Supplemental Information

Polyethylene glycol binding alters human telomere G-quadruplex structure by conformational selection.

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Discussion of equation 7 as a restricted form of the MWC model

The well-known Monod-Wyman-Changeux model[1] as generalized by Eigen[2] posits a preexisting equilibrium between two states A and B, with equilibrium constant L (here denoted K_0), with ligand independent binding constant to each site that differ between the two states (denoted by K_A and K_B), i.e. a three parameter function. The binding sites are assumed to be independent (i.e. no binding cooperativity within a state). Here we consider the possibility that the number of potential binding sites in states A and B may be different, denoted by n and m, respectively. This might arise from an increase in surface area in state B. The general form of the equilibrium constant for this model is:

$$K = K_0(1+x/K_B)^n/(1+x/K_A)^m$$

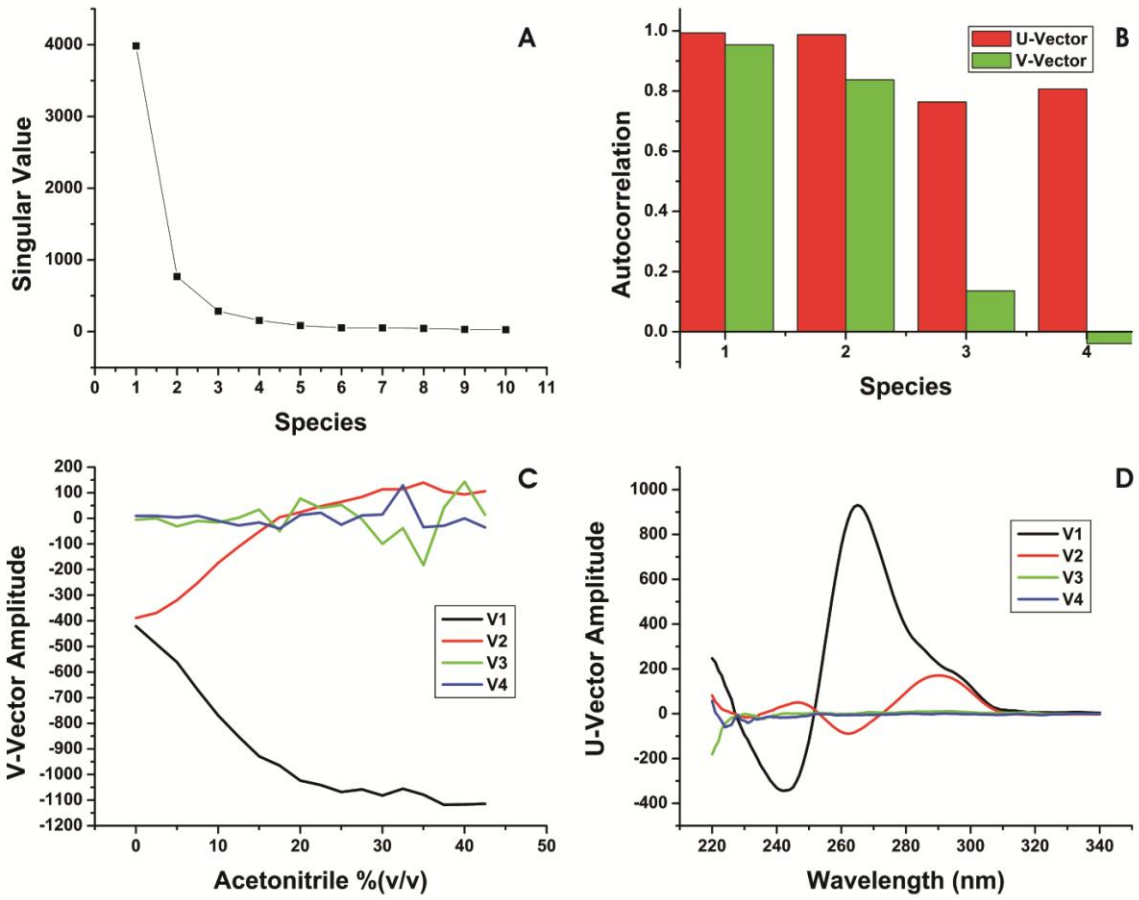
where x is the activity of the ligand. As the titration data can be adequately fitted even to a simple Hill equation, it is clear that the general mechanism of Equation 8 is underdetermined. We consider physical simplifications that reduce to the minimum number of parameters needed to fit the experimental data adequately. If $K_A = K_B$, i.e. there is only differential binding stoichiometries, the above equation reduces to

$$K= K_0(1+x/K_A)^{n-m}$$

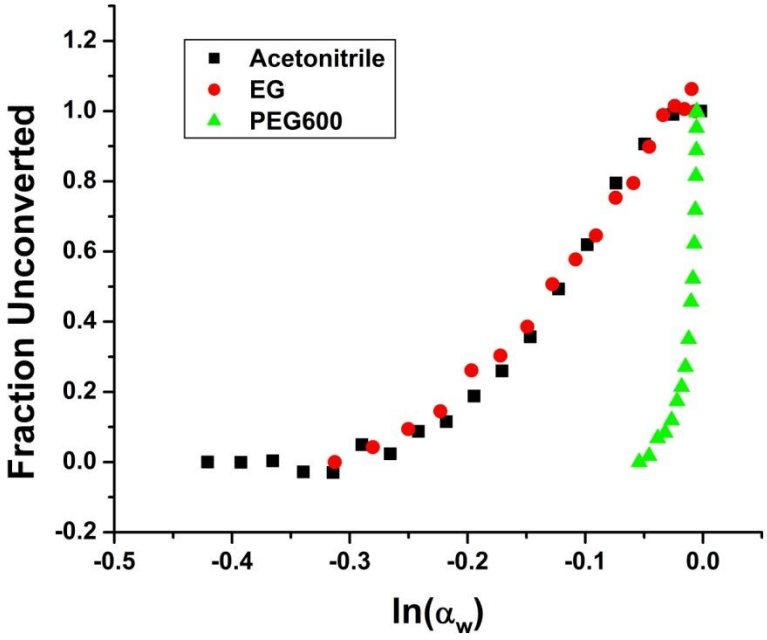
In this instance the apparent stoichiometry is the difference between the two states, analogous to the model of differential hydration. If the value of K_A is very high compared with the maximum value of x, then

$$K= K_0(1+x/K_B)^m$$

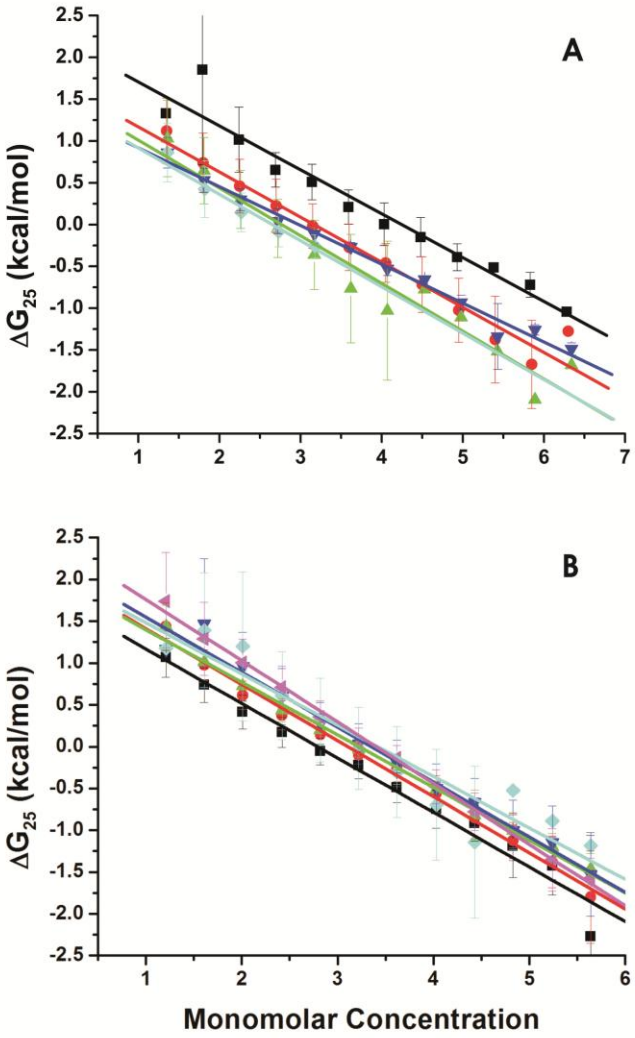
This is exclusive binding, and the stoichiometry is the number of ligand molecule binding to state B. IF n=m, the form reduces to the conventional MWC model.



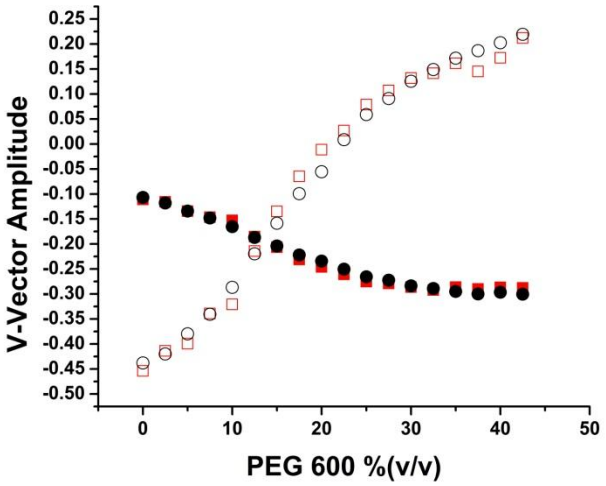
Supporting Information Figure 1. Singular value decomposition (SVD) analysis of the conversion of human telomere G-quadruplex by titration with acetonitrile. All co-solvent titrations completed in this work were analyzed by SVD and resulted in two species significantly contributing to the conversion of the human telomere quadruplex. A) Singular values demonstrate the first two species make up greater than 85% of the observed signal. B) Autocorrelation values indicate only two species are required for accurate analysis of the conversion, with V-autocorrelations falling below the threshold of 0.8 for species beyond the first two. C) V-vectors demonstrate only two significant changes occur during the conversion of human telomere quadruplex by addition of acetonitrile. D) The U-vectors corresponding to the first two species dominate the changes seen during the titration.



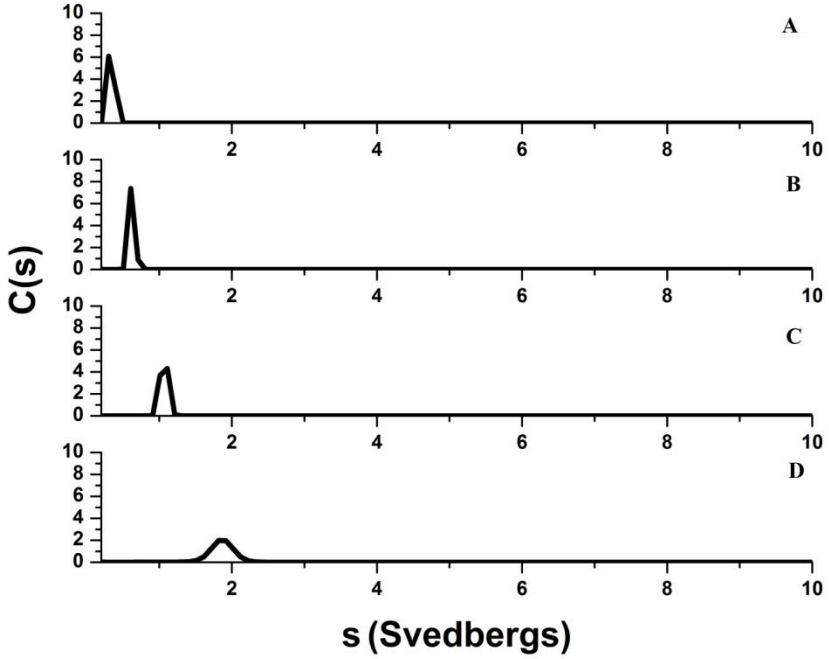
Supporting Information Figure 2. Comparison of the conversion of the hTel22 through addition of acetonitrile (black squares), ethylene glycol (red circles), and PEG 600 (green triangles).



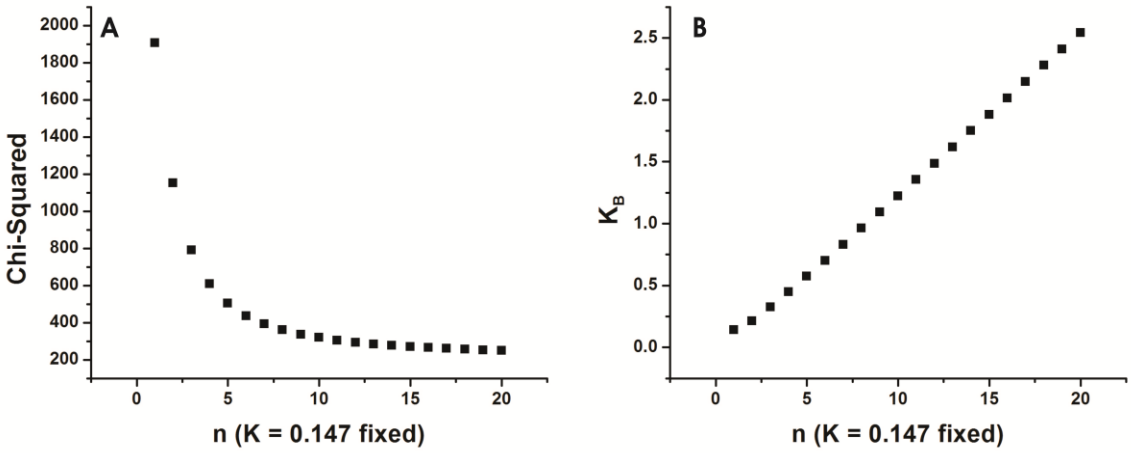
Supporting Information Figure 3. Determination of monomer M-values from linear regression of Gibbs free energy changes (ΔG_{25}) vs. monomolar PEG concentration. A) Ethylene glycol (black), diethylene glycol (red), triethylene glycol (green), PEG 200 (blue), and PEG 400 (cyan). B) PEG 600 (black), PEG 1000 (red), PEG 1500 (green), PEG 3350 (blue), PEG 8000 (cyan), and PEG 10000 (magenta).



Supporting Information Figure 4. PEG 600 titrations conducted at 10X strand concentration monitoring a shift in CD during the conversion of the hTel22. Titrations were conducted at 4 µM (circles) and 40 µM (squares). Strand concentration does not influence the conversion of the hTel22 as monitored by two distinct SVD V-vectors corresponding to 290 nm (closed) and 265 nm (open).



Supporting Information Figure 5. Effect of PEG concentration on hTel22 sedimentation coefficient. Results are plotted as the relative concentration (C(s)) versus uncorrected sedimentation coefficient for PEG concentrations of 30% (A), 20% (B) 10% (C) and 0% (D) in 0.4 M KCl-folding buffer. Data analysis was by Sedfit. Correcting for the measured density and viscosity of the PEG solutions yields the $S_{20,w}$ and f/f_o values shown in Table 2.



Supporting Information Figure 6. Analysis of parameter uncertainty and correlation for fits to Equation 8. A) Error space for estimates of the moles of PEG bound (n). Chi-squared values for the best fit at fixed n values are plotted according to the procedure of Saroff.[3] The plot defines the error space for the parameter n and shows that only a minimum value can be determined. B) Correlation of dissociation constant (K_B) and stoichiometry (n) estimates.

References.

(1) Monod, J.; Wyman, J.; Changeux, J. P. *Journal of molecular biology* **1965**, *12*, 88.

(2) M. Eigen, in S. Claesson (Ed.), *Fast Reactions and Primary Processes in Chemical Kinetics*, Nobel Symposium No. 5, Almqvist and Wiksell, Stockholm, 1967, p. 333.

(3) Saroff, H. A. *Analytical biochemistry* **1989**, *176*, 161.