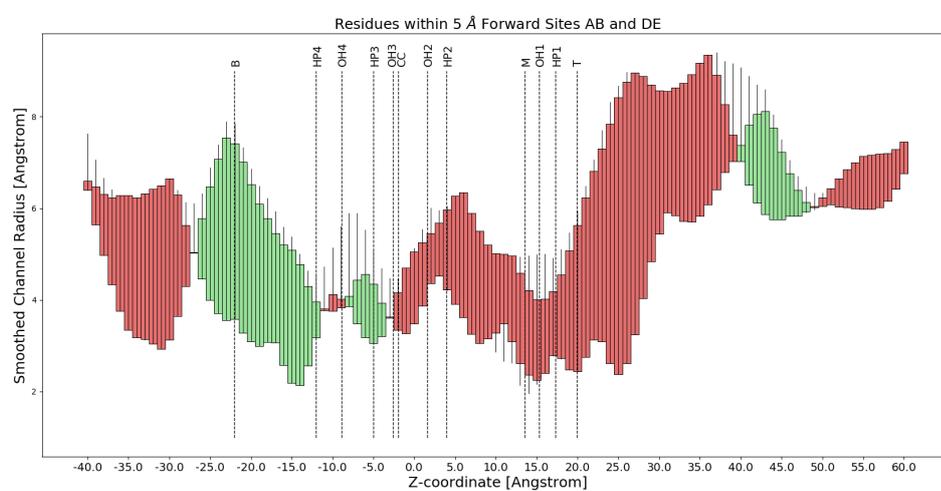


Figure S16: Diagram showing the effect of two GABA molecules binding to both the AB and DE sites. Forward vectors are applied to only those amino acids within 5 Å of the bound GABA. Sometimes as the applied forces went from 0 to 1, the direction changed with an extremum around 0.5; this is shown by the stick parts that overshoot the bars.

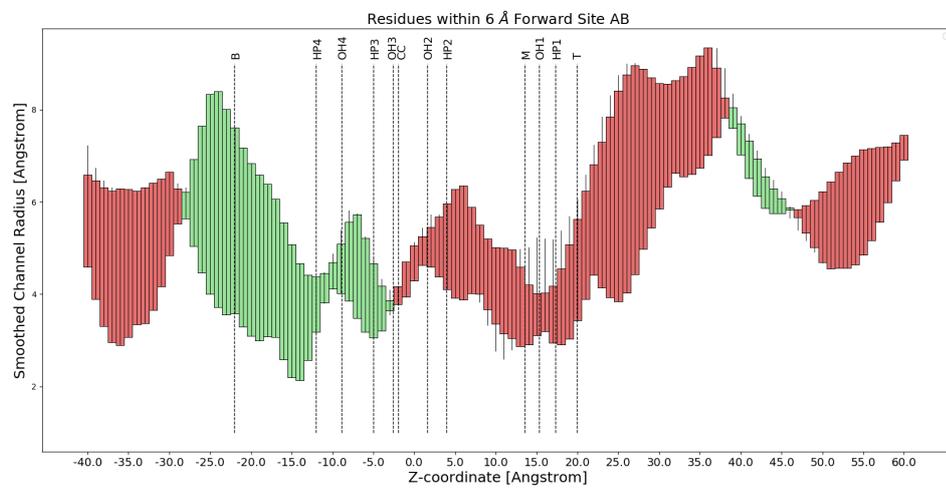


Figure S17: Diagram showing the effect of GABA binding to the AB site. This is the binding site where the  $\beta 2$ -subunit is adjacent to the  $\gamma 2$ -subunit. Forward vectors are applied to only those amino acids within 6 Å of the bound GABA. Sometimes as the applied forces went from 0 to 1, the direction changed with an extremum around 0.5; this is shown by the stick parts that overshoot the bars.

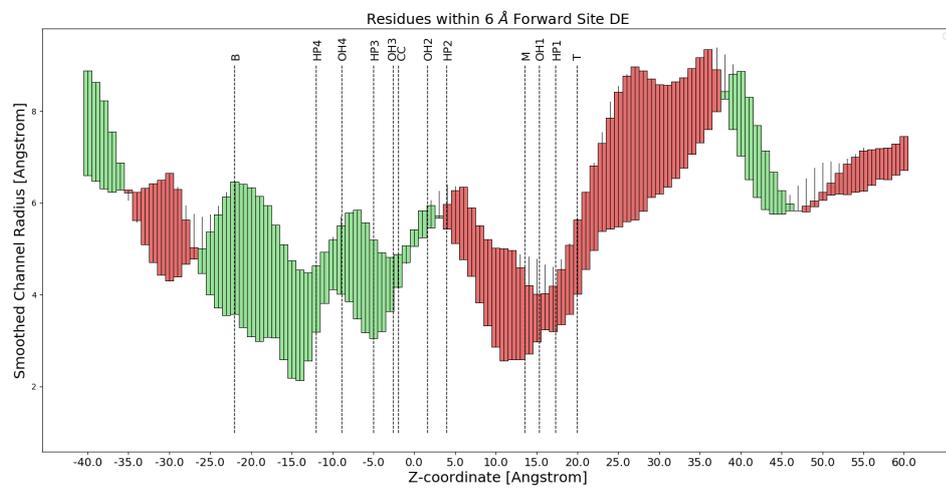


Figure S18: Diagram showing the effect of GABA binding to the DE site. This is the binding site where the  $\alpha 1$ -subunit is adjacent to the  $\gamma 2$ -subunit. Forward vectors are applied to only those amino acids within 6 Å of the bound GABA. Sometimes as the applied forces went from 0 to 1, the direction changed with an extremum around 0.5; this is shown by the stick parts that overshoot the bars.

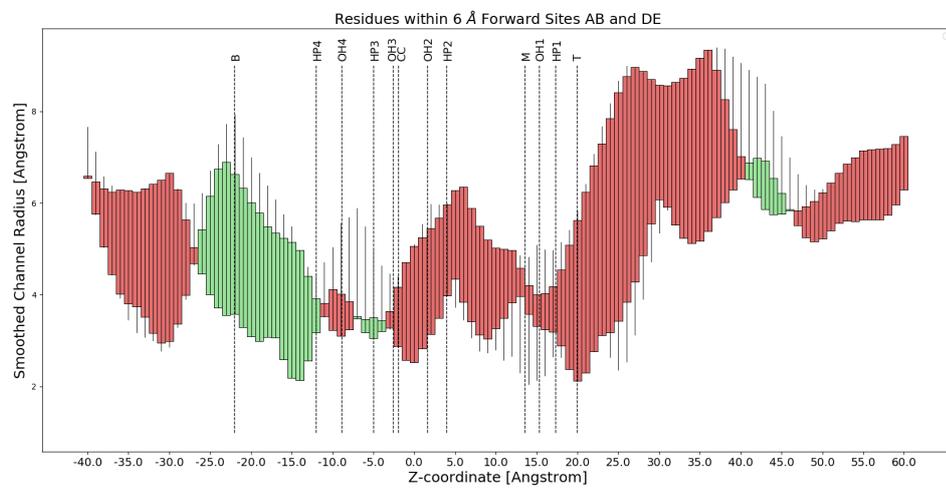


Figure S19: Diagram showing the effect of two GABA molecules binding to both the AB and DE sites. Forward vectors are applied to only those amino acids within 6 Å of the bound GABA. Sometimes as the applied forces went from 0 to 1, the direction changed with an extremum around 0.5; this is shown by the stick parts that overshoot the bars.