

Supporting information

Pulsed EPR Characterization of HIV-1 Protease Conformational Sampling and Inhibitor-Induced Population Shifts

Zhanglong Liu ^a, Thomas M. Casey ^a, Mandy E. Blackburn ^{a,1}, Xi Huang ^{a,2}, Linh Pham ^{a,3}, Ian Mitchell S. de Vera ^{a,4}, Jeffrey D. Carter ^{a,5}, Jamie L. Kear-Scott ^{a,6}, Angelo M. Veloro ^a, Luis Galiano ^{a,7}, Gail E. Fanucci ^{a,*}

^a Department of Chemistry, PO BOX 117200, University of Florida, Gainesville, FL 32611-7200, USA

* Corresponding author: E-mail address: fanucci@chem.ufl.edu (G. E. Fanucci).

¹ Current address: Department of Biochemistry, Chemistry & Physics Programs, University of Central Missouri, MO 64093, USA

² Current address: Boston Biomedical, Inc., Cambridge, MA 02139, USA.

³ Current address: Department of Science and Mathematics, Texas A&M University - Central Texas, Killeen, TX 76549, USA

⁴ Current address: Department of Molecular Therapeutics, the Scripps Research Institute, Jupiter, FL 33458, USA.

⁵ Current address: 3012 Seville St Fort Lauderdale, FL 33304, USA.

⁶ Current address: Department of Biochemistry and Molecular Biology, University of Chicago, IL 60637, USA.

⁷ Current address: Syngenta, Inc., Greensboro, NC, 27419, USA

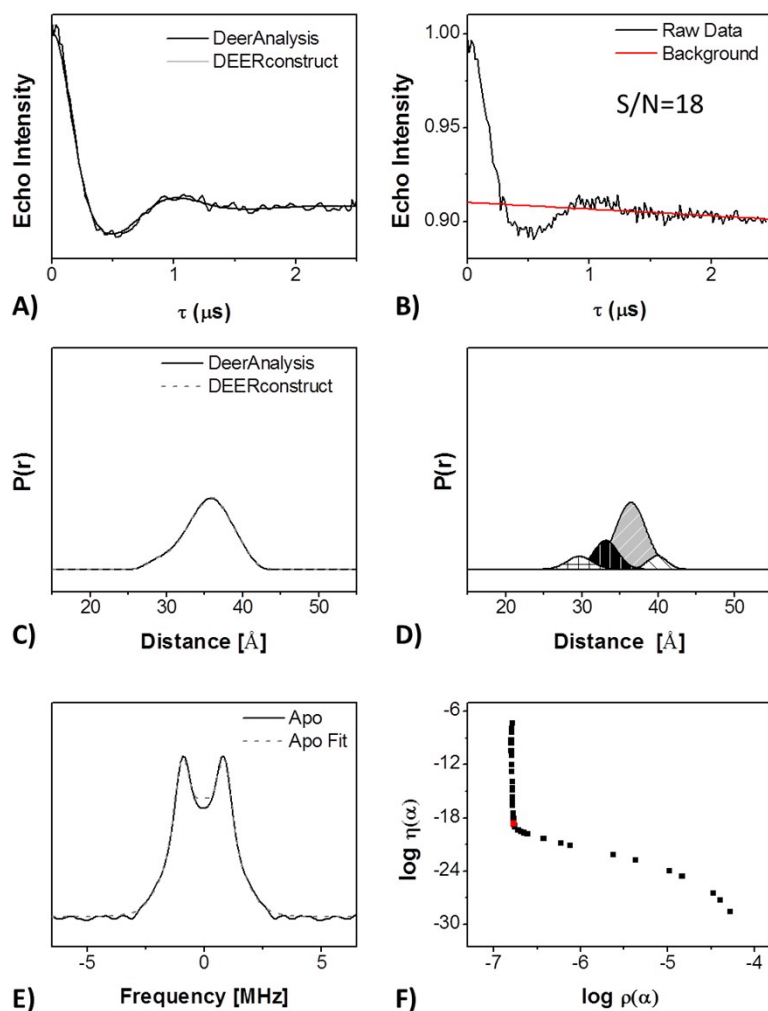


Figure S1. DEER data for apo HIV-1 PR V6, A) Background corrected dipolar evolution curve after the long pass filter in DeerAnalysis (black) and the simulated curve from DEERconstruct (gray); B) Raw dipolar evolution curve and background, the signal to noise ratio (S/N) is shown inset, where the signal is the DEER modulation depth and the noise is 2 times of the standard deviation of the noise curve; C) The corresponding distance profile generated via TKR analysis by DeerAnalysis (black) and the theoretical curve generated from the Gaussian reconstruction by DEERconstruct (gray); D) The individual Gaussian functions used in the reconstruction; E) Frequency domain spectrum; F) L-curve derived from TKR fit to obtain the optimal regulation parameter, the optimal regulation parameter is plot in red.

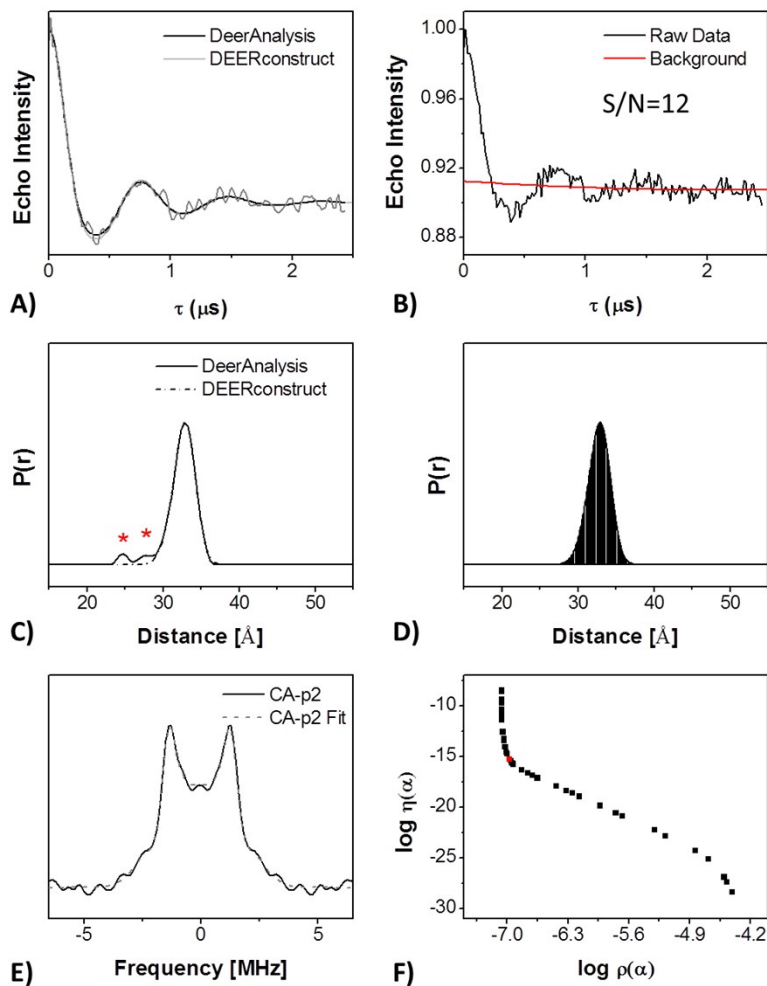


Figure S2. DEER data for CaP2-bound HIV-1 PR V6, A) Background corrected dipolar evolution curve after the long pass filter in DeerAnalysis (black) and the simulated curve from DEERconstruct (gray); B) Raw dipolar evolution curve and background, the signal to noise ratio (S/N) is shown inset, where the signal is the DEER modulation depth and the noise is 2 times of the standard deviation of the noise curve; C) The corresponding distance profile generated via TKR analysis by DeerAnalysis (black) and the theoretical curve generated from the Gaussian reconstruction by DEERconstruct (gray), asterisks indicate that peaks are within the suppression range; D) The individual Gaussian functions used in the reconstruction; E) Frequency domain spectrum; F) L-curve derived from TKR fit to obtain the optimal regulation parameter, the optimal regulation parameter is plot in red.

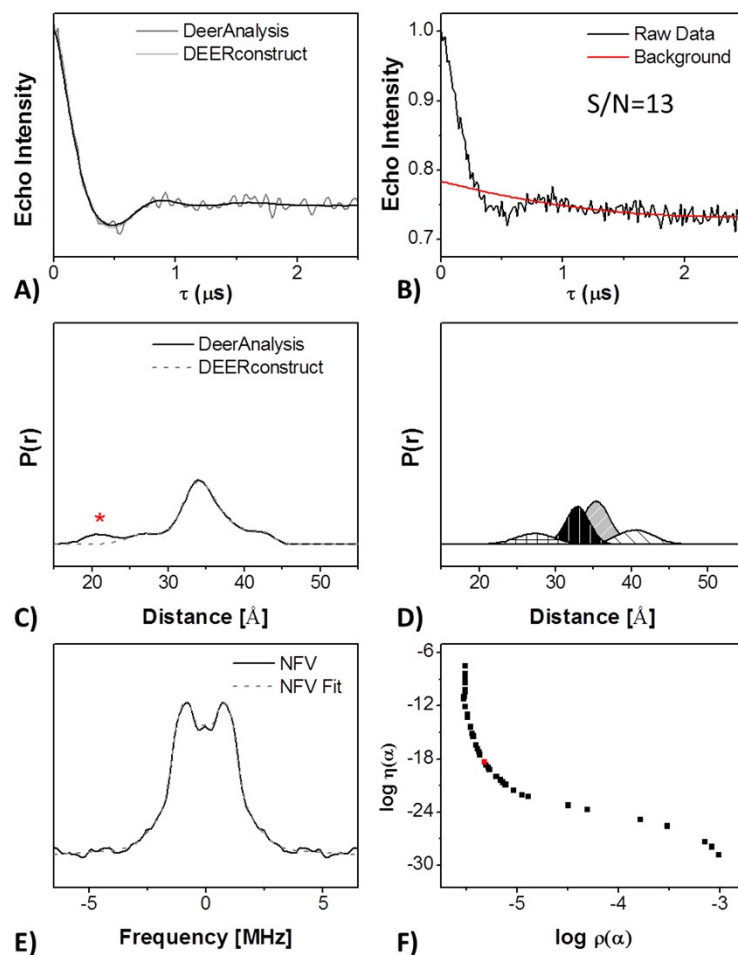


Figure S3. DEER data for NFV-bound HIV-1 PR V6, A) Background corrected dipolar evolution curve after the long pass filter in DeerAnalysis (black) and the simulated curve from DEERconstruct (gray); B) Raw dipolar evolution curve and background, the signal to noise ratio (S/N) is shown inset, where the signal is the DEER modulation depth and the noise is 2 times of the standard deviation of the noise curve; C) The corresponding distance profile generated via TKR analysis by DeerAnalysis (black) and the theoretical curve generated from the Gaussian reconstruction by DEERconstruct (gray), asterisks indicate that peaks are within the suppression range; D) The individual Gaussian functions used in the reconstruction; E) Frequency domain spectrum; F) L-curve derived from TKR fit to obtain the optimal regulation parameter, the optimal regulation parameter is plot in red.

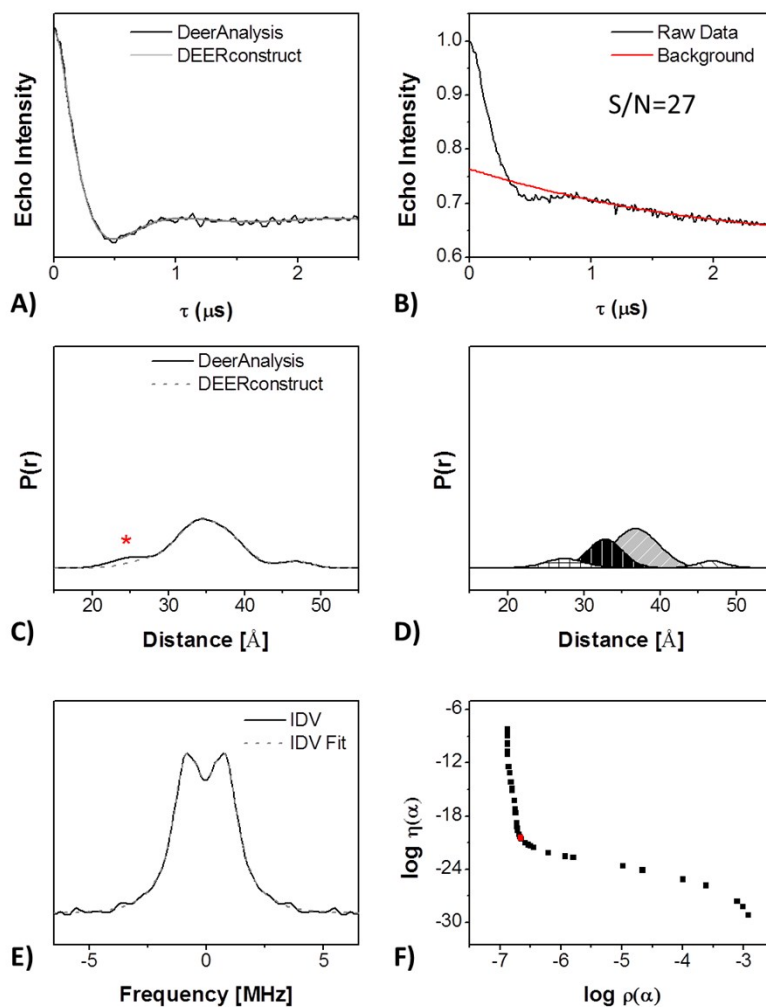


Figure S4. DEER data for IDV-bound HIV-1 PR V6, A) Background corrected dipolar evolution curve after the long pass filter in DeerAnalysis (black) and the simulated curve from DEERconstruct (gray); B) Raw dipolar evolution curve and background, the signal to noise ratio (S/N) is shown inset, where the signal is the DEER modulation depth and the noise is 2 times of the standard deviation of the noise curve; C) The corresponding distance profile generated via TKR analysis by DeerAnalysis (black) and the theoretical curve generated from the Gaussian reconstruction by DEERconstruct (gray), asterisks indicate that peaks are within the suppression range; D) The individual Gaussian functions used in the reconstruction; E) Frequency domain spectrum; F) L-curve derived from TKR fit to obtain the optimal regulation parameter, the optimal regulation parameter is plot in red.

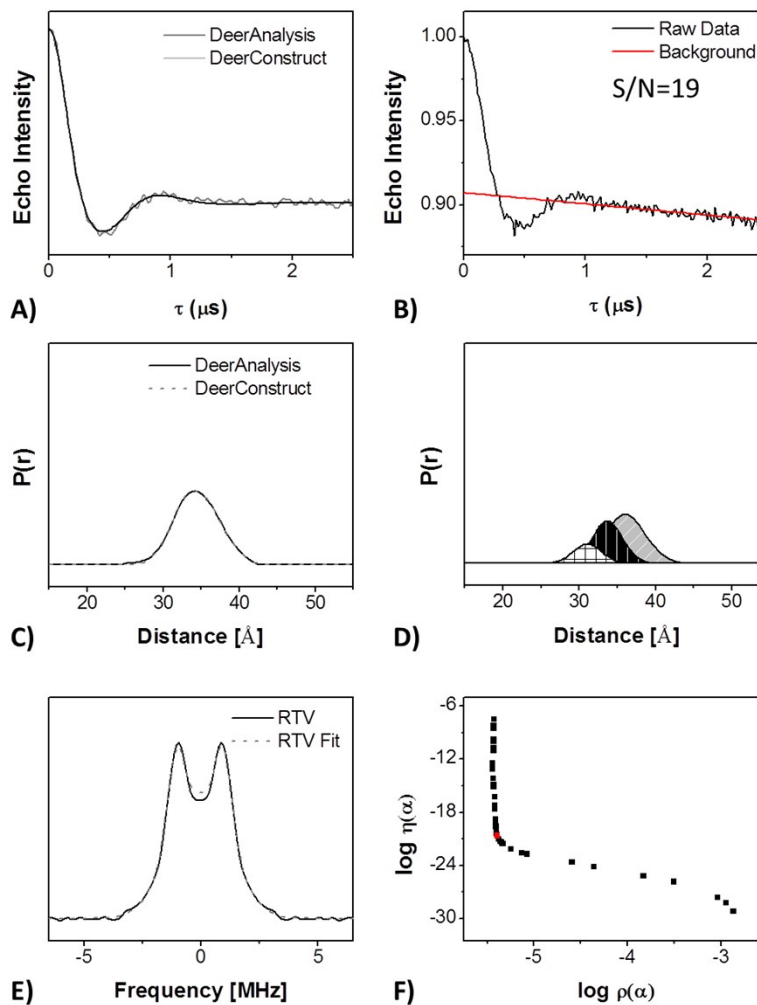


Figure S5. DEER data for RTV-bound HIV-1 PR V6, A) Background corrected dipolar evolution curve after the long pass filter in DeerAnalysis (black) and the simulated curve from DEERconstruct (gray); B) Raw dipolar evolution curve and background, the signal to noise ratio (S/N) is shown inset, where the signal is the DEER modulation depth and the noise is 2 times of the standard deviation of the noise curve; C) The corresponding distance profile generated via TKR analysis by DeerAnalysis (black) and the theoretical curve generated from the Gaussian reconstruction by DEERconstruct (gray). D) The individual Gaussian functions used in the reconstruction; E) Frequency domain spectrum; F) L-curve derived from TKR fit to obtain the optimal regulation parameter, the optimal regulation parameter is plot in red;

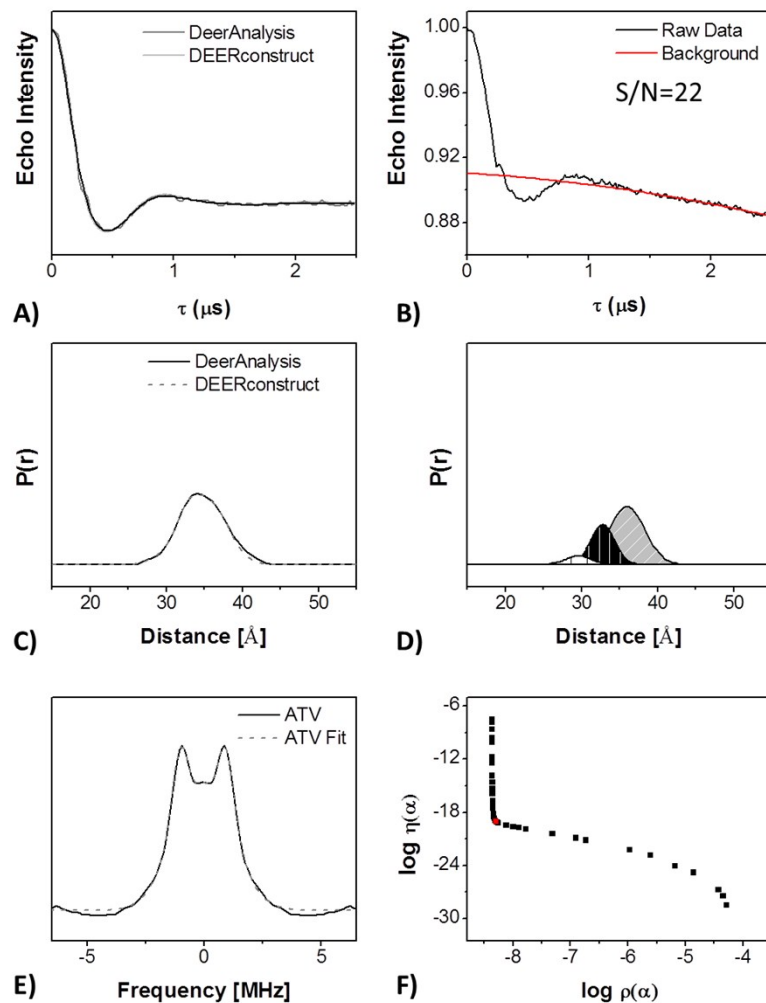


Figure S6. DEER data for ATV-bound HIV-1 PR V6, A) Background corrected dipolar evolution curve after the long pass filter in DeerAnalysis (black) and the simulated curve from DEERconstruct (gray); B) Raw dipolar evolution curve and background, the signal to noise ratio (S/N) is shown inset, where the signal is the DEER modulation depth and the noise is 2 times of the standard deviation of the noise curve; C) The corresponding distance profile generated via TKR analysis by DeerAnalysis (black) and the theoretical curve generated from the Gaussian reconstruction by DEERconstruct (gray). D) The individual Gaussian functions used in the reconstruction; E) Frequency domain spectrum; F) L-curve derived from TKR fit to obtain the optimal regulation parameter, the optimal regulation parameter is plot in red;

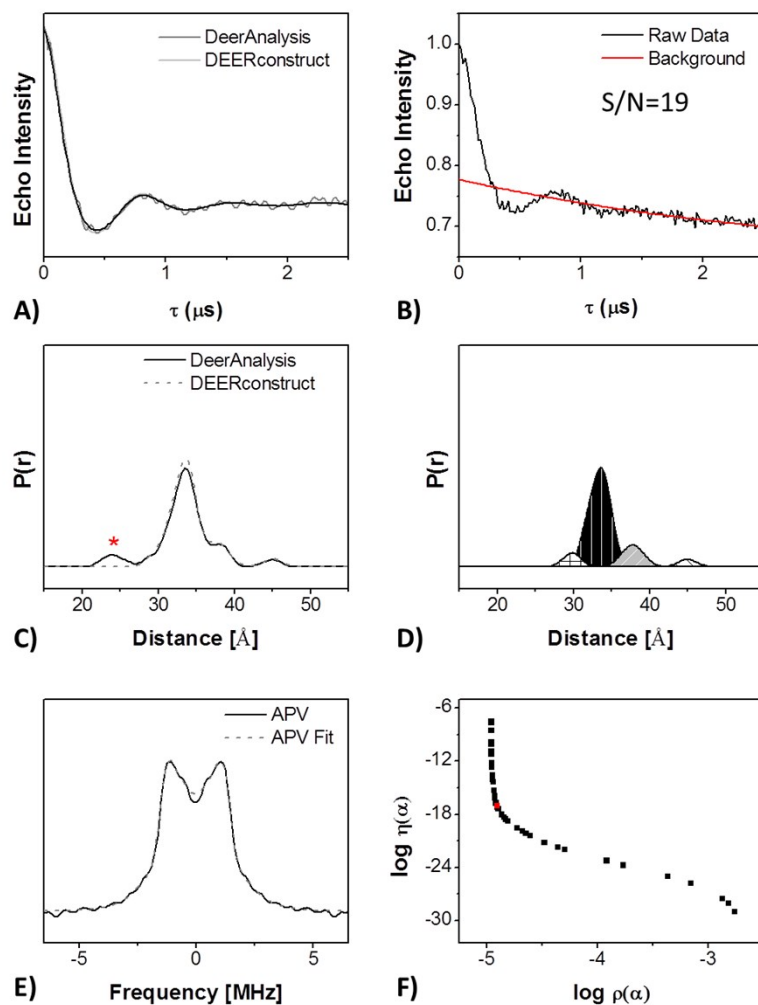


Figure S7. DEER data for APV-bound HIV-1 PR V6, A) Background corrected dipolar evolution curve after the long pass filter in DeerAnalysis (black) and the simulated curve from DEERconstruct (gray); B) Raw dipolar evolution curve and background, the signal to noise ratio (S/N) is shown inset, where the signal is the DEER modulation depth and the noise is 2 times of the standard deviation of the noise curve; C) The corresponding distance profile generated via TKR analysis by DeerAnalysis (black) and the theoretical curve generated from the Gaussian reconstruction by DEERconstruct (gray), asterisks indicate that peaks are within the suppression range; D) The individual Gaussian functions used in the reconstruction; E) Frequency domain spectrum; F) L-curve derived from TKR fit to obtain the optimal regulation parameter, the optimal regulation parameter is plot in red.

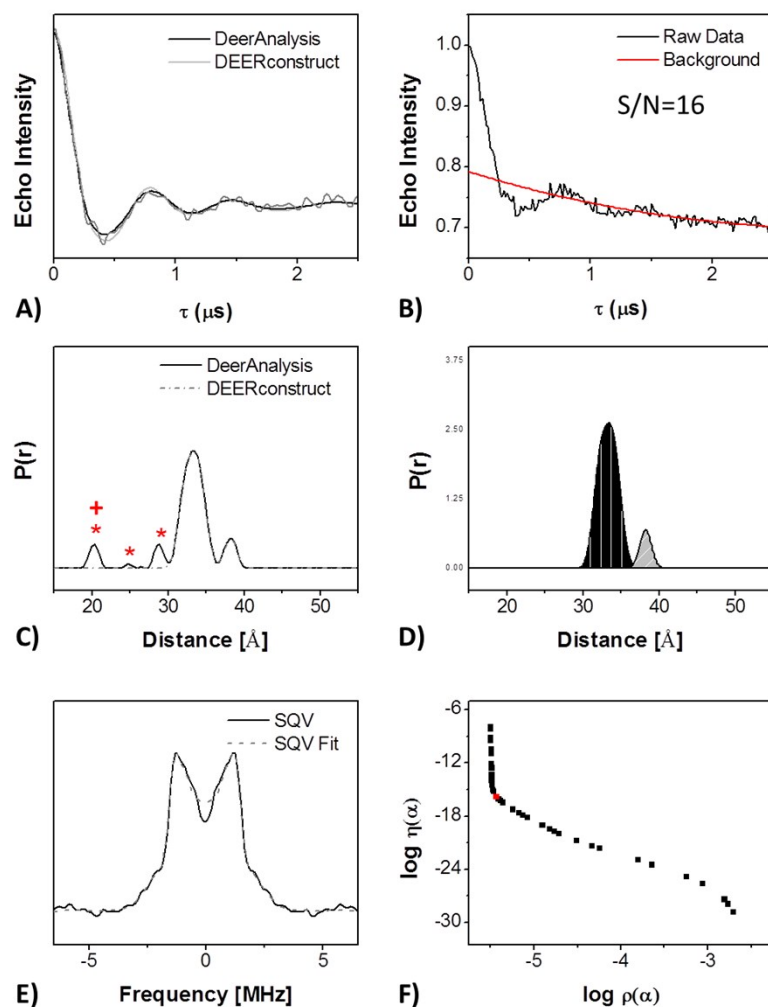


Figure S8. DEER data for SQV-bound HIV-1 PR V6, A) Background corrected dipolar evolution curve after the long pass filter in DeerAnalysis (black) and the simulated curve from DEERconstruct (gray); B) Raw dipolar evolution curve and background, the signal to noise ratio (S/N) is shown inset, where the signal is the DEER modulation depth and the noise is 2 times of the standard deviation of the noise curve; C) The corresponding distance profile generated via TKR analysis by DeerAnalysis (black) and the theoretical curve generated from the Gaussian reconstruction by DEERconstruct (gray), asterisks indicate that peaks are within the suppression range, “+” indicates that the peak is presumed to be an artifact of processing as it is near the lower limit of the generally accepted range that is measurable using DEER; D) The individual Gaussian functions used in the reconstruction; E) Frequency domain spectrum; F) L-curve derived from TKR fit to obtain the optimal regulation parameter, the optimal regulation parameter is plot in red.

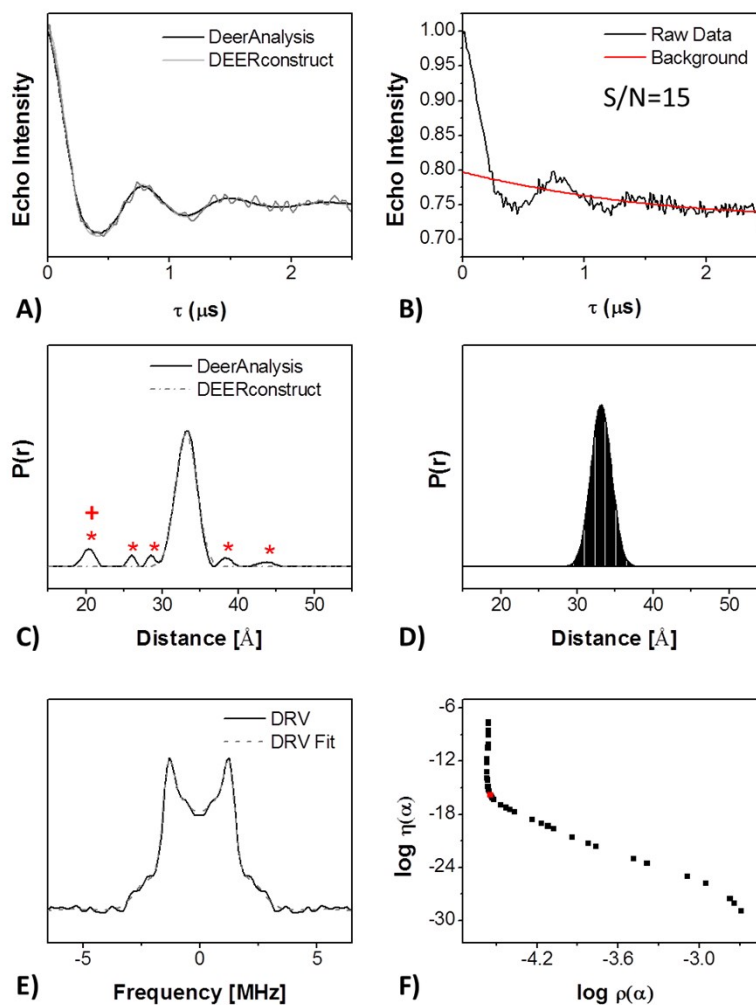


Figure S9. DEER data for DRV-bound HIV-1 PR V6, A) Background corrected dipolar evolution curve after the long pass filter in DeerAnalysis (black) and the simulated curve from DEERconstruct (gray); B) Raw dipolar evolution curve and background, the signal to noise ratio (S/N) is shown inset, where the signal is the DEER modulation depth and the noise is 2 times of the standard deviation of the noise curve; C) The corresponding distance profile generated via TKR analysis by DeerAnalysis (black) and the theoretical curve generated from the Gaussian reconstruction by DEERconstruct (gray), asterisks indicate that peaks are within the suppression range, “+” indicates that the peak is presumed to be an artifact of processing as it is near the lower limit of the generally accepted range that is measurable using DEER; D) The individual Gaussian functions used in the reconstruction; E) Frequency domain spectrum; F) L-curve derived from TKR fit to obtain the optimal regulation parameter, the optimal regulation parameter is plot in red.

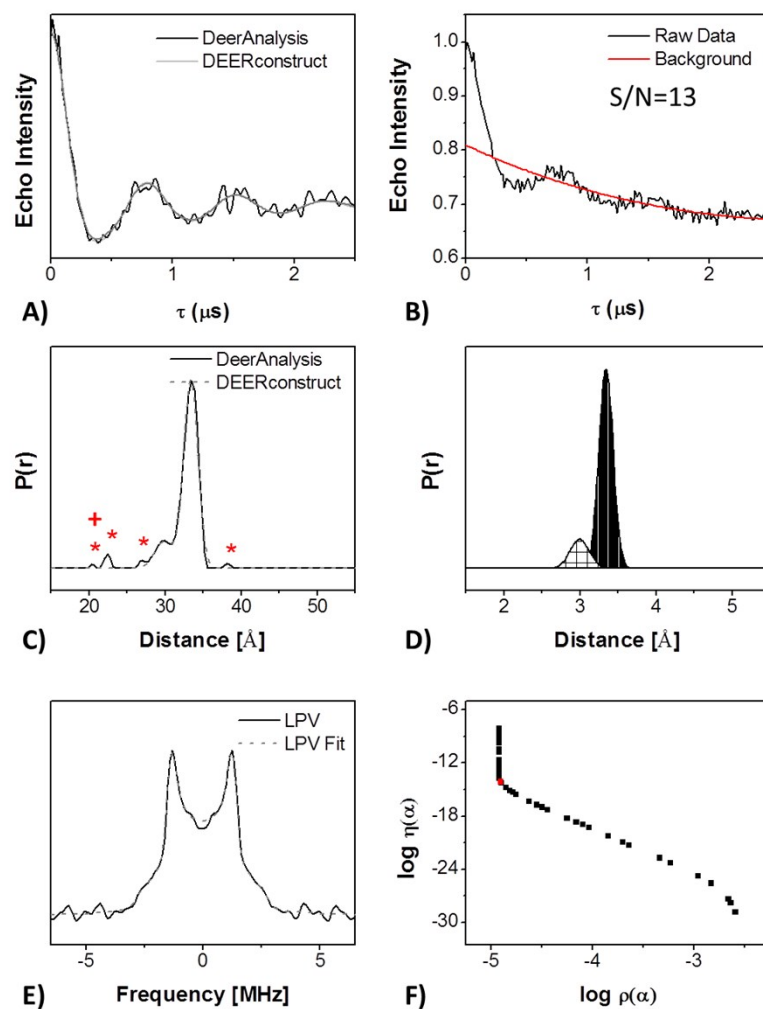


Figure S10. DEER data for LPV-bound HIV-1 PR V6, A) Background corrected dipolar evolution curve after the long pass filter in DeerAnalysis (black) and the simulated curve from DEERconstruct (gray); B) Raw dipolar evolution curve and background, the signal to noise ratio (S/N) is shown inset, where the signal is the DEER modulation depth and the noise is 2 times of the standard deviation of the noise curve; C) The corresponding distance profile generated via TKR analysis by DeerAnalysis (black) and the theoretical curve generated from the Gaussian reconstruction by DEERconstruct (gray), asterisks indicate that peaks are within the suppression range, “+” indicates that the peak is presumed to be an artifact of processing as it is near the lower limit of the generally accepted range that is measurable using DEER; D) The individual Gaussian functions used in the reconstruction; E) Frequency domain spectrum; F) L-curve derived from TKR fit to obtain the optimal regulation parameter, the optimal regulation parameter is plot in red.

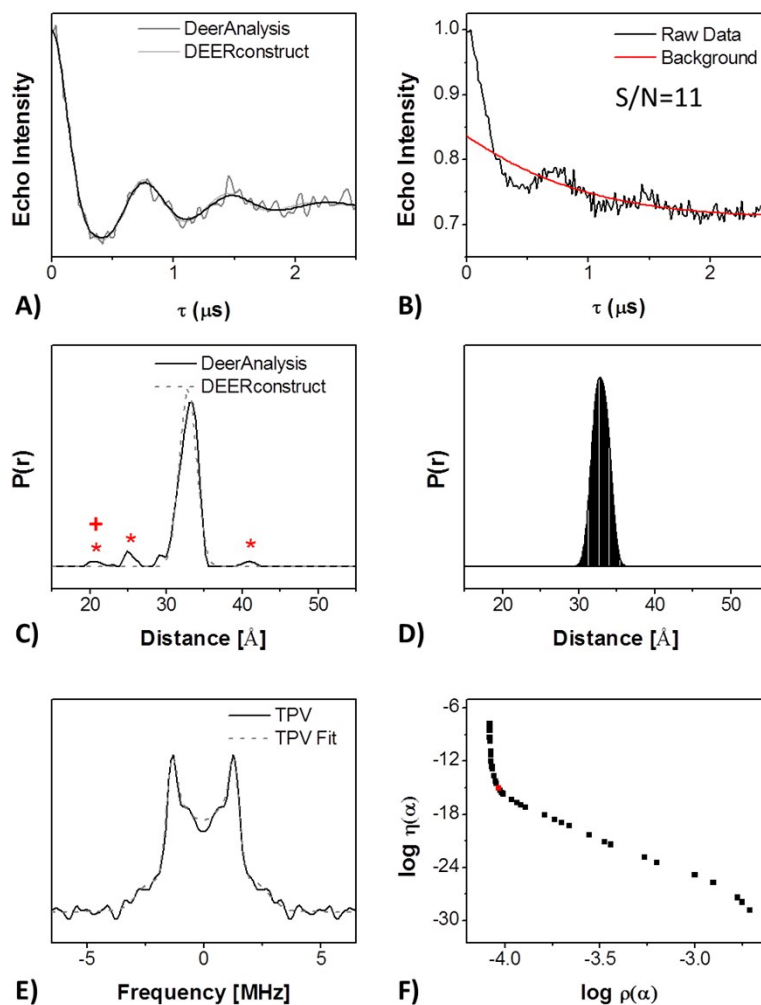


Figure S11. DEER data for TPV-bound HIV-1 PR V6, A) Background corrected dipolar evolution curve after the long pass filter in DeerAnalysis (black) and the simulated curve from DEERconstruct (gray); B) Raw dipolar evolution curve and background, the signal to noise ratio (S/N) is shown inset, where the signal is the DEER modulation depth and the noise is 2 times of the standard deviation of the noise curve; C) The corresponding distance profile generated via TKR analysis by DeerAnalysis (black) and the theoretical curve generated from the Gaussian reconstruction by DEERconstruct (gray), asterisks indicate that peaks are within the suppression range, “+” indicates that the peak is presumed to be an artifact of processing as it is near the lower limit of the generally accepted range that is measurable using DEER; D) The individual Gaussian functions used in the reconstruction; E) Frequency domain spectrum; F) L-curve derived from TKR fit to obtain the optimal regulation parameter, the optimal regulation parameter is plot in red.