



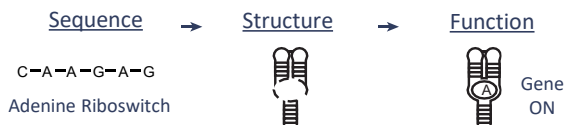
Ensembles Link RNA Sequence to Function

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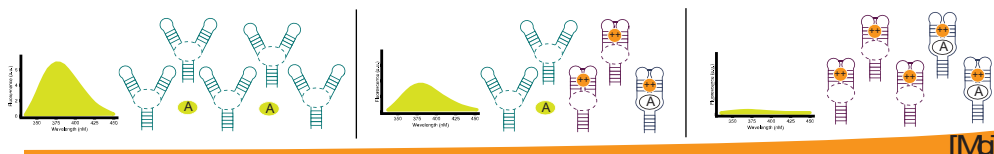
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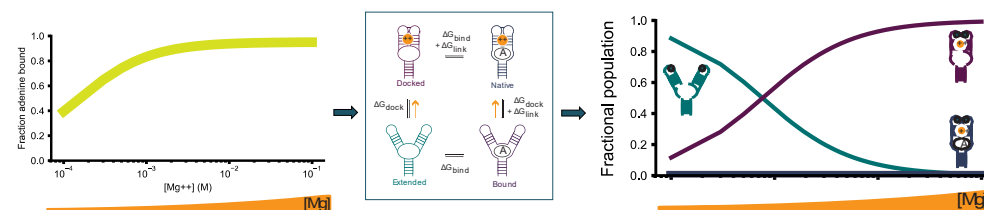
Goal: Predict how sequence changes translate to functional changes



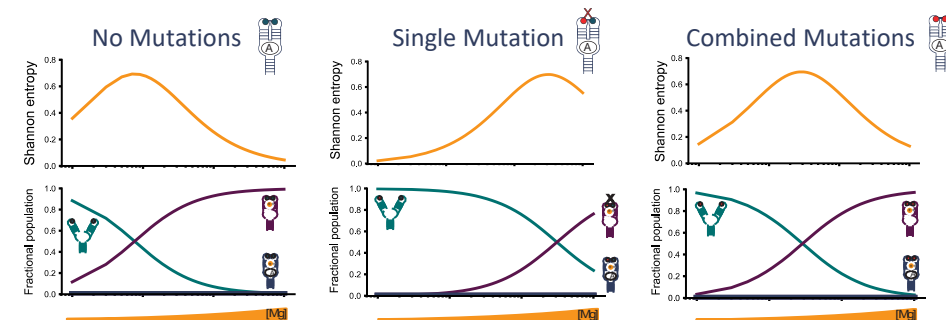
Step 1: Measure the effect of a mutation on adenine binding



Step 2: Calculate how the mutation redistributes the ensemble



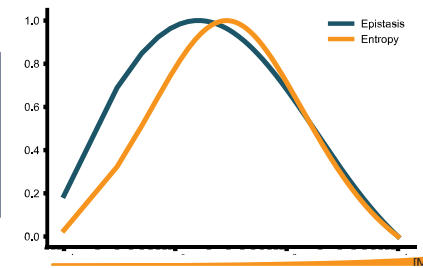
Step 3: Analyze ensemble diversity for mutations alone and together



Results: Adenine riboswitch exhibits ensemble epistasis

Future Directions:

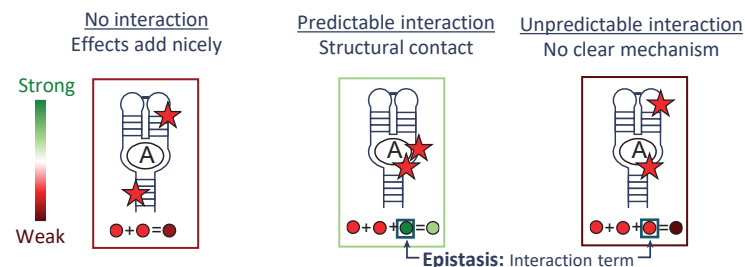
✓ Epistasis (mutational interaction) increases as the ensemble becomes more diverse



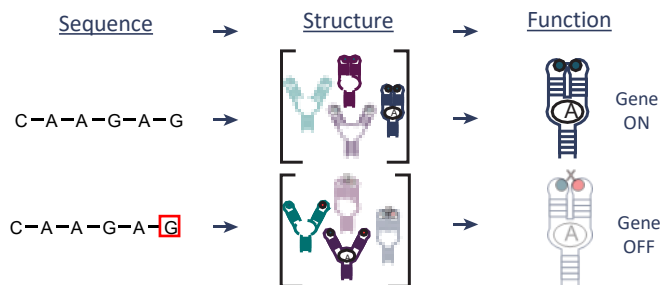
- Measure all combinations of five mutations (32 variants)
- Understand mechanism of each mutational interaction
- Incorporate ensembles into mutation prediction models

Acknowledgements: Harms Lab, Widom Lab, Presidential Undergraduate Research Scholars Program

Challenge: Mutations can interact with each other



Theory: Mutations interact through the ensemble

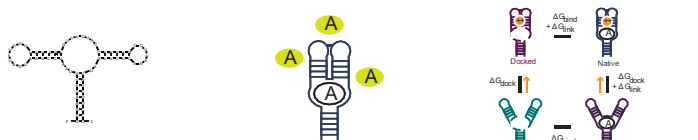


Ingredients for Ensemble Epistasis:

Molecule adopts 3+ conformations, mutations affect conformations differently

Question: Do RNA molecules exhibit ensemble epistasis?

Model system: Adenine Riboswitch



Simple chemistry and structure

Binds fluorescent adenine

Ensemble influenced by Mg++