Supplementary Material

Insights into the structural stability of Bax from molecular dynamics simulations at high temperatures

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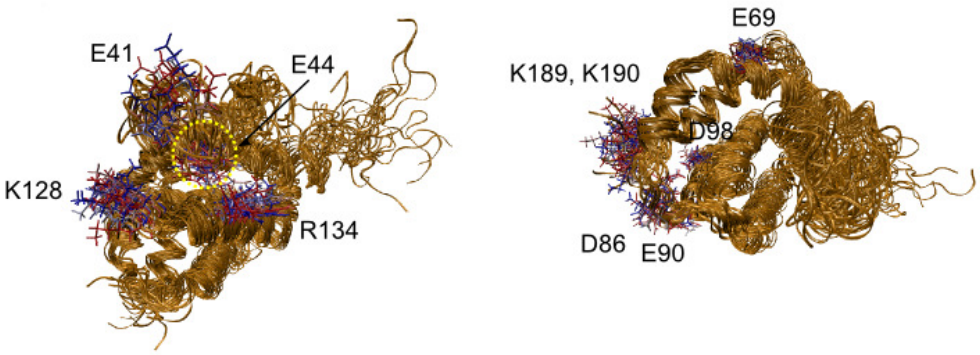

Fig. S1. NMR models. All 20 NMR models from the PDB file are shown (PDB ID: 1F16). The color coding representation for the residues ranges from red for model 1 to blue for model 20.

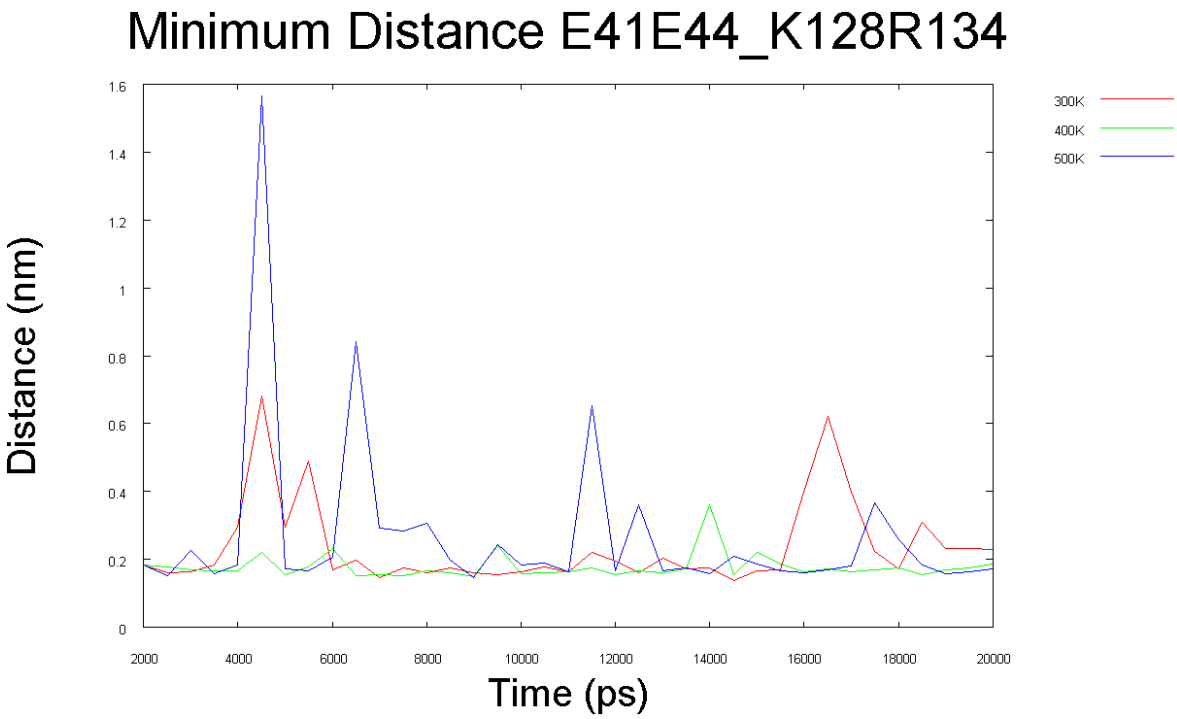

Fig. S2. Minimum distance between E41E44-K128R134. Two sets are defined, one that contains E41 and E44 and the other K128 and R134. The minimum distance between a pair formed with one element of each set is shown in this figure to be close to the van der Waals distance (0.16 nm) at several times in all MD simulations. This proximity is important in the stability of Bax because it prevents the separation of the hairpin formed by αH1 and αH2 from the hydrophobic core (αH5 and αH6).

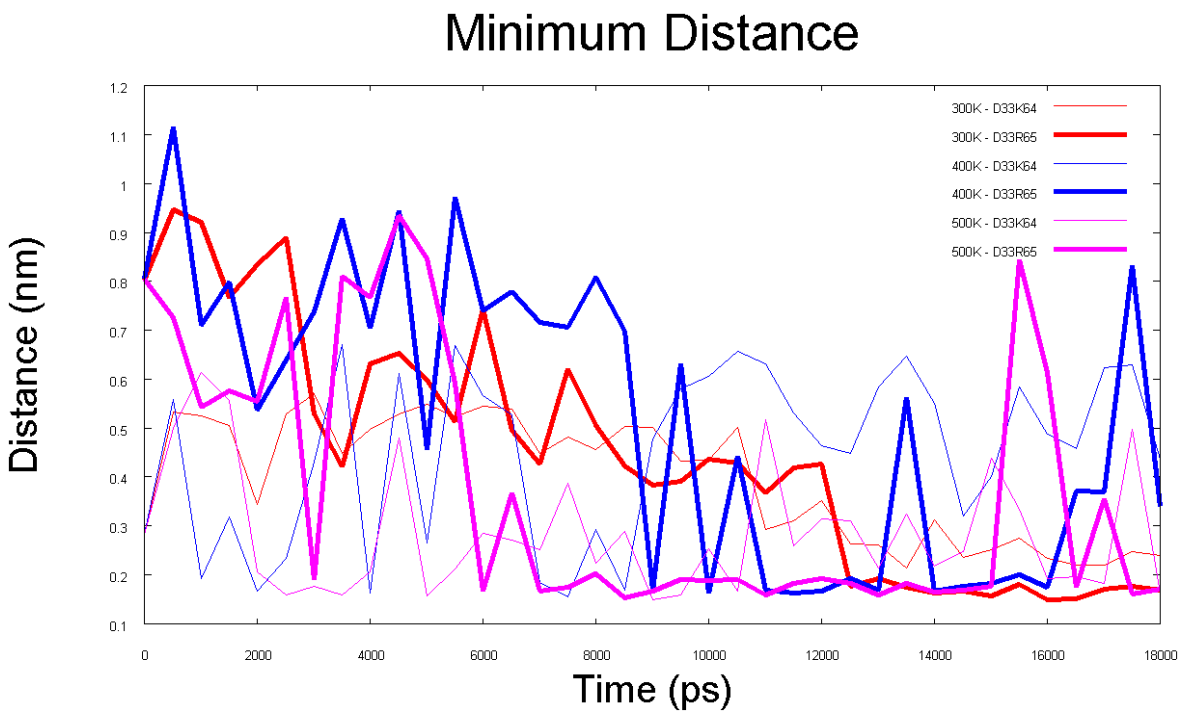

Figure S3. Minimum distance between D33-K64R65. The distance between D33 and these basic residues in αH2 is short even at 500 K.

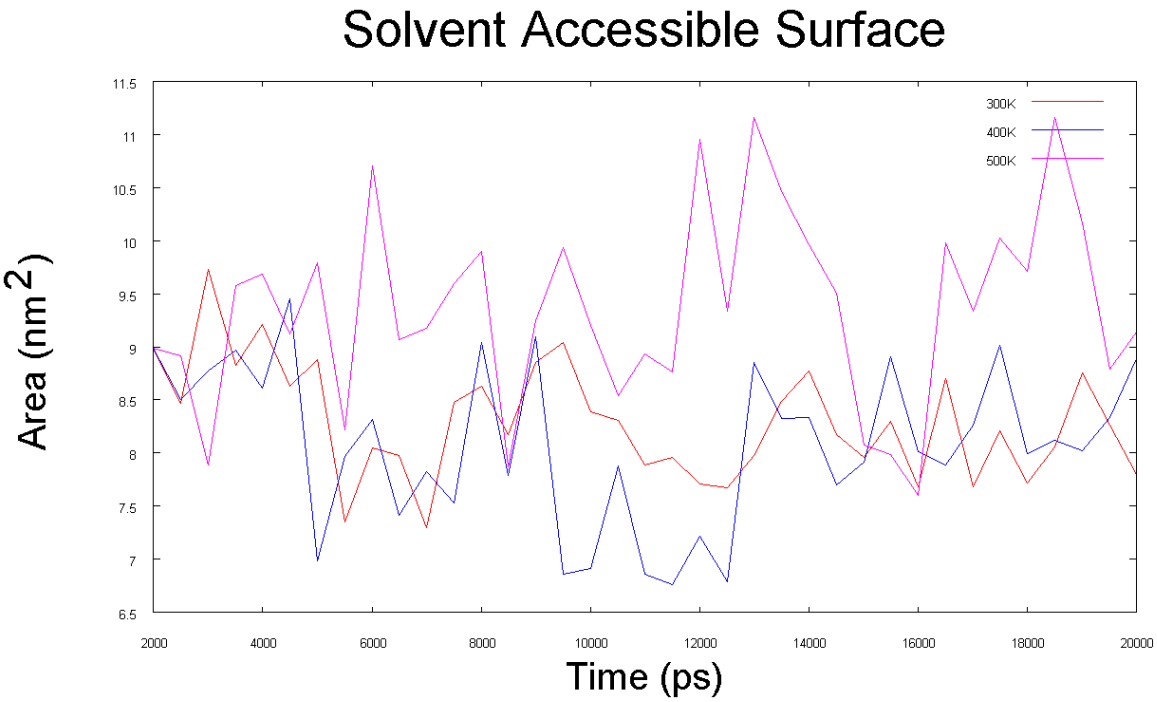

Fig. S4. SASA12-24. Solvent Accessible Surface Area of residues 12-24 (epitope 6A7). The values remain below 11.5 nm2 in all simulations. The residues that cover the epitope allow for enough space for the solvent but block the corresponding antibody.

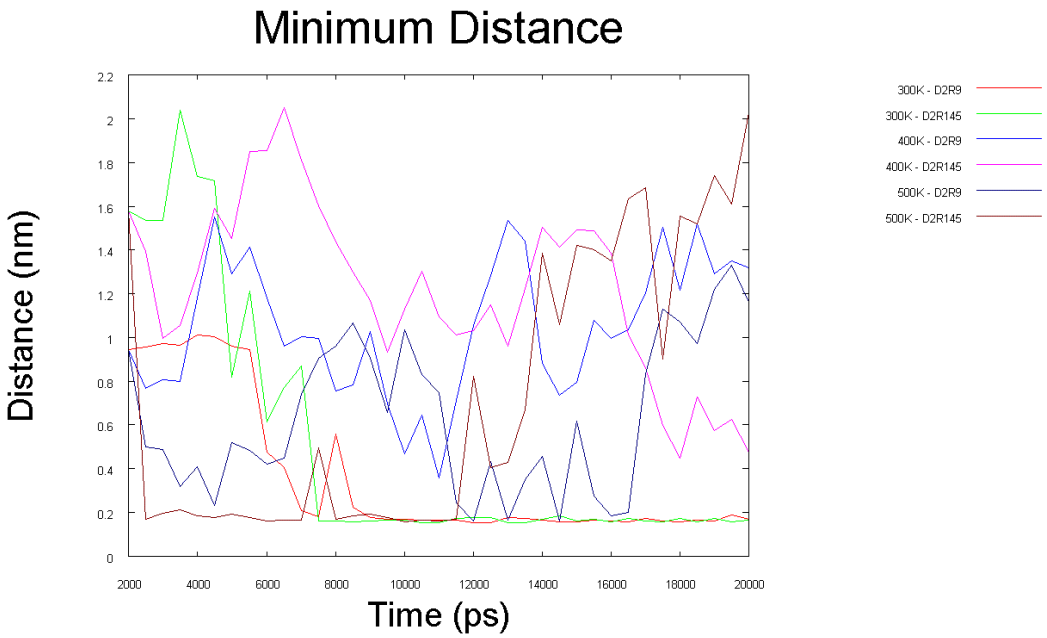

Fig. S5. Minimum distance between D2R9-D2R145. The proximity of D2 and R145 stabilizes the bending of LpNt and the proximity of D2 and R145 keeps LpNt covering the epitope 6A7 (residues 12-24). The minimum values observed are below 0.2 nm, which leaves them close to the van der Waals distance of 0.16 nm. Interestingly, this proximities are more pronounced at 500 K than they are at 400 K and are not present in the conformation at 2 ns but appear later in the MD simulations.

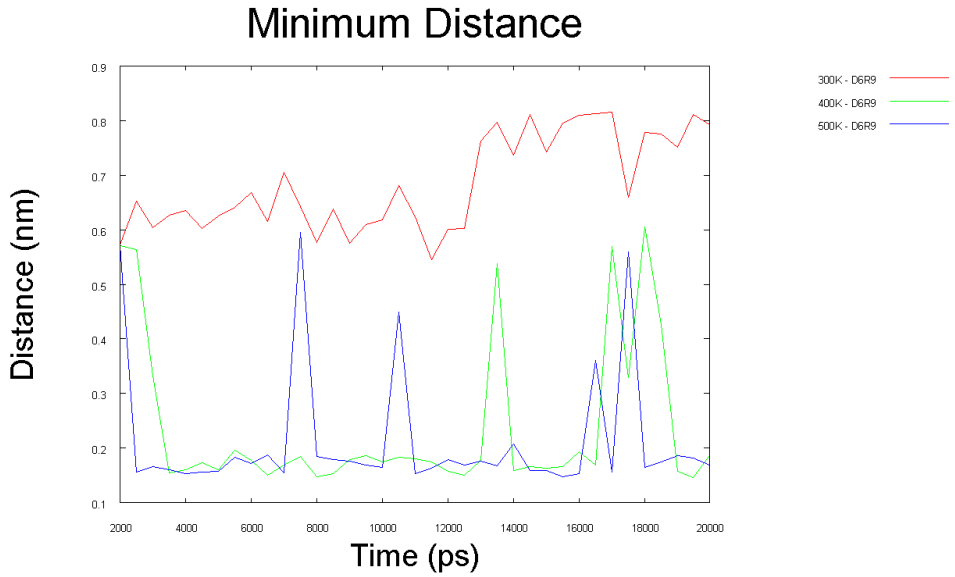

Fig. S6. Minimum distance between D6-R9. The proximity of D6 and R9 contributes to the stabilization of the bending of LpNt that facilitates its function of covering the epitope 6A7. Interestingly, this proximity is only observed in the MD simulations at high temperatures. The minimum distance is close to the van der Waals distance (0.16 nm) at 400 K and 500 K.

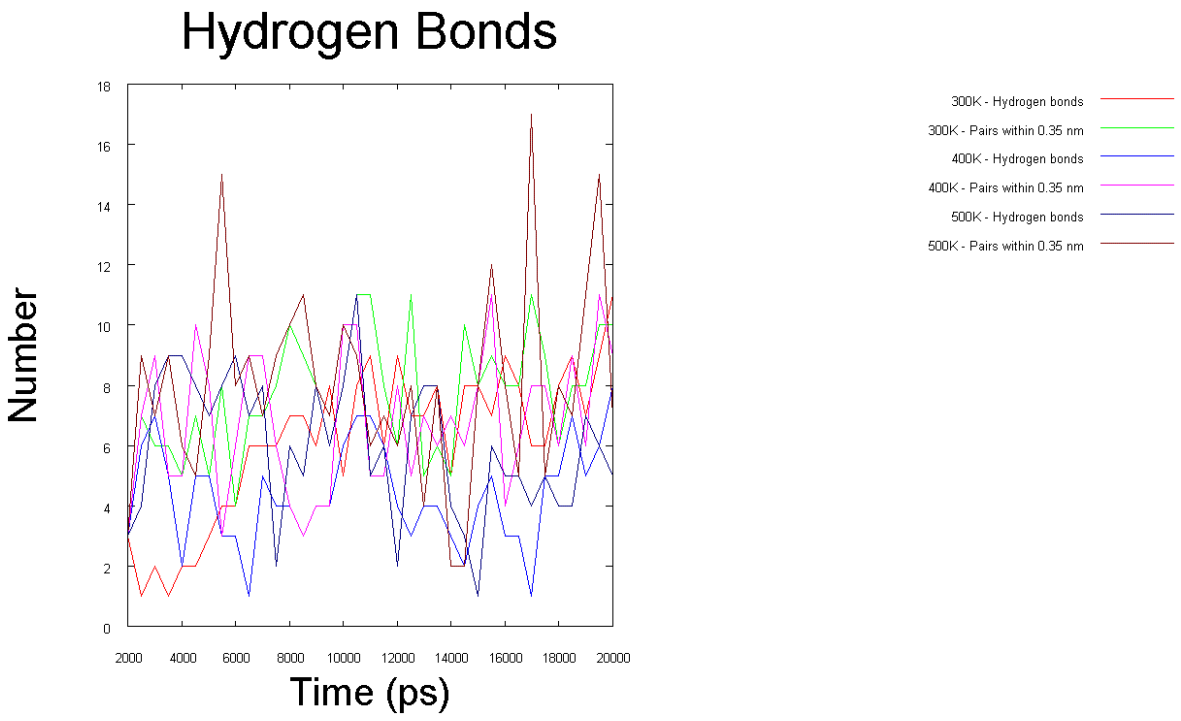

Fig. S7. Hydrogen bonds between LpNt and the rest of the protein. All simulations show a net increase in the number of hydrogen bonds between LpNt and the rest of the protein, helping to keep it close to the core. Pairs within 0.35 nm are likely to have a favorable interaction, and their number is also increased in all simulations, thus contributing to the the proximity of LpNt and the core of Bax.

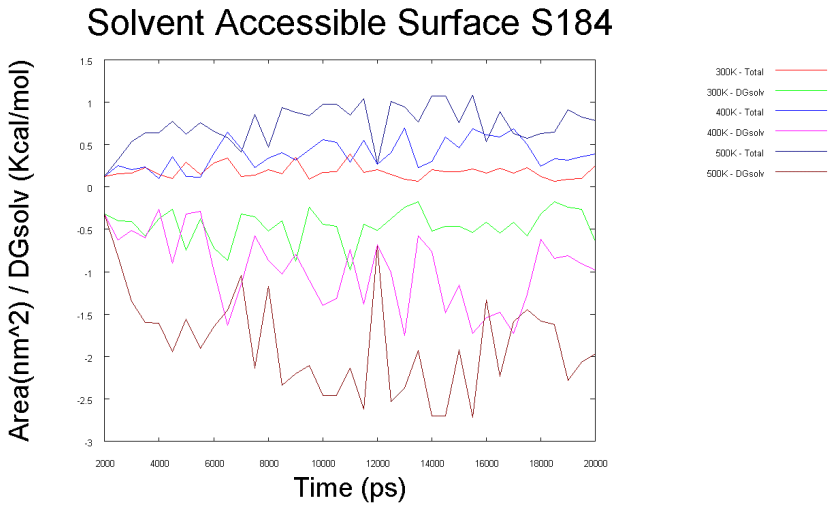

Fig. S8. SASA of S184. The exposure of S184 can be followed in this figure. At 300 K, the value of its SASA is always below 0.5 nm^2, whereas it is above this value intermitently at 400 K and for most of the time at 500 K. This exposure is also noticeable in the free energy of solvation (ΔGsolv), where the values are lowest for the MD simulations at high temperatures.

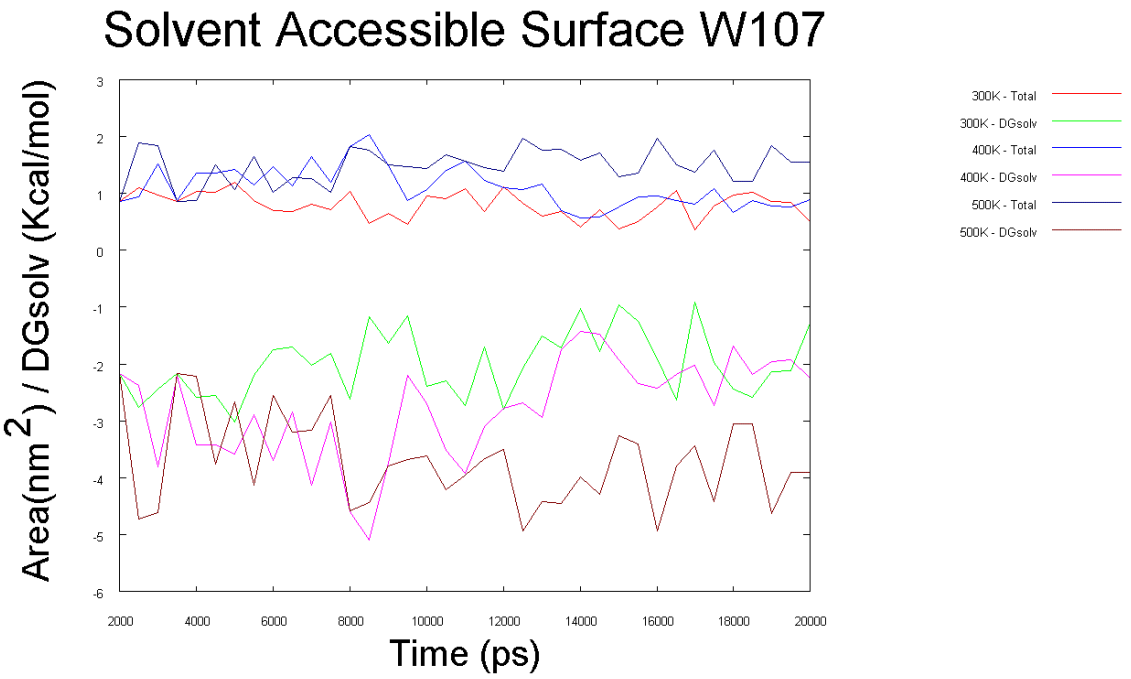

Fig. S9. SASA of W107. The exposure of W107 can be followed in this figure. At 300 K, the SAS area remains close to 1 nm^2, whereas it is closer to 2 nm^2 at several points at 400 K and for most of the simulation at 500 K. This exposure is also noticeable in the free energy of solvation (ΔGsolv), where the values are lowest for the simulation at 500 K.

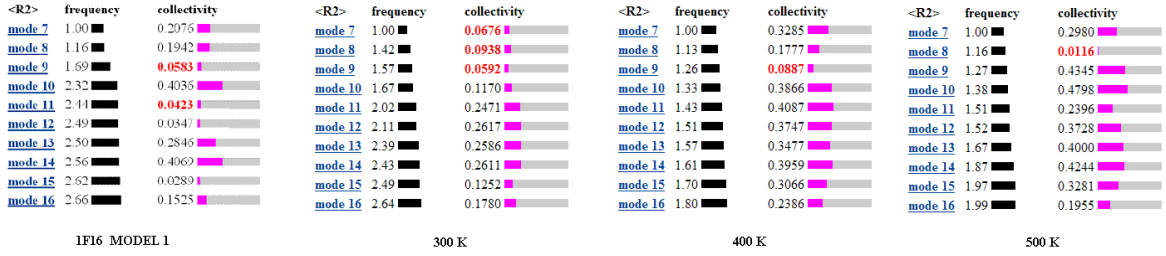

Fig. S10. Normal Mode Analysis. The first ten nontrivial modes are displayed. The leftmost was performed on the first NMR model of the structure from the PDB. The rest were performed on the final structure for each simulation. Low collectivity modes at 300 K are mostly due to LpNt as it is for the NMR structure. At 400 and 500 K these modes include large mobility of Lp1-2, Lp5-6, αH4 and BH2.