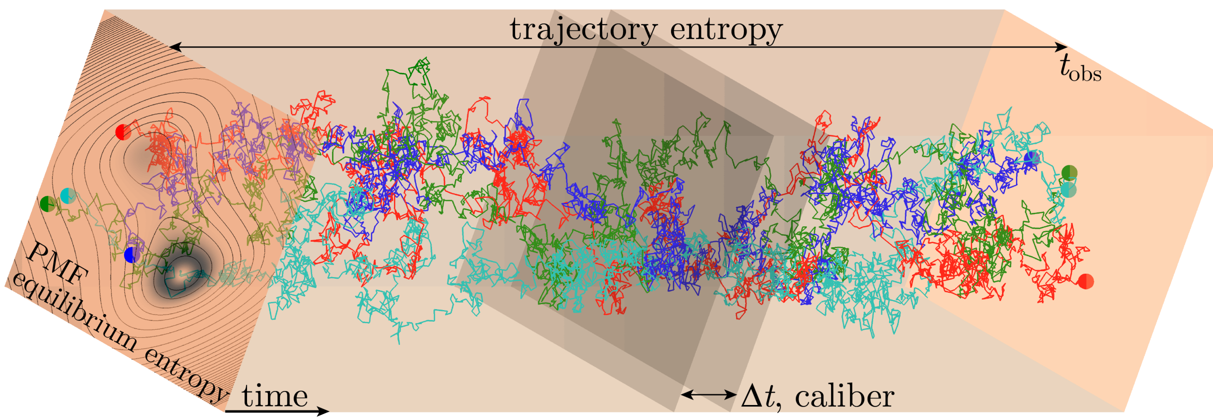
Information Thermodynamics and Bayesian Optimization:

Applications to Single Molecule Experiments



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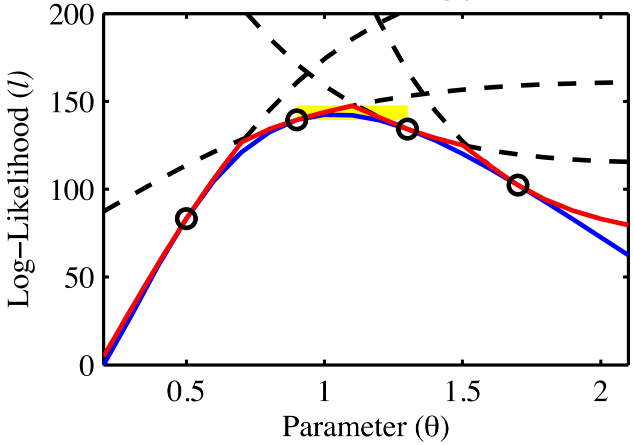
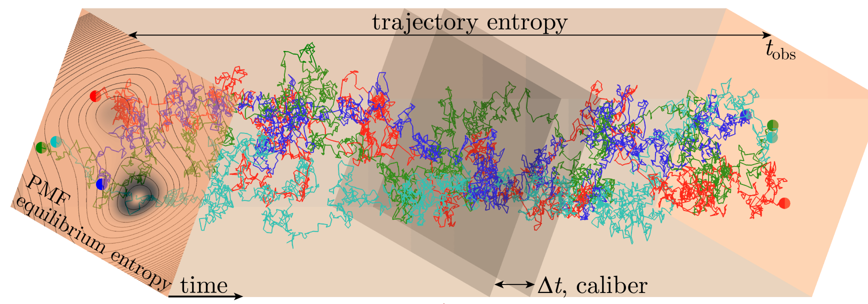
Trajectory Entropy and Information Thermodynamics for Analyzing Complex Systems

Likelihood "Energy"

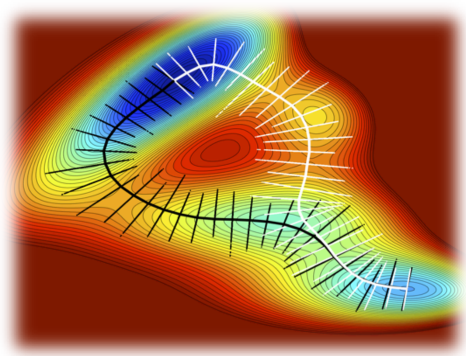


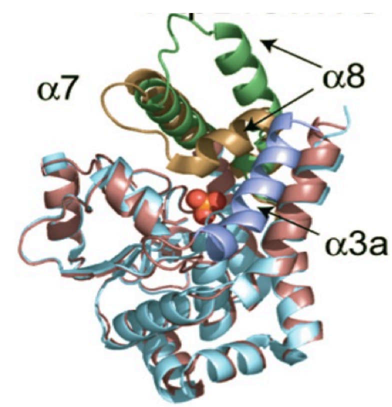
Prior "Entropy"



- Experiment
- Simulation

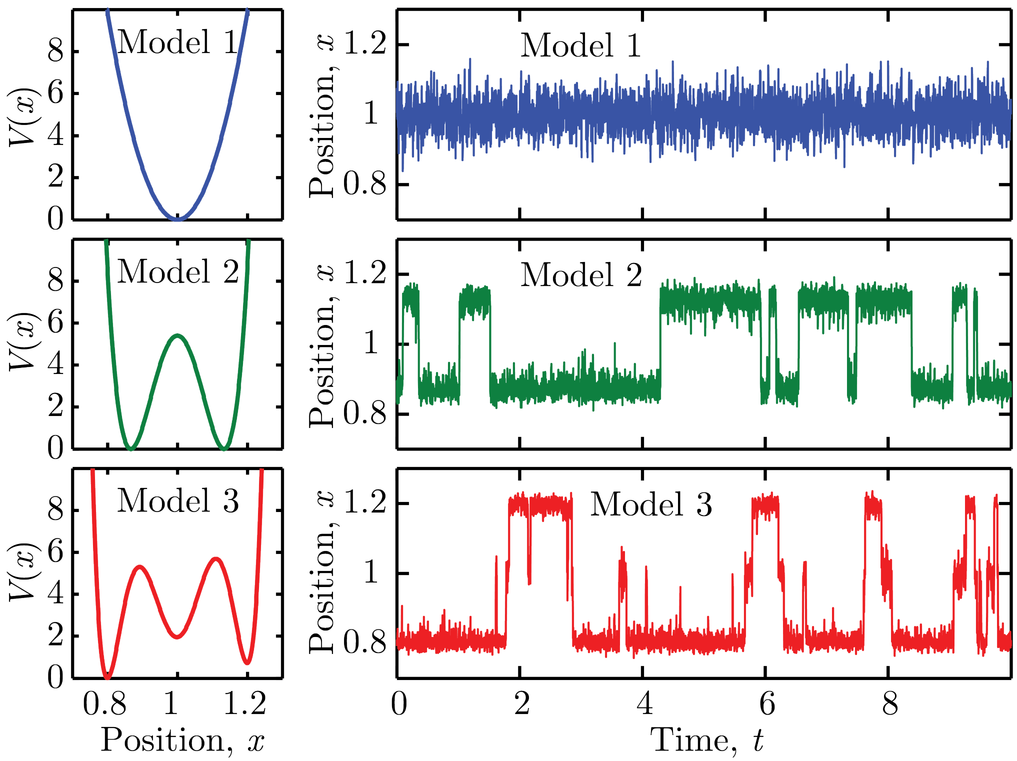
Posterior
"Least Informative Model"





$$\mathcal{P}(Model|Data) = \frac{\overbrace{P(Data|Model)}^{\text{Likelihood}}\ \overbrace{P(Model)}^{\text{Prior}}}{P(Data)}$$

Information Content of Langevin Dynamics as coarse-grained model of system dynamics



$$\dot{x} = \beta D F(x) + \sqrt{2D} dW_t$$

- Balance between
  - Random fluctuations
  - Deterministic forcing
- Information content

$\propto$

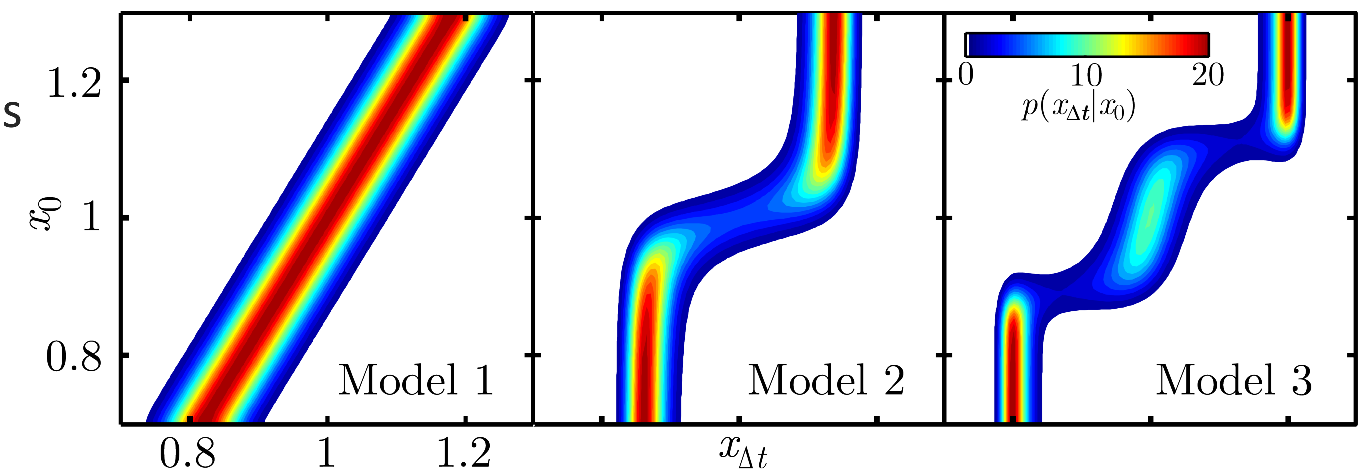
- -(Entropy)

Entropy	1-well	2-well	3-well
$\int dx\, p_{eq}(x) \ln p_{eq}(x)$	1.683	1.683	1.683

Dynamic Correlations Measured by Jaynes Caliber

$$S(\Delta t) = -\int dx_0 dx_{\Delta t}\; p(x_{\Delta t}, x_0) \ln p(x_{\Delta t}|x_0)$$

- Jaynes Caliber
  - Markov Process
  - Discrete Time
  - Finite States

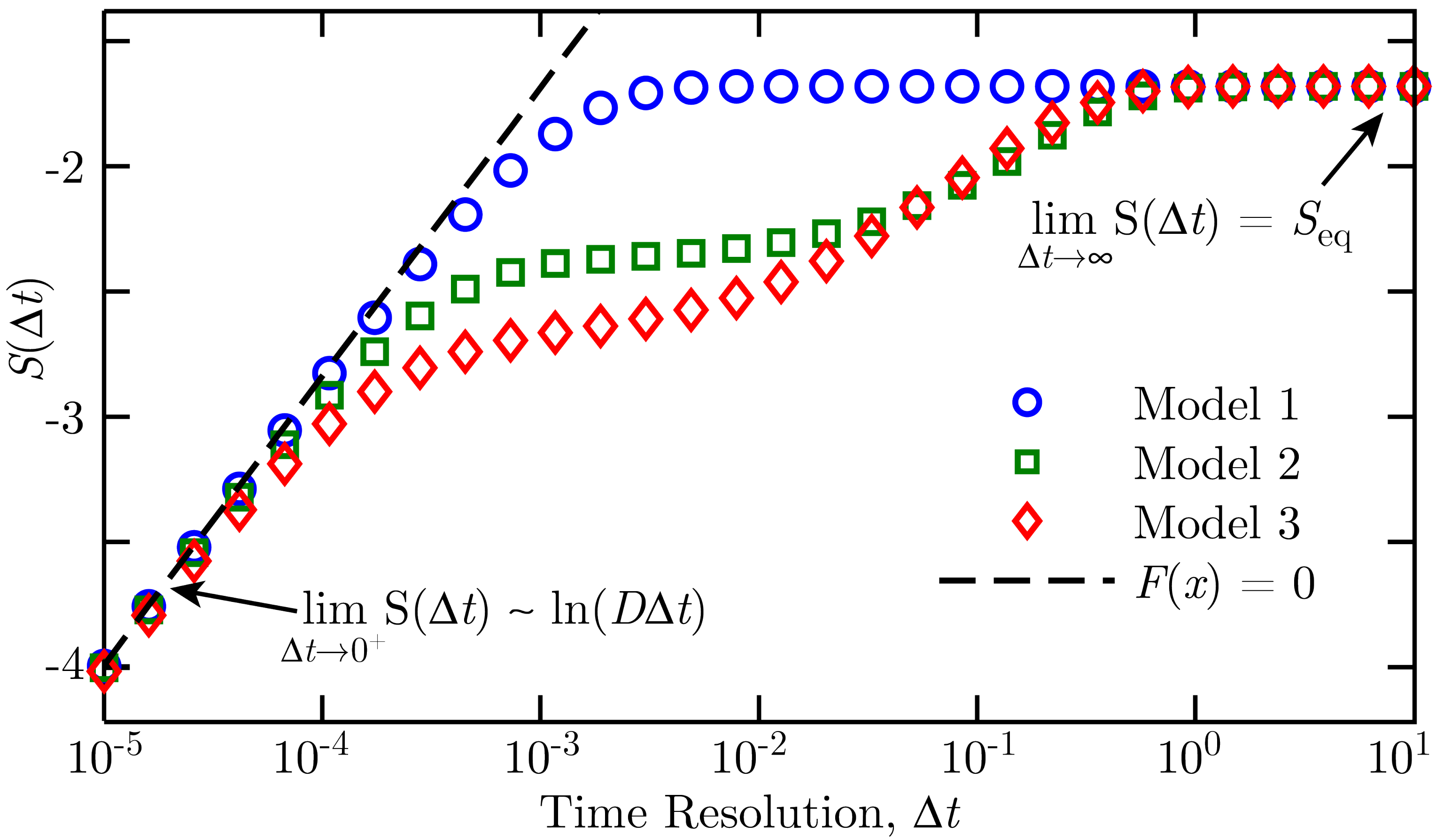


- Information of:
  - Conditional propagator (from Fokker-Planck)
  - Dynamic correlations

$$\frac{\partial p(x_t|x_0)}{\partial t} = D\frac{\partial^2 p}{\partial x_t^2} - \frac{\partial}{\partial x_t}\left(\frac{DF(x_t)}{k_B T}p\right)$$

Captures Dynamic Complexity, but, Divergence in Continuum limit due to Weiner Process

$$S(\Delta t) = -\int dx_0 dx_{\Delta t}\, p(x_{\Delta t}, x_0) \ln p(x_{\Delta t}|x_0)$$



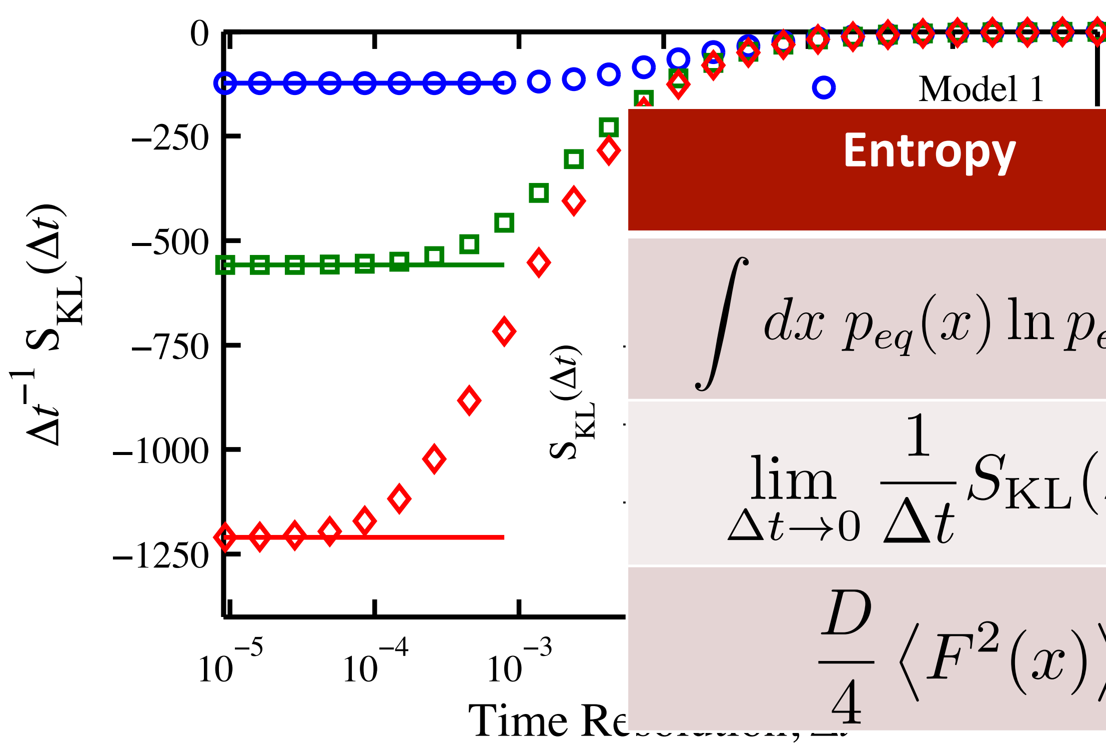
Dynamic Information as KL-Divergence w.r.t reference diffusion process

$$S_{\mathrm{KL}}(\Delta t) = -\int dx_0 dx_{\Delta t} p(x_{\Delta t}, x_0) \ln \frac{p(x_{\Delta t}|x_0)}{q(x_{\Delta t}|x_0)}$$

F(x)=0

- p & q balance into continuum limit

$$p(x_{\Delta t}|x_0) \propto q(x_{\Delta t}|x_0) \to \delta(x_{\Delta t} - x_0)$$



Entropy	1-well	2-well	3-well
$\int dx\, p_{eq}(x) \ln p_{eq}(x)$	1.683	1.683	1.683
$\lim_{\Delta t \to 0} \frac{1}{\Delta t} S_{\mathrm{KL}}(\Delta t)$	123.6	558.6	1,210
$\frac{D}{4} \langle F^2(x) \rangle_{eq}$	123.5	558.7	1,211

Entropy Measure as Path Integral over Trajectory Ensemble w.r.t reference pure diffusion process

$$\mathcal{S} \equiv -\int_0^{t_{\mathrm{obs}}} \mathcal{D}X(t)\; \mathcal{P}[X(t)] \ln \frac{\mathcal{P}[X(t)]}{\mathcal{Q}[X(t)]}$$

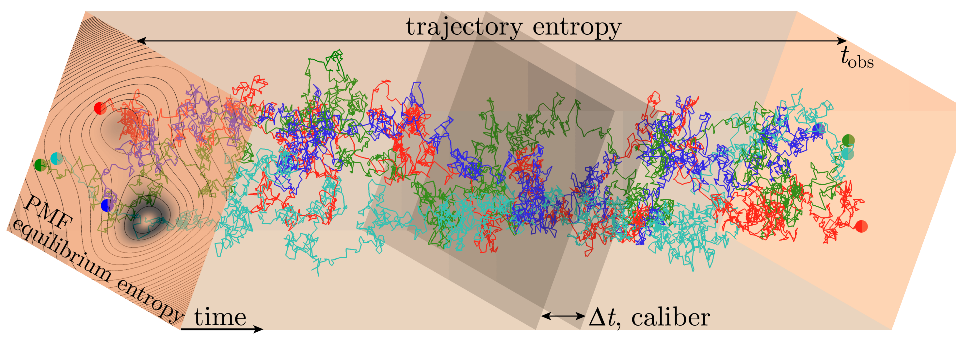
- Path probability from Onsager Machlup action

$$\mathcal{P}[X(t)] = e^{-E^{\mathrm{OM}}[X(t)]}/\mathcal{Z}$$

$$E^{\mathrm{OM}}[X(t)] = \frac{1}{4}\int_0^{t_{\mathrm{obs}}} dt\; \frac{\dot{x}_t^2}{D} + DF^2(x_t) + 2DF'(x_t)$$

- Expectation of OM Action

$$\mathcal{S} = \left\langle E^{\mathrm{OM}}[X(t)] \right\rangle_{X(t)} + \ln \frac{\mathcal{Z}}{\mathcal{Z}_{\mathrm{ref}}}.$$



Analytic Entropy Functional for Continuous Stochastic Dynamics

$$\mathcal{S} = -t_{\text{obs}} \frac{D}{4} \left\langle F^2(x) \right\rangle_{\text{eq}} + \frac{1}{4} \left\langle \int_0^{t_{\text{obs}}} dt \, \frac{\dot{x}_t^2}{D} - \frac{\dot{x}_t^2}{D_{\text{ref}}} \right\rangle_{X(t)} + \ln \frac{\mathcal{Z}}{\mathcal{Z}_{\text{ref}}}$$

1. Exchange space/time integrals. 2. Derivatives of partition function

- Deterministic Force reduces entropy
- Stochastic Diffusion increases entropy

$$\boxed{\mathcal{S}[F(x), D] = S_{\text{eq}} - \frac{t_{\text{obs}} D}{4} \left\langle F^2(x) \right\rangle_{\text{eq}} + \lim_{\Delta t \to 0^+} \frac{t_{\text{obs}}}{2\Delta t} \ln D}$$

$$\rho_{\text{eq}}(x) = \sqrt{p_{\text{eq}}}(x); \quad \langle F^2(x) \rangle_{\text{eq}} \Leftrightarrow \int dx \left(\nabla \rho_{\text{eq}(x)} \right)^2$$

Haas, Yang, Chu *In Review*

Understanding Dynamics through Maximum Entropy Optimization - Mean First Passage Time Constraint

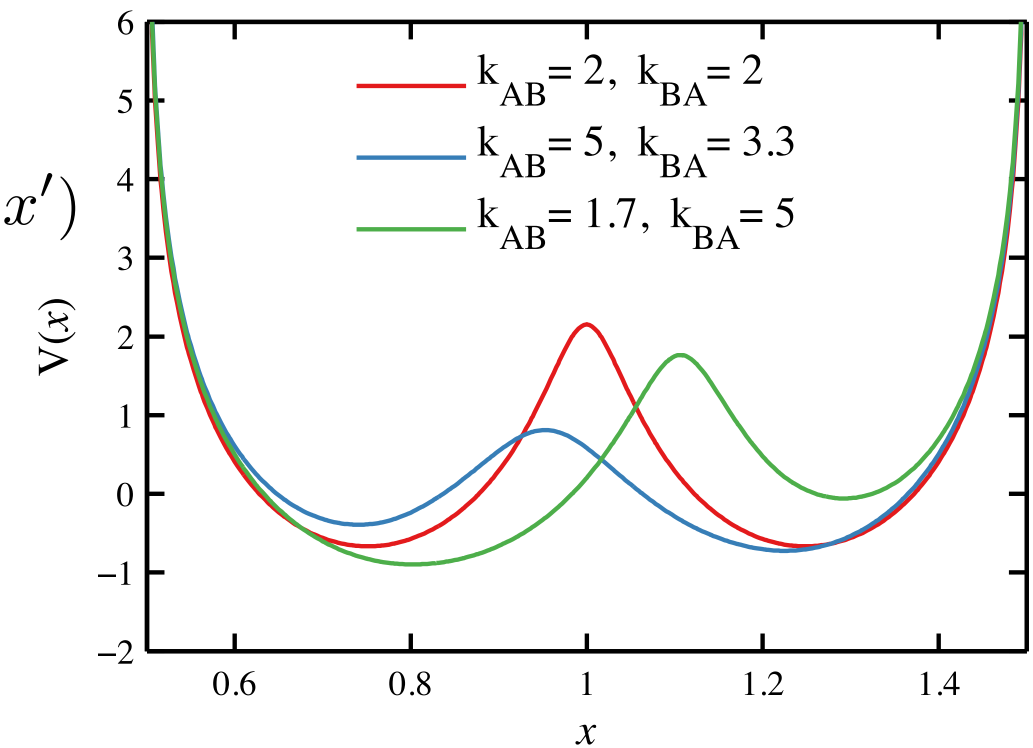
- Maximum Entropy Optimization

$$\max_{\rho(x)} \Big(-\underbrace{t_{\text{obs}} D \langle \rho_{\text{eq}} | \nabla \cdot \nabla | \rho_{\text{eq}} \rangle}_{\text{Entropy}} + \sum_i \omega_i \underbrace{\left(\langle \rho_{\text{eq}} | \boldsymbol{C}_i | \rho_{\text{eq}} \rangle - C_i \right)}_{\text{Constraint}} \Big)$$

- Mean First-Passage Time

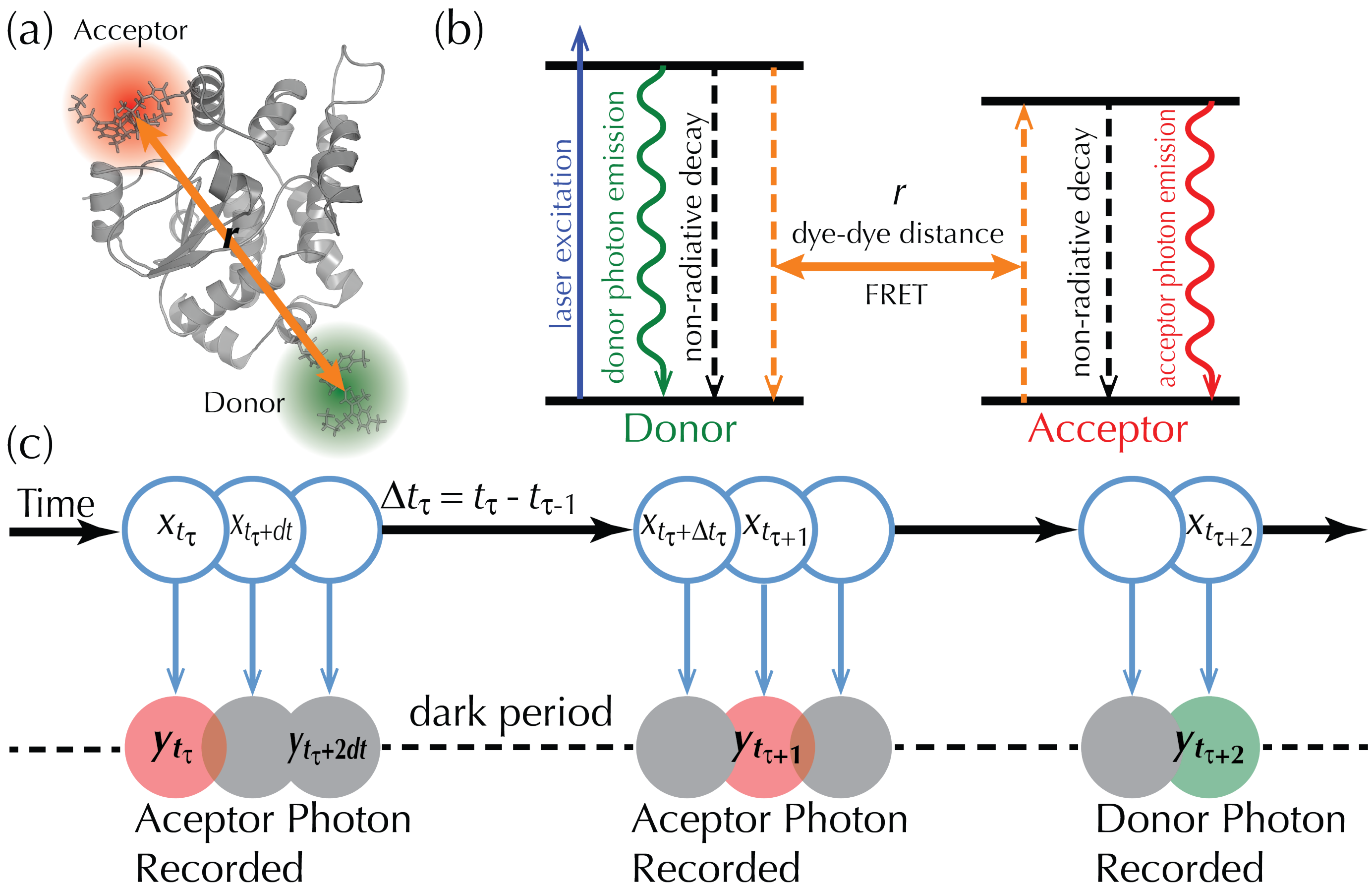
$$\frac{1}{D} \int_{x_A}^{x_B} dx\ \rho^{-2}(x) \int_{x_L}^{x} dx'\ \rho^2(x')$$

- Hammond-Leffler postulate
  - Transition state for endothermic near products



Haas, Yang, Chu **JCP** (2013)

Likelihood of Force Profile, Diffusion from single-molecule FRET

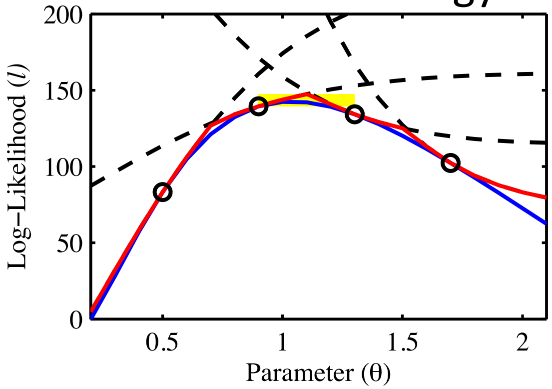


$$\mathcal{P}[Y(t)|\rho, D] = \langle \alpha_{t_0} | e^{-\boldsymbol{H}\Delta t_1} \boldsymbol{y}_1 e^{-\boldsymbol{H}\Delta t_2} \boldsymbol{y}_2 \dots e^{-\boldsymbol{H}\Delta t_{N_\mathrm{P}}} \boldsymbol{y}_{N_\mathrm{P}} | \beta_{t_\mathrm{exp}} \rangle$$

Haas, Yang, Chu **JPCB** (2013)

Bayesian Posterior with Entropy Prior Gives Optimal model and is Equivalent to Free Energy

Likelihood "Energy"



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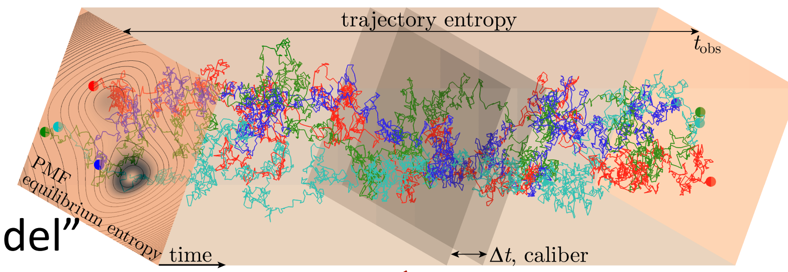
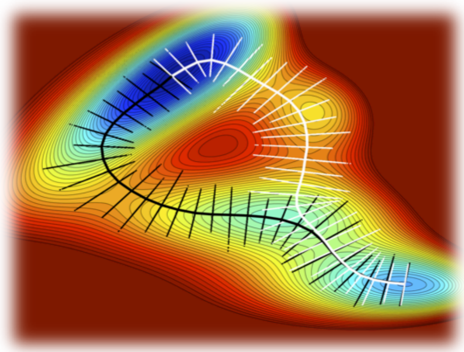


Posterior
"Least Informative Model"



$$\mathcal{P}[\rho(x),\eta_F,\eta_D|Y(t)] \propto \mathcal{P}[Y(t)|\rho(x)]e^{-\eta_F D\langle\rho|\nabla^2|\rho\rangle}e^{-\eta_D \ln(D)}p(\eta_F,\eta_D)$$

OPTIMAL MODEL $$\rho(x)^* = \arg\max_{\rho} \mathcal{P}[\rho(x),\eta_F,\eta_D|Y(t)]$$

HYPER-PARAMETERS $$P(\eta_F,\eta_D|Y(t)) = \int D\rho(x)\mathcal{P}[\rho(x),\eta_F,\eta_D|Y(t)]$$

Thermodynamics of simulation, experiment combined with entropy to make inference about dynamics

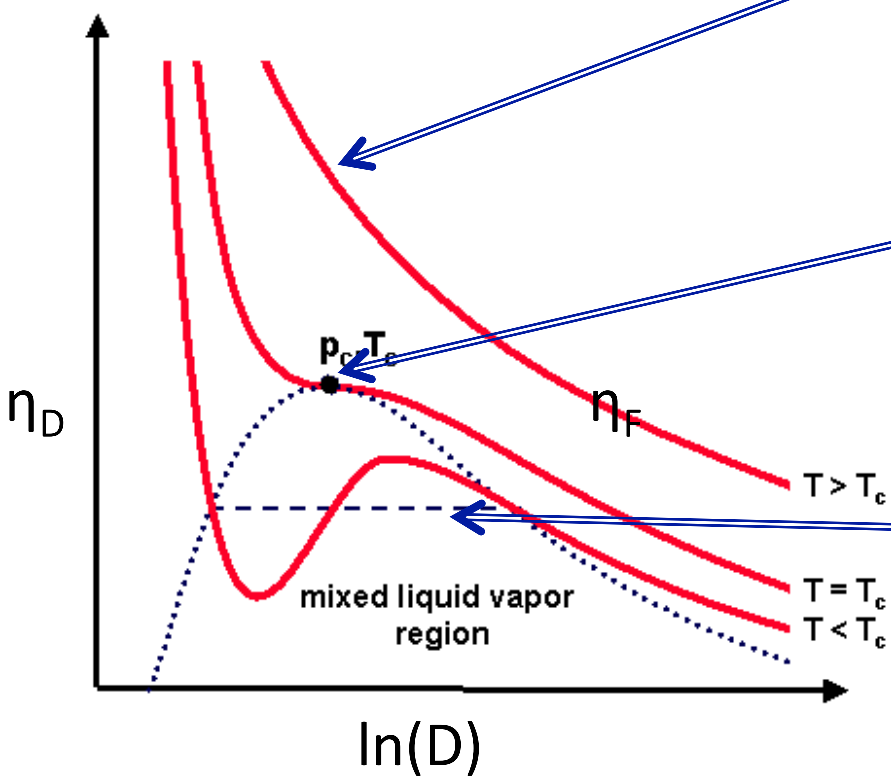
$$-\ln P(\eta_F, \eta_D | Data) = \langle U \rangle + \eta_F \langle S \rangle + \eta_D \langle ln(D) \rangle$$

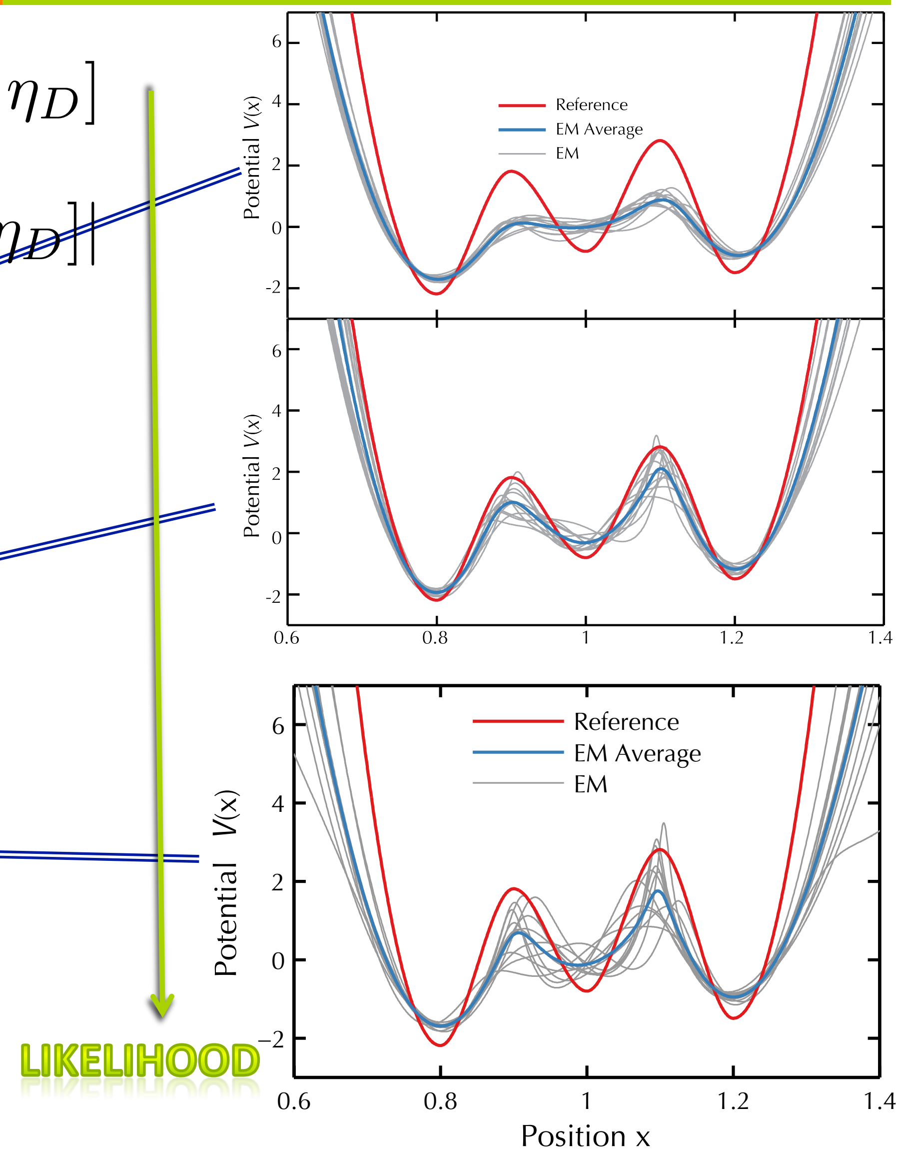
$$G(\eta_F, \eta_D) = -\ln P(\eta_F, \eta_D | Data)$$

	Static	**Dynamic**
Microstate	x	X(t)
Sufficient Statistic	g(r)	$\varrho_{eq}(x)$
Internal Energy	U[g(r)]	-ln $P(\varrho_{eq}(x) \mid data)$
Entropy	$p_{eq} \ln p_{eq}$	$(d\varrho_{eq}(x)/dx)^2$
Work	P,V	η_D, ln(D)
Temperature	T	η_F

Phase Transitions and Critical Point in Bayesian Optimization. Optimal complexity from smFRET!

$$G(\eta_F, \eta_D) \approx -\ln \max_{\rho(x)} \mathcal{P}[\rho(x), \eta_F, \eta_D] + \ln |\nabla_\rho \nabla_\rho \mathcal{P}[\rho(x), \eta_F, \eta_D]|$$





Thank you

- Conclusion:

$$D\langle F^2(x)\rangle_{\mathrm{eq}}$$

- github.com/krhaas/AIChE2013