

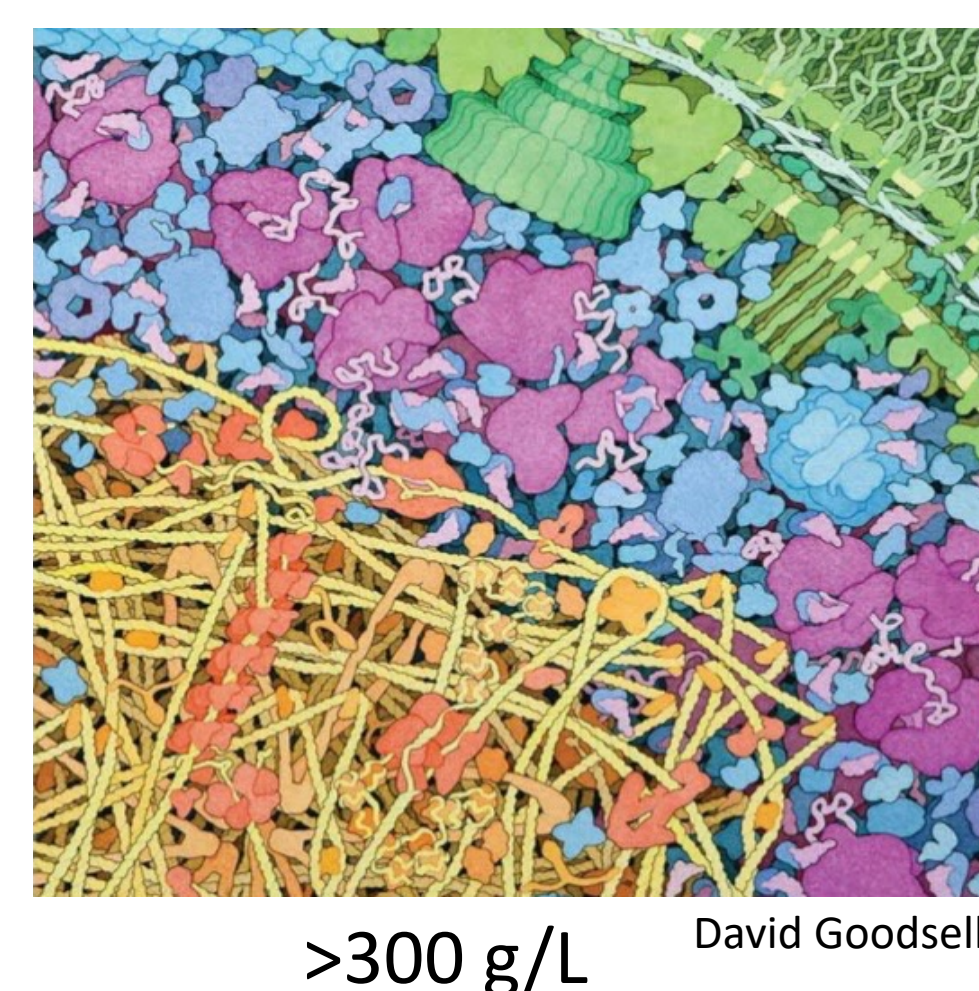


# Protein Dimer Stability in Concentrated Solutions of Sugar Polymers

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## Background and Significance



>300 g/L David Goodsell

...BUT



<10 g/L

Classic Crowding Models:  $\Delta G_{D \rightarrow M}^{\circ'} \approx -T\Delta S_{D \rightarrow M}^{\circ'}$

New Model:  $\Delta G_{D \rightarrow M}^{\circ'} = \Delta H_{D \rightarrow M}^{\circ'} - T\Delta S_{D \rightarrow M}^{\circ'}$

Soft interactions

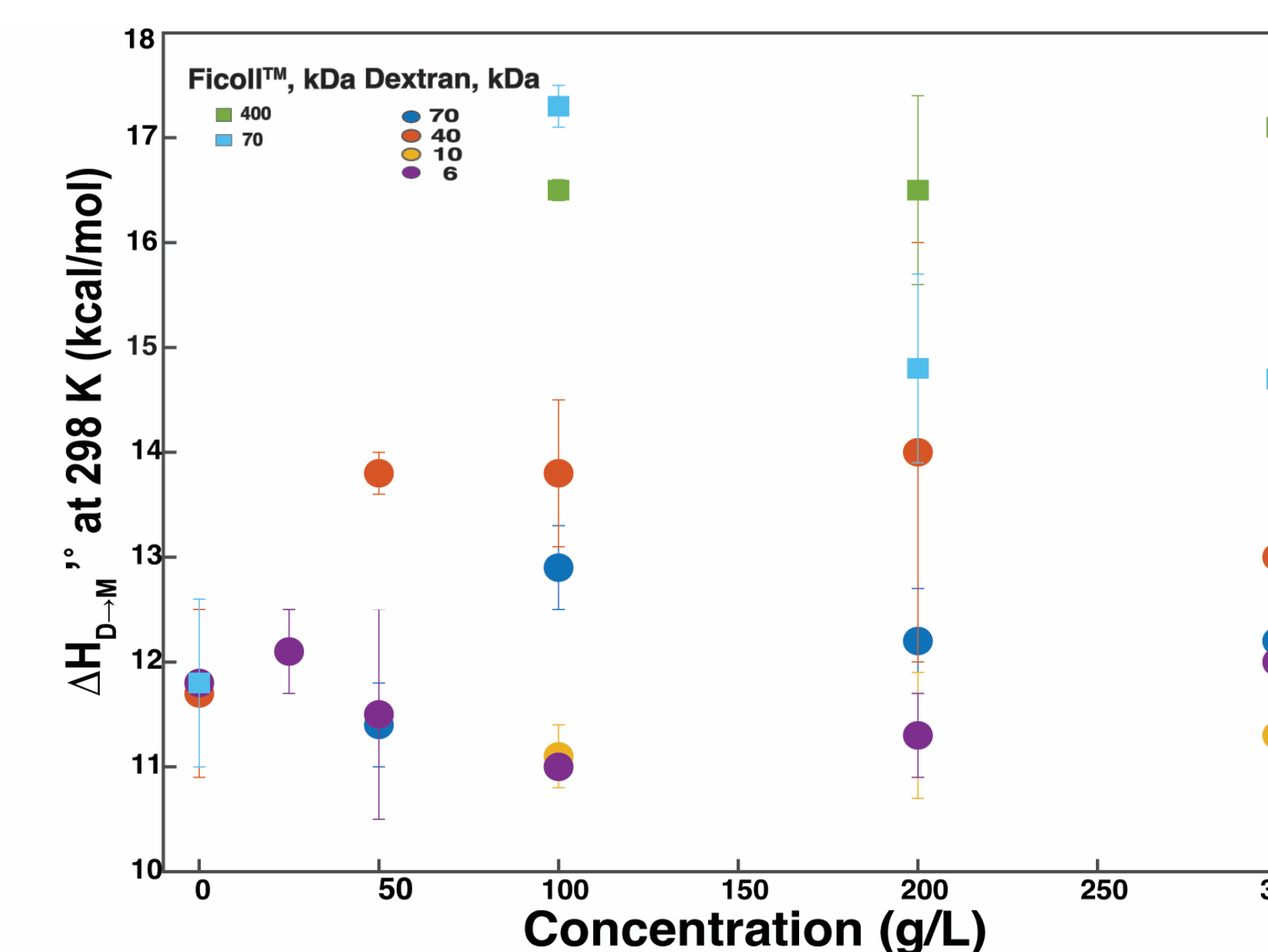
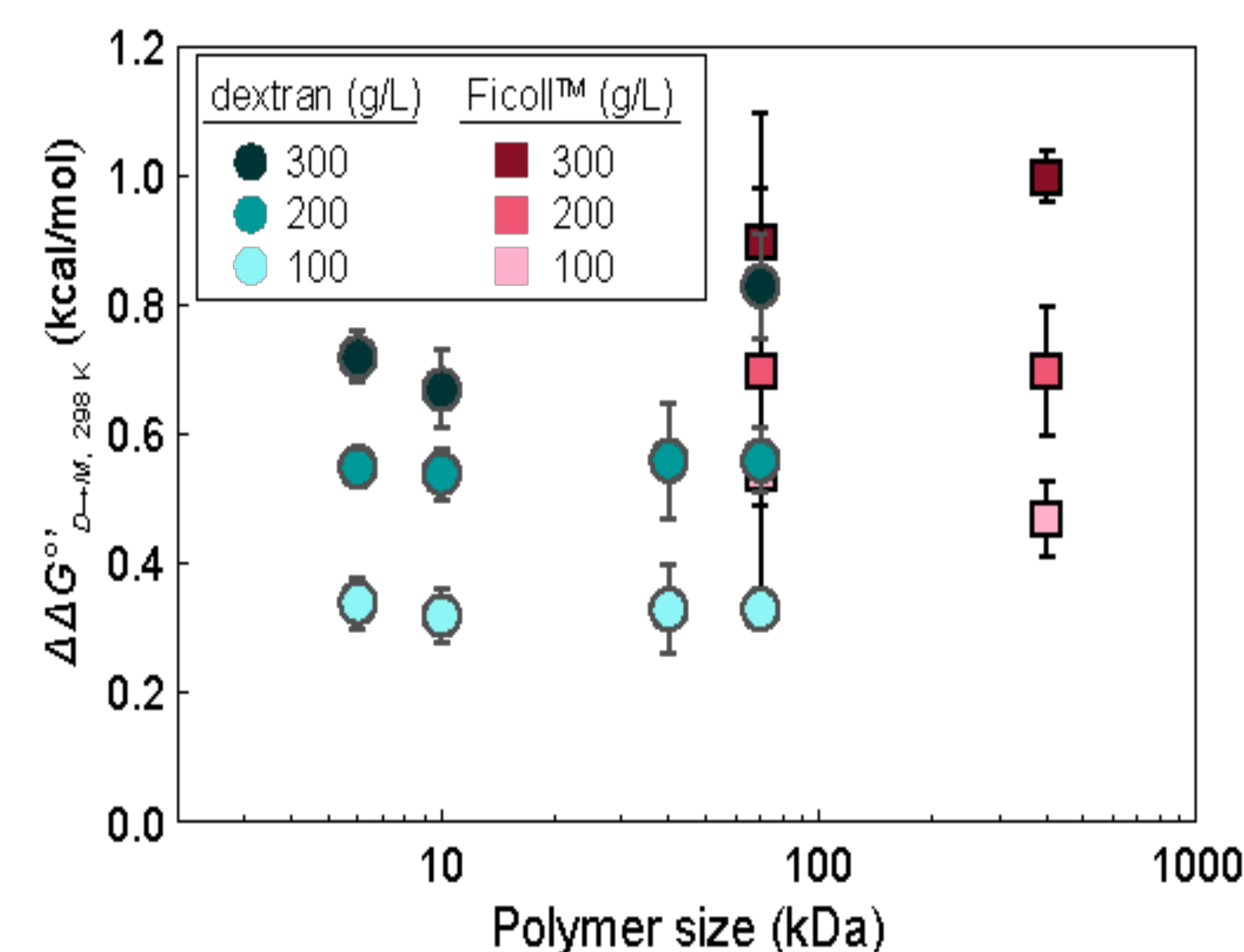
Hardcore repulsions  
Soft interactions

Dimer  $\rightleftharpoons$  monomer equilibrium quantified by <sup>19</sup>F NMR:

$$\Delta G_{D \rightarrow M}^{\circ'} = -RT \ln \left( \frac{\text{Population Monomer}}{\text{Population Dimer}} \right)$$

- Cytoplasm is crowded; macromolecular concentrations can exceed 300 g/L
- But most research done in dilute buffers with less than 10 g/L.
- Classic crowding theory only predicts entropic effect, not enthalpic effects
- We use two synthetic crowder: dextran the polymer of glucose and Ficoll™ the polymer of sucrose
- We quantified the free energy & enthalpy of dissociation.

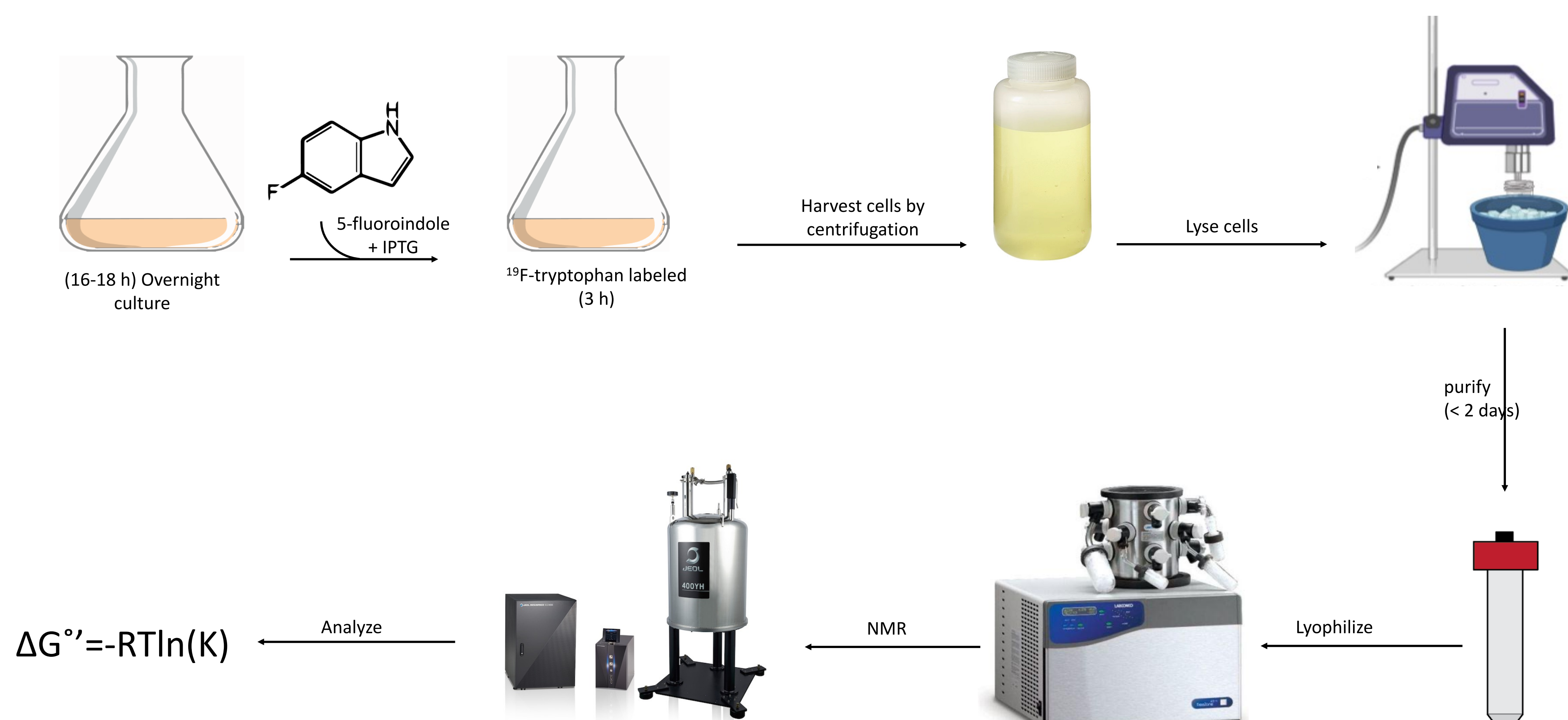
## Results



- $\Delta\Delta G_{D \rightarrow M}^{\circ'}$  measures dimer stability
- Increasing polymer concentration increases stability
- Size of crowder has negligible effect on dimer stability
- Shape of polymer may affect dimer stability

- Enthalpy is non-zero
- Hence, classic crowding model is insufficient
- Enthalpic contribution to dimer stability may depend on polymer size and shape

## Methods



## Conclusions

- Crowding has a stabilizing effect
- Enthalpy affects protein-complex stability
- Need model to better understand effects of crowding on protein-complex stability

## References and Acknowledgements

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