

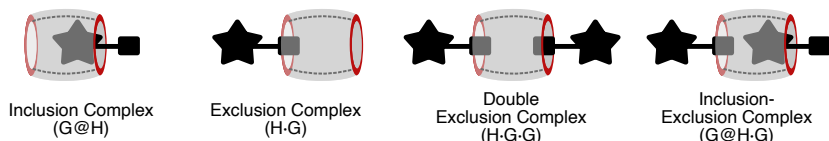
# A Simulation-Guided Method to Tackle Supramolecular Complexity and Save Me Time

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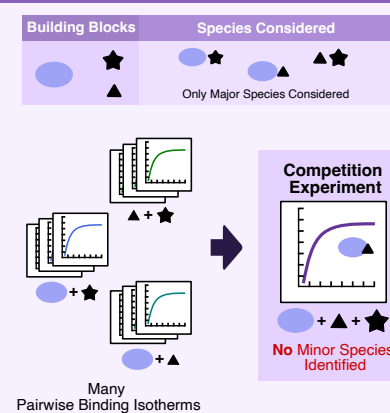
## Background

**Supramolecular chemistry** is a branch of chemistry that studies weak, reversible intermolecular interactions.<sup>1</sup>

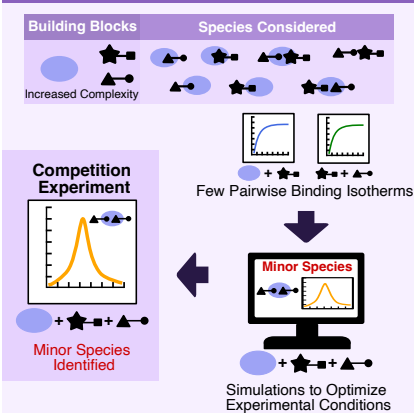
**Supramolecular complexity** refers to the idea that there are multiple distinct host-guest complexes (species) in solution leading to new properties.



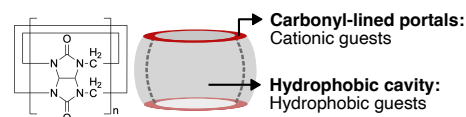
### Reductionist Approach



### Holistic Simulation-Experiment Approach

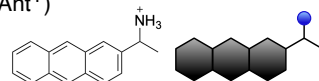


**Host:** Cucurbit[7]uril (CB[7])



**Fluorescent Guest:**

1-(2-Anthryl)ethylammonium cation (Ant<sup>+</sup>)



**Objectives:**

1. Use simulations in a non biased way to determine major and minor species before doing experiments.
2. Reduce the number of preliminary experiments needed to explore supramolecular complexity.

## Methods

### Equilibrium Estimation.py (EE.py)

1. Generate all possible species for defined building blocks.
2. Generate equations for concentration of all species.

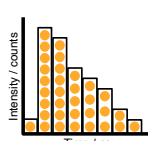
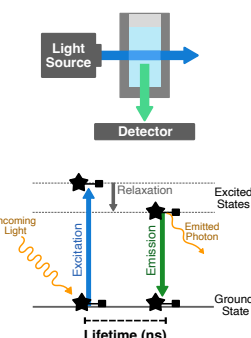
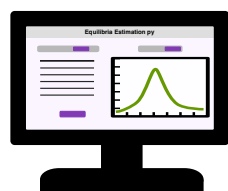
$$[M_{\text{free}}] = M_i - \sum_{\text{all } S} N_M \times [S]$$

3. Solve for concentrations based on  $K_a$  values and initial concentrations.

### Steady-State Fluorescence and Time-Correlated Single Photon Counting (TCSPC)

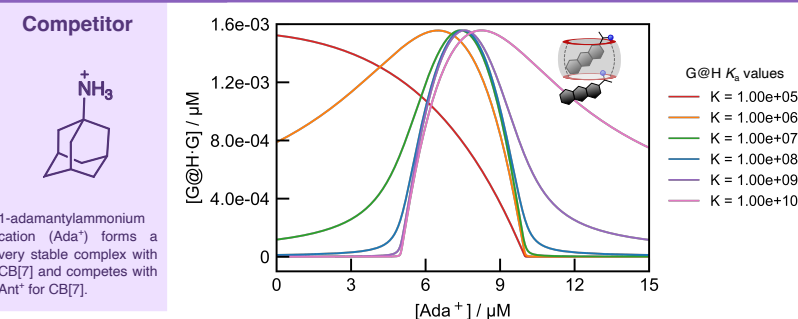
**Steady-State:** Constant excitation and emission. Measures total intensity – cannot discriminate between fluorophores.<sup>2</sup> Was used to investigate the change in fluorescence as a competitor was added.

**TCSPC:** Pulsed excitation and emission decays. Measures the delay between excitation and emission. Was used to confirm the existence of multiple species in the solution.



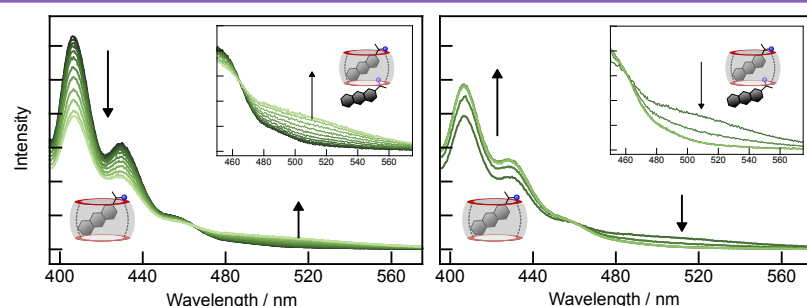
## Results

### Initial Simulation



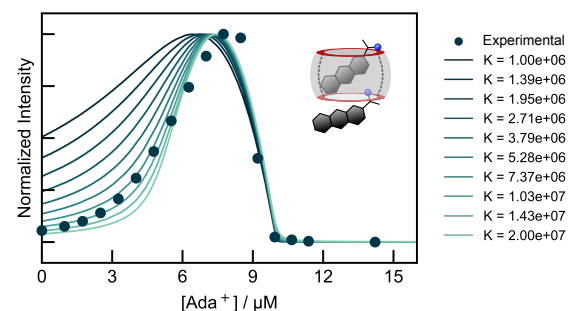
**Figure 1.** [Ant@CB[7]-Ant] for simulated titration of 5 μM Ant<sup>+</sup> and 10 μM CB[7] with Ada<sup>+</sup>.  $K_a$  of the Ant@CB[7] species was varied.

### Competitive Binding Experiment



**Figure 2.** Change in fluorescence spectra when titrating 5 μM Ant<sup>+</sup> and 10 μM CB[7] with 290 μM Ada<sup>+</sup>. (Left) 0 – 8.5 μM Ada<sup>+</sup> (right) 8.5 – 14.2 μM Ada<sup>+</sup>.

### Minor Species Acquired



**Figure 3.** Normalized experimental intensity over 480–540 nm (circles) and simulated concentration profiles of Ant<sup>+</sup>@CB[7]-Ant<sup>+</sup> at various  $K_a$  values for Ant<sup>+</sup>@CB[7] (lines).

## Conclusions

I developed a simulation methodology that informed experimental design and predicted an emergent property. This methodology minimized the time spent in the lab to characterize a supramolecular system and its complexity.

**Future work:** use this approach to investigate a more complex system with multiple hosts.

**Estimated Time Saved:**

Estimated number of binding isotherms prevented = 7 x (3 replicates) = 21 isotherms  
Time per isotherm (including preparation and processing) = 8 hours / isotherm

A total of **168 hours saved** ~ 4 weeks of full time work

## Acknowledgements

We acknowledge and respect the Lək̓ʷəŋən (Songhees and X̱w̱sep̱əm/Esquimalt) Peoples on whose territory the university stands, and the Lək̓ʷəŋən and W̱SÁNEĆ Peoples whose historical relationships with the land continue to this day.

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1. Menger, F. M. Supramolecular Chemistry and Self-Assembly. *PNAS* **2002**, *8* (99), 4818–4822. <https://doi.org/10.1073/pnas.062524299>.

2. He, W.; Guo, Z. Molecular Imaging: Chemistry and Applications. In *Comprehensive Inorganic Chemistry II: From Elements to Applications*; Reedijk, J., Poepelmeier, K. Eds.; Elsevier Ltd, 2013; Vol. 8, pp 733–780. <https://doi.org/10.1016/B978-0-08-097774-4.00805-6>.