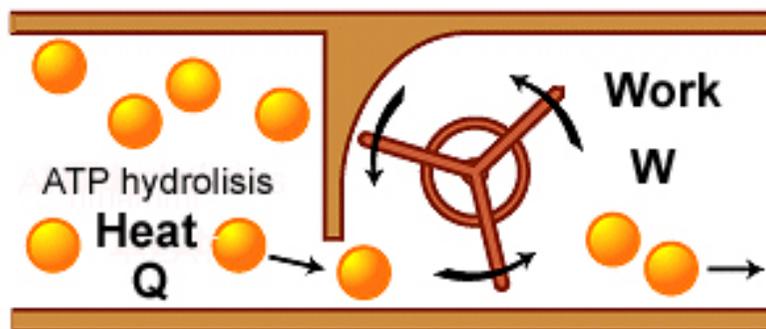


Tradeoff between dissipation and uncertainty in helicases

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How are the helicase speed (rate V), the fluctuations (diffusion D) and the entropy production (S) related?

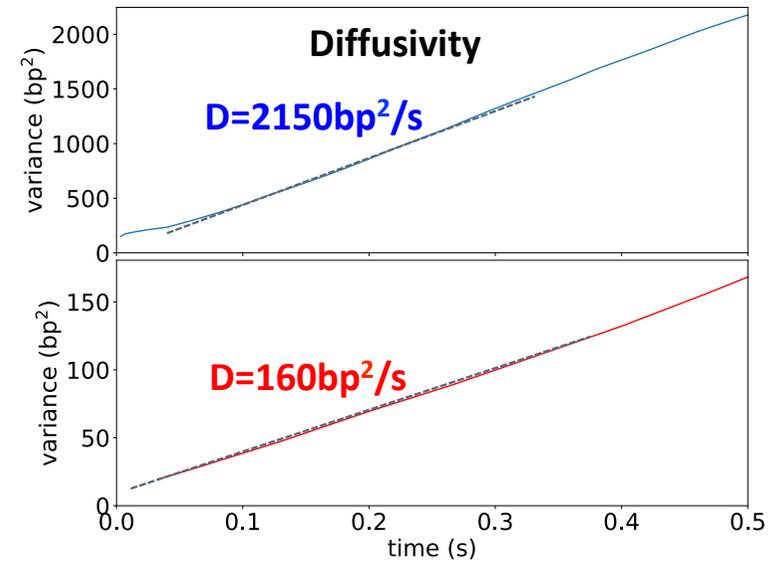
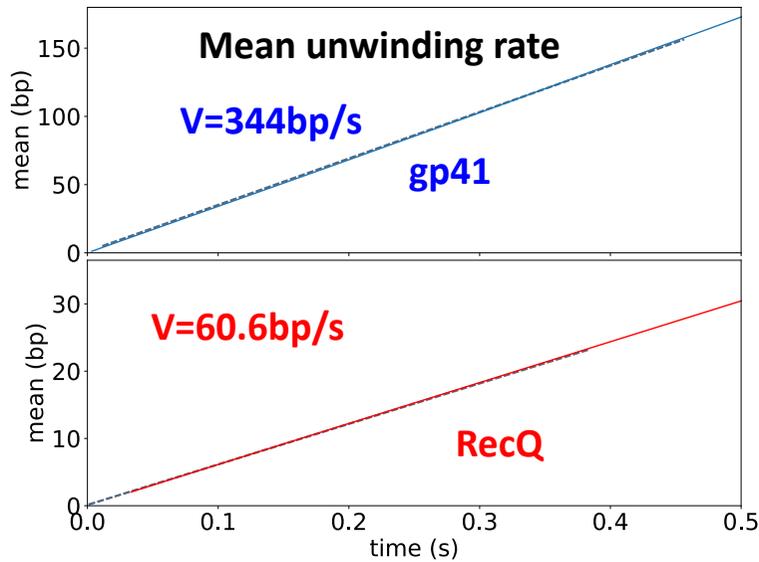
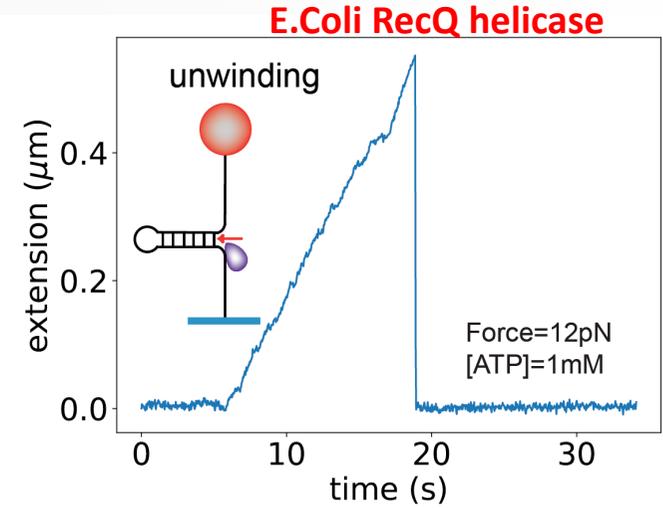
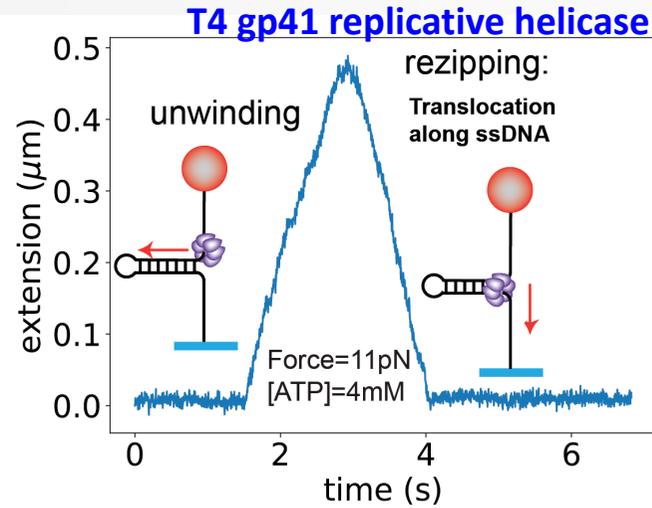
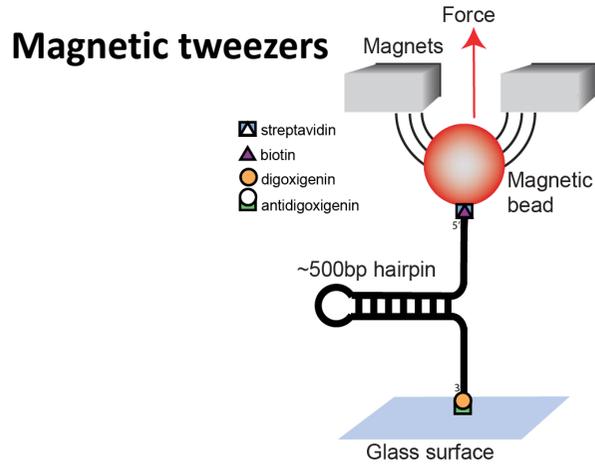
A lower bound for the trade-off Q is given by the thermodynamic uncertainty relation (TUR) [1,2]:

$$Q = \frac{S_{bp}}{k_B} \frac{2D}{v} \geq 2$$

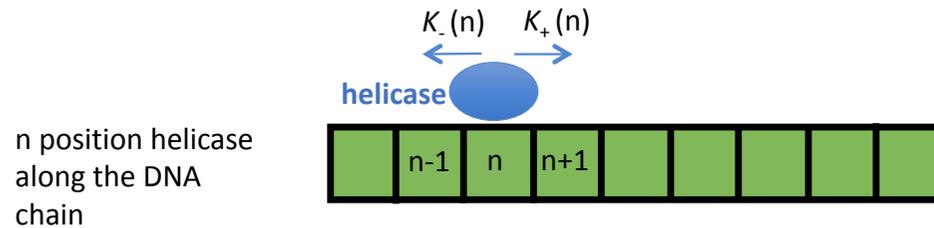
[1] Barato, A. C., & Seifert, U. (2015). Thermodynamic uncertainty relation for biomolecular processes. Physical review letters, 114(15), 158101.

[2] Pietzonka, P., Ritort, F., & Seifert, U. (2017). Finite-time generalization of the thermodynamic uncertainty relation. Physical Review E, 96(1), 012101.

Following DNA unwinding trajectories of two different helicases



Simple model for helicase motion: Biased random walk (BRW)



Energies involved in a single unwinding/translocation step:

$\Delta\mu \approx 20-25k_B T$ (ATP hydrolysis)

$\Delta G_{bp} \approx 2-3k_B T$ (DNA base-pairing energies)

$\Delta G_{act} \approx 0$ (gp41 passive helicase) $\Delta G_{act} \approx 2k_B T$ (RecQ active helicase) [3]

$W_F < 3k_B T$ (work by the external force $< 15pN$)

Rates fulfill detailed balance:

$$K_- = \exp\left(\frac{-\Delta\mu}{k_B T}\right)$$

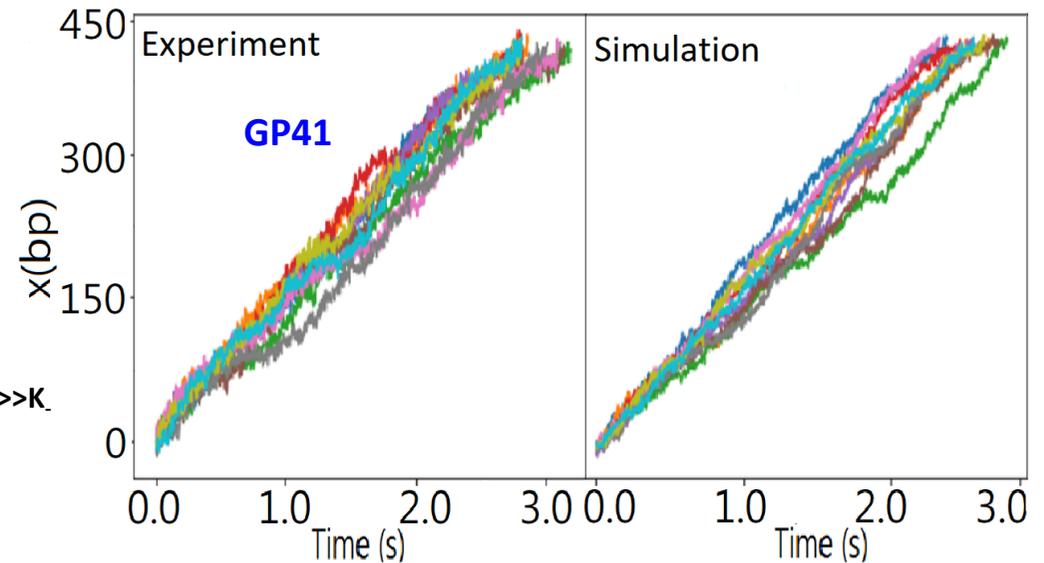
$$K_+ = \exp\left(\frac{-\Delta G_{bp}(n) + W_F + DG_{act}}{k_B T}\right)$$

Homogeneous sequence: $\Delta G_{bp} = cte$, $K_+ \gg K_-$

$$V = K_+ - K_- \approx K_+$$

$$D = \frac{K_+ + K_-}{2} \approx \frac{K_+}{2}$$

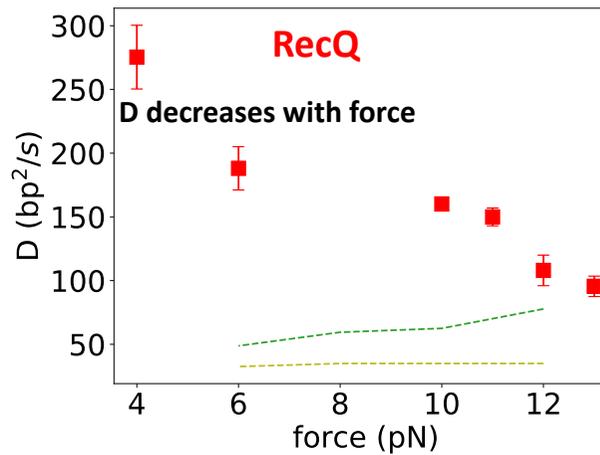
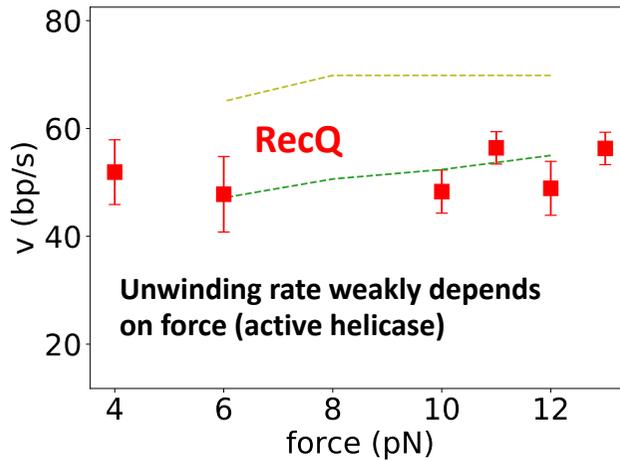
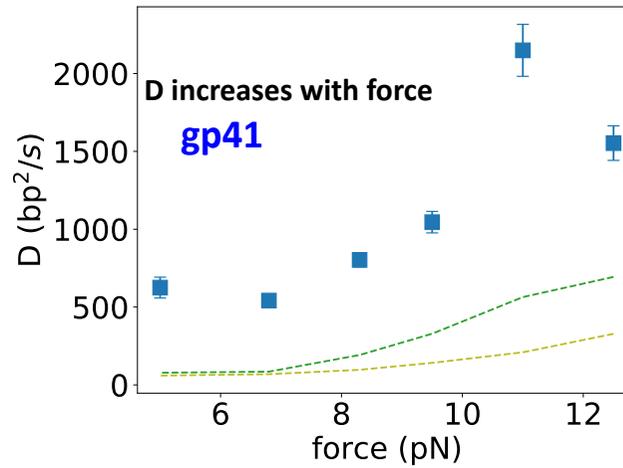
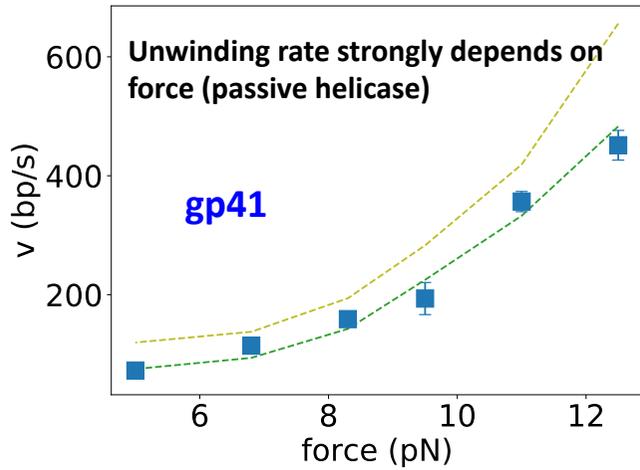
Simulations random walk + Langevin dynamics for the magnetic bead using DNA chain with the specific heterogeneous DNA sequence



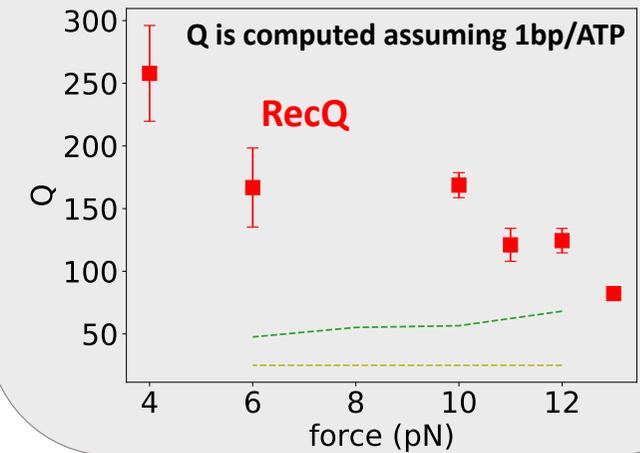
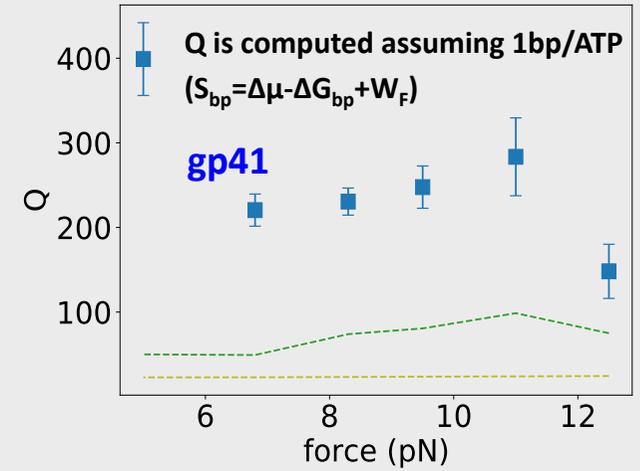
[3] Manosas, M., Xi, X. G., Bensimon, D., & Croquette, V. (2010). Active and passive mechanisms of helicases. *Nucleic acids research*, 38(16), 5518-5526.

Force analysis

■ gp41 ■ RecQ Unwinding (exp) - - - BRW heterogenous sequence
- BRW homogenous sequence

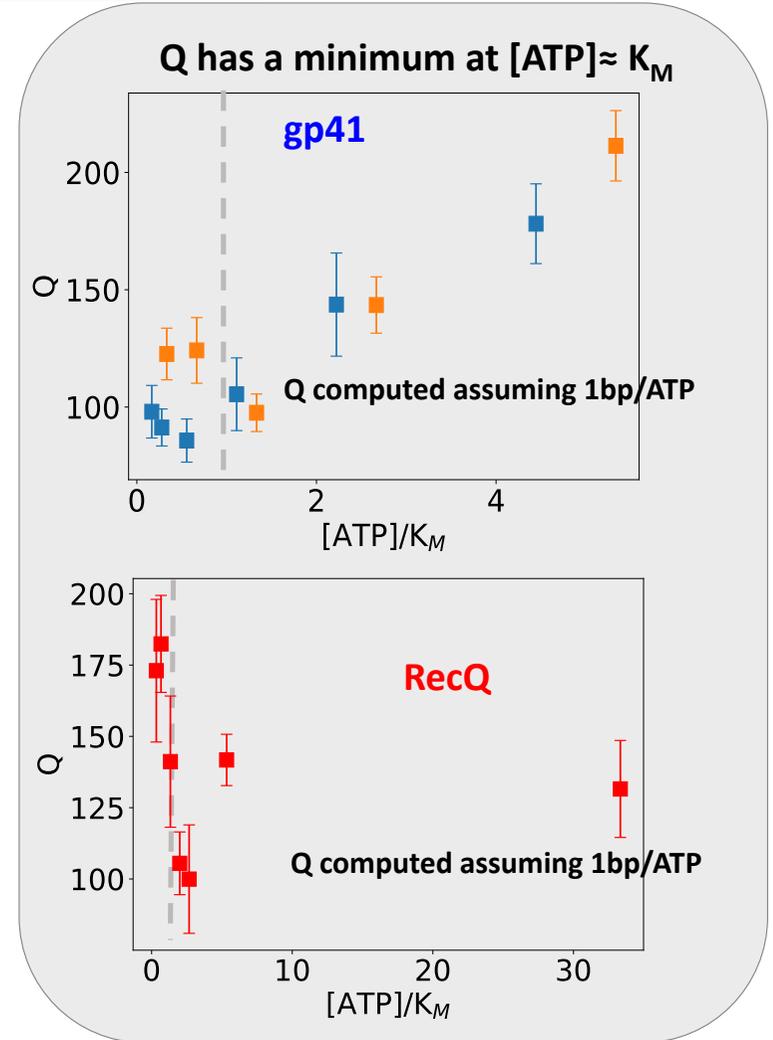
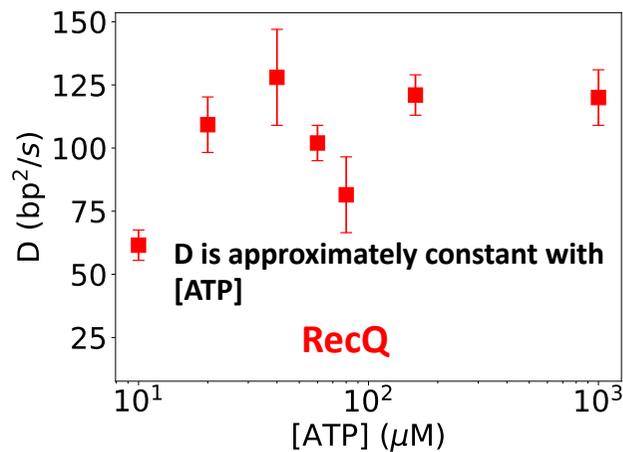
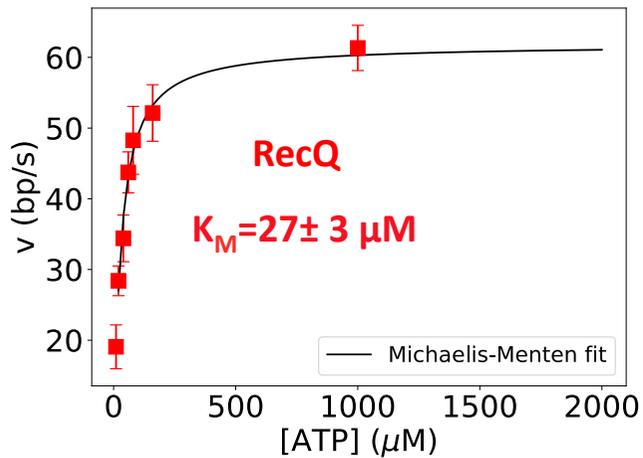
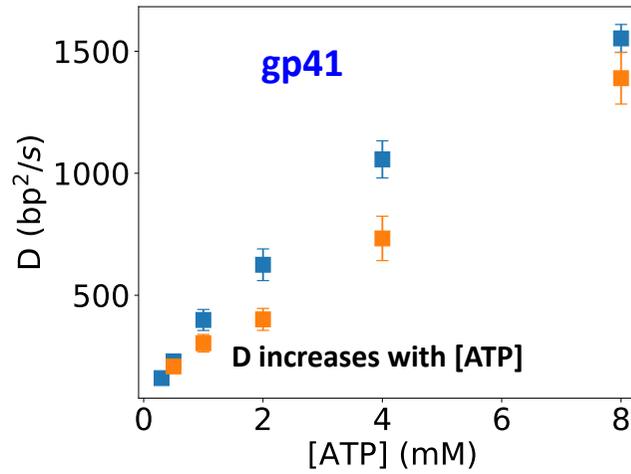
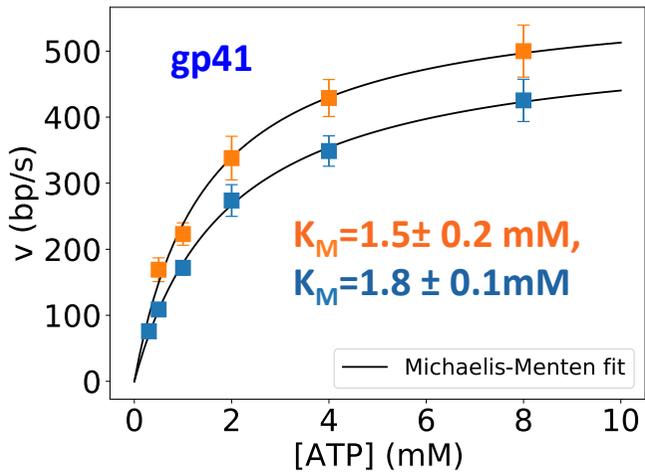


BRM predicts lower Q
Q decreases with the applied force



ATP analysis

■ gp41 ■ RecQ Unwinding (exp) ■ Translocation (exp)



Conclusions and Future perspectives

- **The trade-off Q depends on external conditions, such as the $[ATP]$ and the external force**
- **Besides the differences between gp41 and RecQ (different values for V , D and their force dependence) both helicases present similar Q values ($Q \approx 100-400$) that decrease with the external force**
- **Both helicases minimize Q at a ATP concentration around $[ATP] \approx K_M$ as predicted in theoretical studies [4]**
- **A simple model for helicase motion based on a biased random walk does underestimate the experimental diffusivity and Q trade-off.**
- **We envision to extend the model to include: (i) the ATP hydrolysis reaction with different mechano-chemical couplings and, (ii) a helicase off-pathway pausing state.**
- **We plan to investigate other experimental factors that could affect the Q trade-off, such as the temperature and salt concentration**

[4] Song, Y., & Hyeon, C. (2021). Thermodynamic uncertainty relation to assess biological processes. The Journal of Chemical Physics, 154(13), 130901.