

Hyeon and Thirumalai's 2003 paper

Can energy landscape roughness of proteins and RNA be measured by using mechanical unfolding experiments? [1]

I'm skeptical about **H&T eq. 8** to **H&T eq. 9**, so I'll rework as much of their math as I am capable of...

$$f^* = \frac{k_B T}{\Delta x(f^*)} \left[\log \left(\frac{r_f \Delta x(f^*)}{v_D(f^*) e^{-\beta \Delta F_0^\ddagger(f^*) k_B T}} \right) + \log \left(1 + f^* \frac{\Delta x(f^*)'}{\Delta x(f^*)} - \frac{\Delta F_0^\ddagger(f^*)'}{\Delta x(f^*)} + \frac{v_D(f^*)'}{v_D(f^*)} \cdot \frac{k_B T}{\Delta x(f^*)} \right) + \log \left(\langle e^{\beta F_1} \rangle \right)^2 \right] \quad \text{H&T eq. 8}$$

We simplify by dropping the 2nd term ("In obtaining Eq. 9, we have assumed that the second term in Eq. 8 is small."), and defining $\alpha \equiv k_B T$, $\rho \equiv \log \left(\frac{r_f \Delta x(f^*)}{v_D(f^*) e^{-\beta \Delta F_0^\ddagger(f^*) k_B T}} \right)$, and $e^{\beta \epsilon} \equiv \langle e^{\beta F_1} \rangle$, yielding

$$f^* = \frac{\alpha}{\Delta x(f^*)} \left(\rho + \frac{\epsilon^2}{\alpha^2} \right) \quad (1)$$

We obtain our version of **H&T eq. 9** by taking two measurements of equal mode force

$$0 = f_1^* - f_2^* \quad (2)$$

$$= \frac{1}{\Delta x(f^*)} \left(\alpha_1 \rho_1 + \frac{\epsilon^2}{\alpha_1} - \alpha_2 \rho_2 - \frac{\epsilon^2}{\alpha_2} \right) \quad (3)$$

$$\epsilon^2 \left(\frac{1}{\alpha_2} - \frac{1}{\alpha_1} \right) = \alpha_1 \rho_1 - \alpha_2 \rho_2 \quad (4)$$

$$\epsilon^2 \cdot \frac{\alpha_1 - \alpha_2}{\alpha_1 \alpha_2} = \quad (5)$$

$$\epsilon^2 = \frac{\alpha_1 \alpha_2}{\alpha_1 - \alpha_2} (\alpha_1 \rho_1 - \alpha_2 \rho_2) \quad (6)$$

$$\epsilon^2 = \frac{k_B T_1 k_B T_2}{k_B T_1 - k_B T_2} \left[k_B T_1 \log \left(\frac{r_{f1} \Delta x_1(f^*)}{v_{D1}(f^*) e^{-\beta_1 \Delta F_0^\ddagger(f^*)_1 k_B T_1}} \right) - k_B T_2 \log \left(\frac{r_{f2} \Delta x_2(f^*)}{v_{D2}(f^*) e^{-\beta_2 \Delta F_0^\ddagger(f^*)_2 k_B T_2}} \right) \right] \quad (7)$$

Which is different from **H&T eq. 9** by the sign in the prefactor, and the replacement $v_D(f^*) \rightarrow k(f^*)$.

$$\epsilon^2 = \frac{k_B T_1 k_B T_2}{k_B T_2 - k_B T_1} \left[k_B T_1 \log \left(\frac{r_{f1} \Delta x_1(f^*)}{v_{D1}(f^*) k_B T_1} \right) - k_B T_2 \log \left(\frac{r_{f2} \Delta x_2(f^*)}{v_{D2}(f^*) k_B T_2} \right) \right] \quad \text{H&T eq. 9}$$

Alternatively, noting that $\Delta x(f^*)$ can vary as a function of temperature, we follow Nevo et al. in keeping it in. Using $\delta \equiv \Delta x(f^*)$

$$0 = f_1^* - f_2^* \quad (8)$$

$$= \frac{\alpha_1 \rho_1}{\delta_1} + \frac{\epsilon^2}{\delta_1 \alpha_1} - \frac{\alpha_2 \rho_2}{\delta_2} - \frac{\epsilon^2}{\delta_2 \alpha_2} \quad (9)$$

$$\epsilon^2 \left(\frac{1}{\delta_2 \alpha_2} - \frac{1}{\delta_1 \alpha_1} \right) = \frac{\alpha_1 \rho_1}{\delta_1} - \frac{\alpha_2 \rho_2}{\delta_2} \quad (10)$$

$$\epsilon^2 \cdot \frac{\delta_1 \alpha_1 - \delta_2 \alpha_2}{\delta_1 \delta_2 \alpha_1 \alpha_2} = \frac{\delta_2 \alpha_1 \rho_1 - \delta_1 \alpha_2 \rho_2}{\delta_1 \delta_2} \quad (11)$$

$$\epsilon^2 = \frac{\alpha_1 \alpha_2}{\delta_1 \alpha_1 - \delta_2 \alpha_2} (\delta_2 \alpha_1 \rho_1 - \delta_1 \alpha_2 \rho_2) \quad (12)$$

$$\epsilon^2 = \frac{k_B T_1 k_B T_2}{\Delta x_1(f^*) k_B T_1 - \Delta x_2(f^*) k_B T_2} \left[\Delta x_2(f^*) k_B T_1 \log \left(\frac{r_{f1} \Delta x_1(f^*)}{k_1(f^*) k_B T_1} \right) - \Delta x_1(f^*) k_B T_2 \log \left(\frac{r_{f2} \Delta x_2(f^*)}{k_2(f^*) k_B T_2} \right) \right] \quad (13)$$

References

- [1] C. Hyeon and D. Thirumalai. *Can energy landscape roughness of proteins and RNA be measured by using mechanical unfolding experiments?*. PNAS **100**, 18, 10249-10253 (2003).

<http://www.pnas.org/>