quarantine lab meeting, an update on the random walk binding model: adjusting terms in the Hamiltonian and partition function for reliable calculations of transition probabilities

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rewriting the Hamiltonian

to more easily code up, and interpret, the Hamiltonian for additional base pair mismatches, we will introduce elementary rearrangements, from which we obtain an equivalent expression for the Hamiltonian,

$$\exp(-\mathcal{H}) = \exp\Bigg(- \frac{1}{(|\{\mathrm{mat}\}|+2)^3} \sum_{i\sim j} \mathcal{J}_{ij}\sigma_i\sigma_j - \frac{1}{(|\{\mathrm{mis}\}|+2)^3} \sum_{i\not\sim j} \mathcal{J}_{ij}(1-\sigma_i\sigma_j)\Bigg) \; ,$$

$$\Leftrightarrow \prod_{i\sim j} \exp\Bigg(- \frac{1}{(|\{\mathrm{mat}\}|+2)^3} \mathcal{J}_{ij}\sigma_i\sigma_j\Bigg) \prod_{i\not\sim j} \exp\Bigg(- \frac{1}{(|\{\mathrm{mis}\}|+2)^3} \mathcal{J}_{ij}(1-\sigma_i\sigma_j)\Bigg) \; ,$$

with $\mathcal{J}_{ij} = |N-j|$ if $\sigma_i = \sigma_j$ and $\mathcal{J}_{ij} = 1-|N-j|$ otherwise

the next step: expressing the probability measure μ for binding configurations

from the equivalent expression of $\exp(-\mathcal{H})$, one can form a probability measure, for additional base pair mismatches, with an expression of the form

$$\mu(N, N_{\mathrm{mis}}, |X_{\mathrm{mis}}|) = \frac{\prod_{i\sim j} \exp\bigg(- \frac{1}{(|\{\mathrm{mat}\}|+2)^3} \mathcal{J}_{ij}\sigma_i\sigma_j \bigg) \prod_{i\not\sim j} \exp\cdots}{1 + \lambda_c e^{-\beta\epsilon_{\mathrm{PAM}}} + N_{\mathrm{mis}} \sum_{\mathrm{mis}} \lambda_{\mathrm{mis}} e^{-\lambda_{\mathrm{mis}} X_{\mathrm{mis}}}} \ ,$$

which in retrospect, from expressions of the Hamiltonian and partition function that I have proposed last semester, **account** for:

- redefining contributions from $\mathcal{H}$, individually for base pair matches and mismatches,
- accompanying normalizations N_{mat} and N_{mis},
- appropriately weighing the exponential factor in the numerator of μ, so as to accurately weigh unfavorable binding configurations

rigorous formulation of the choice of free parameters in the Hamiltonian and partition function

with μ, one can appropriately choose $\lambda_c, \lambda_{\mathrm{mis}} << 1$, in addition to an N_{mis} parameter, so that:

- μ comparatively assigns sufficiently lower values within the sample space of binding configurations to sequences with new mismatches,
- from such probabilistic assignments, we can use the value of the dimensionless probability to capture the decay in transition probabilities,
- calculate visits of the random walk at N.

Remark from plots in the last presentation: The visits of the random walk to the position of binding all appeared to be of almost of the same magnitude because the exponential parameter for base pair mismatches, if not multiplied by N_{mis}, alters the assignment of the probability measure with very little precision! With N_{mis}, we are able to decrease the value of μ for additional base pair mismatches, which multiplicatively can be used to calculate transition probabilities

future directions for next week's meeting

to construct transition probability sequences, for next week's progress it is imperative to

- enforce consistent values of the λ_c, λ_{mis}, ϵ_{PAM}, λ_{mis} parameters, all of which satisfy the condition $<< 1$ in Specht, Xu, Lambert (2019)
- construct a sequence $\{N_i\}_{i \in \mathbf{N}}$, dependent on the position of base pair mismatch, so that for a base pair mismatch at i, there exists N_i so that μ for the modified binding sequence assigns a lower probabilistic value of successful binding at N
- I have generated values for 1 base pair mismatch from the new formula of μ, and am generalizing the formula to account for additional base pair mismatches, possibly for mismatches in succession but not more than 3 mismatches total, to apply code from the previous presentation to compute visits of the random walk, from sequences of transition probabilities