Boulder Summer School:

Lecture #1 → Representing Behavior I
(or: Philosophy & Worms)

→ What business does a theoretical physicist have studying behavior?
(i.e. if not spherically, how should we model a cow?)

→ To bridge scales & extract important coarse-grained descriptions

Q: Why is this absurd?
→ Many scales
→ Far removed from underlying "mechanism"
→ Apparently qualitative

⟹ Need a quantitative language for behavior that we can take seriously

E.g. DNA → base pairs, amino acids, binding affinities, ...

Neurons → membrane voltage, spikes, firing rates, ...

Behavior → ?

→ How do we ~~[illegible]~~ take a complicated creature like an animal & represent it in a manner condusive to experimental & theoretical interrogation?

→ Great! But how?

⇒ How have biologists attempted this?

1) Paradigms (e.g. rat in a maze or center-out task)

→ embody measurement in the experiment

2) Coarse Measurements (e.g. velocity, # of beam crosses)

→ pre-planned coarse-graining

3) Intuition (e.g. manual annotation)

→ assumes discrete behavioral types & the form they take

Q: How can we build on these methods to create a rich, yet comprehensible, measurement of an animals movements?

~~→ To start, look at data~~
~~(C. elegans, Stephens et al, PLOS Comp Bio, 2008)~~

Why is this difficult?

→ continuous or discrete?

→ What length scale?

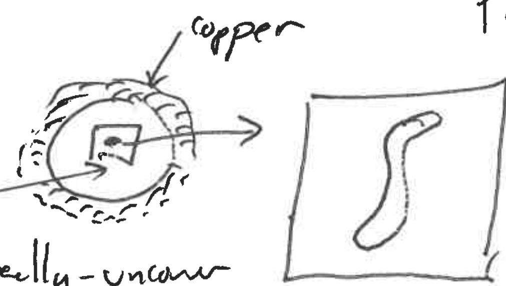
→ What time scale?

→ How to tell time points apart (distance metric)?

→ start by looking at data

Crawling Behavior in C. elegans (Stephens et al, PLoS Comp Bio, 2008) & Stephens et al, PNAS 2011

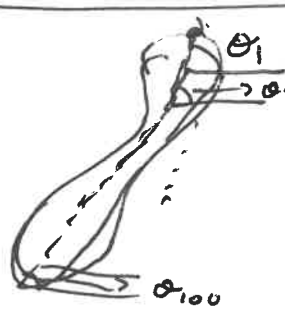
Experiment: Will Ryu



Q: Can we mathematically uncover the essential dynamics of the worm as it moves?

Choice #1: How to describe the worm?

options:
a) center of mass
b) mid-point
c) centerline → Try this! (connects movement at small ~~body~~ scale to movement at body scale)
d) full 2D area

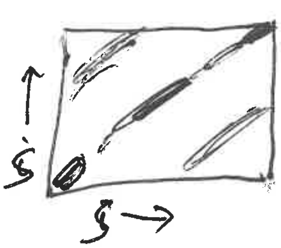


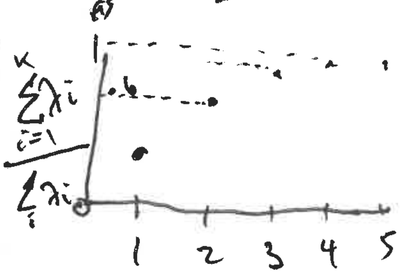
→ set so that $\langle \theta_i^{(t)} \rangle_i = 0 \ \forall t$

(rotational invariance) → another choice

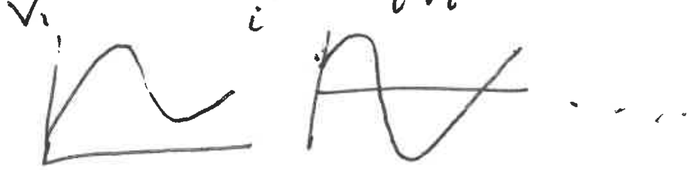
→ Now have 100 time series. Do we need all of them? No!

$C_{ij} = \langle (\theta_i - \langle\theta_i\rangle)(\theta_j - \langle\theta_j\rangle)\rangle_t$ → covariance matrix



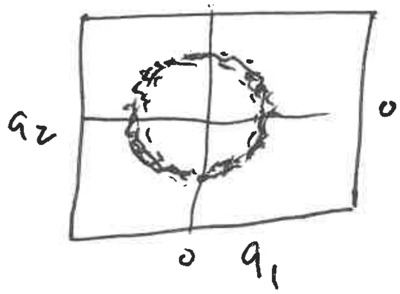


$$C = \sum_i \lambda_i v_i v_i^T$$



Look at projections onto 1^{st} 2 modes:

PDF



$$a_i(t) = \left(\vec{\theta}(t) - \langle \vec{\theta}(t) \rangle_t\right) \cdot \hat{V}_i$$

→ Well-described by a phase variable $\phi = \tan^{-1} \frac{a_2}{a_1}$

→ One variable describes ~ 1/2 of all postural variance!

Can we write-down a model for the dynamics of this one variable?

Idea: Model as a "Langevin-like" model

$$\frac{d\phi(t)}{dt} = w(t), \quad \frac{dw(t)}{dt} = \overbrace{F[\phi(t), w(t)]}^{\text{Deterministic}} + \overbrace{\sigma[\phi(t), w(t)]\,\eta(t)}^{\text{Stochastic}}$$

$$\langle \eta(t)\eta(t+t') \rangle = \delta(t-t')$$

In practice: After some basic filtering & such, calculate $\phi(t)$ & $w(t)$ from data

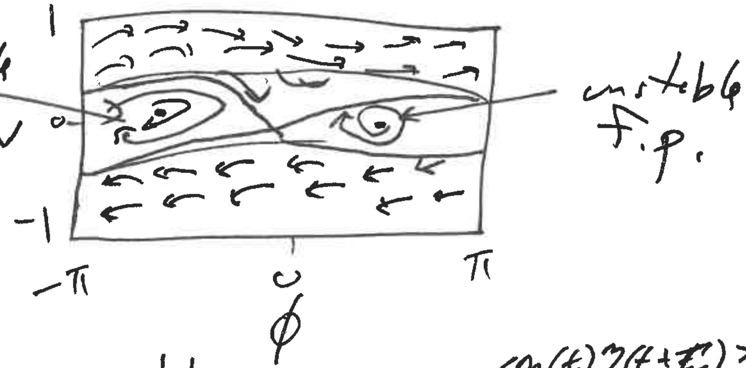
Assume that $\langle \sigma[\phi(t), w(t)]\,\eta(t) \rangle = 0$

→ optimal R.M.S. estimate of $F[\phi(t), w(t)] = \langle \dot{w} \mid \phi, w \rangle$

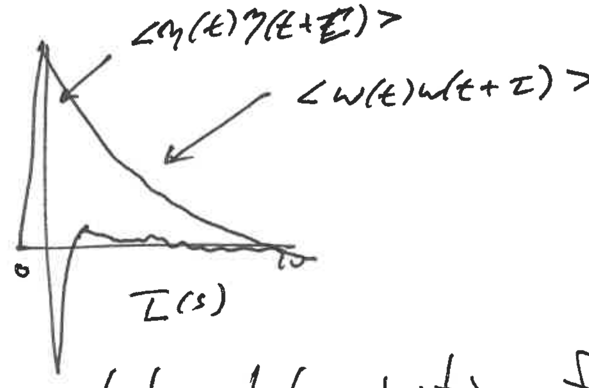
Fit $F(\phi, w) = \sum_{m=-5}^{5} \sum_{p=0}^{5} \alpha_{m,p} w^p e^{-im\phi}$ (Fourier series in ϕ, polynomial expansion in w)

$$\sigma^2(\phi, w) = \left\langle \left(\dot{w}(t) - F(\phi(t), w(t))\right)^2 \,\middle|\, \phi, w \right\rangle_t$$

$F[\phi, w]$



Look at noise correlations:



τ is short $\longrightarrow$

$\rightarrow$ we are happy that we've separated deterministic from stochastic dynamics

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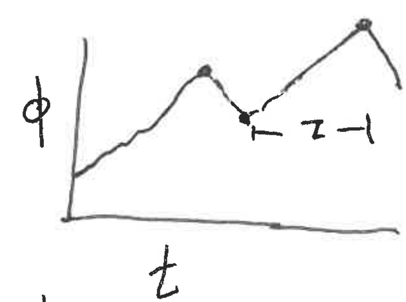
But can we predict anything?

1) Reversal Frequency $\longrightarrow$

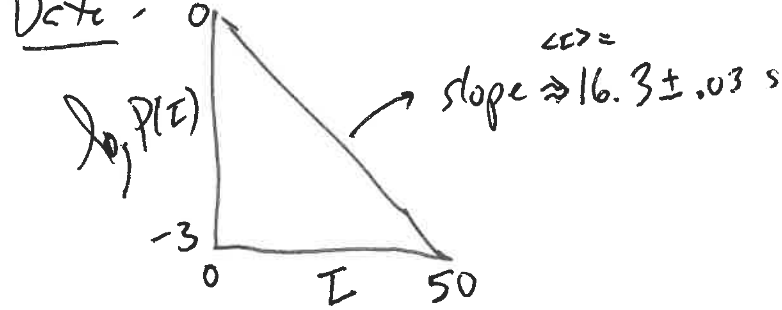


Can we predict the distribution of survival times in the forward state?

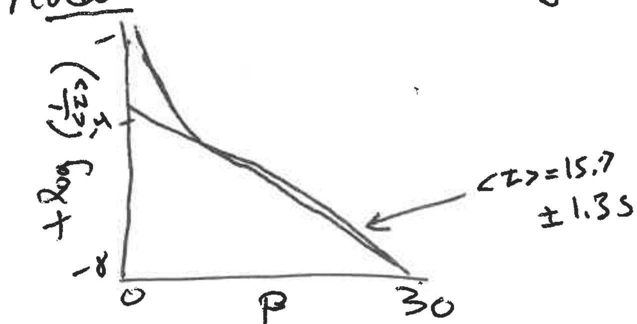
$\rightarrow$ Let's assume that transitions are brief & well-separated in time $\longrightarrow$ should be no memory

$$\Longrightarrow P(\tau) \sim \exp\left[\frac{-\tau}{\langle\tau\rangle}\right]$$

Data:



Model: Scale $\sigma^2(\phi, w)$ by β



(5) Note: The model didn't even have to have had reversals!

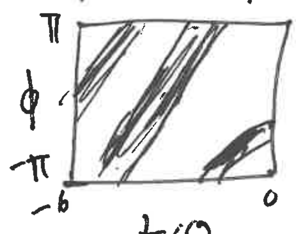
2) Stereotypy → Behaviors performed often & repeatably

In theories of stochastic barrier crossing, often stereotyped patterns of trajectories occur (if barrier much larger than the noise). We have a "Langevin" eqn!

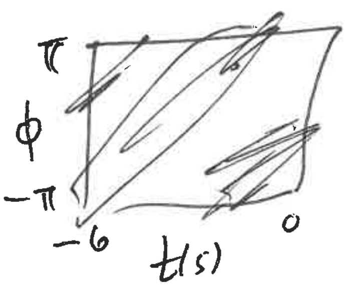
Let $t = 0$ → time of a trajectory exiting the forward state

Compute: $p(\phi | t)$ for model & data

Model:



Data:



!

→ stereotypy in transition structure emerges naturally from the noise-driven crossing of a dynamical barrier!

Lastly: Can we use these measurements to gain insight into biology?

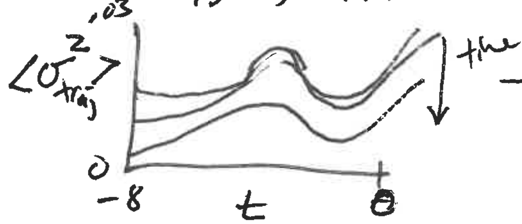
⟹ Worms get hungry. No food on the plate, so more likely to make longer "runs"! Break data up into 3 ~10 minute recordings, fit each to $\frac{dw}{dt} = (\quad)$

1) All 3 models fit well (& reproduce what we saw before)

2) $F(\phi, w)$ is roughly unchanged

3) $\sigma^2(\phi, w)$ alters

Predicts that the worm controls its behavior by controlling noise



→ noise decreases with time, implying longer escape times & straighter trajectories

Inspiration & Challenges for Applying to other Organisms

Inspiration	Challenge
→ Use a simple representation of movement ~~???~~ to describe low-d posture	→ It's a worm (limbs, other things are more complicated, have complicated units)
→ Reconstructed ~~3~~ 2-d dynamical system to describe movements	→ other animals, this is less likely to work (higher-d)
→ Made out-of-sample predictions about behavior & control	→ More difficult because posture ⟷ dynamics mapping will be more complicated
→ Single time scale emerges	→ Multiple time scales in most problems

This is all about how one behavior evolves in time. How does the animal "choose" how to proceed?

→ More next time