Title: A stochastic explanation for observed local-to-global foraging states in *Caenorhabditis elegans*

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Abstract:

Abrupt changes in behavior can often be associated with changes in underlying behavioral states. When placed off food, the foraging behavior of *C. elegans* can be described as a change between an initial local-search behavior characterized by a high rate of reorientations, followed by a global-search behavior characterized by sparse reorientations. This is commonly observed in individual worms, but when numerous worms are characterized, only about half appear to exhibit this behavior. We propose an alternative model that predicts both abrupt and continuous changes to reorientation that does not rely on behavioral states. This model is inspired by molecular dynamics modeling that defines the foraging reorientation rate as a decaying parameter. By stochastically sampling from the probability distribution defined by this rate, both abrupt and gradual changes to reorientation rates can occur, matching experimentally observed results. Crucially, this model does not depend on behavioral states or information accumulation. Even though abrupt behavioral changes do occur, they may not necessarily be indicative of abrupt changes in behavioral states, especially when abrupt changes are not universally observed in the population.

Text:

The search for food in the absence of informative sensory cues is an essential animal behavior[1]. In the short-term, animals tend to perform a random walk[2], however over longer periods, animals tend to alter their search strategy[1,3]. *Caenorhabditis elegans* and *Drosophila melanogaster* larva appear to progressively increase their diffusion constant by decreasing their rates of reorientation[3]. However in separate studies[4,5], individual worms appear to make an abrupt change from a high to low rate of reorientation. This behavior has been described as a switch from a local to global search strategy[5]. In Lopez *et al*[4]., the foraging behaviors of individual worms were tracked for 45 minutes after being removed from food. As observed previously[3], the

reorientation rate from this study followed an exponential decay (Fig. 1A), but as observed in Calhoun *et al*[5], half the worms appeared to execute switch-like decisions with abrupt changes in their reorientation rate (Fig. 1C), while other worms did not appear to do this (Fig. 1D). Whether or not a worm performed a decision was defined by fitting individual reorientation data to two lines (Fig. 1B). If the slope difference between the two lines was large, the worm was labelled as making a decision, and the intersect between the two lines determined the decision-time[4] (Fig. 1D). When the experimental data are plotted according to these parameters, the resulting distributions are continuous along both axes, with no clear boundary between deciders and non-deciders.

Why do some worms appear to make a decision, while others do not? In aggregate, the number of reorientations (Ω) over time appear to follow a simple saturating exponential curve (Fig. 1E),

$$\dot{\Omega} = \alpha e^{-\gamma t} \tag{1}$$

$$\Omega(t) = \alpha'(1 - e^{-\gamma t}) \tag{2}$$

where $\alpha' = \alpha/\gamma$. Despite the average conforming to a simple saturating curve, individual trajectories produce a wide diversity of trajectories which sometimes conform to an apparent switch, while others do not. If the worms are executing a decision, this would seem to indicate only a fraction of the worms decide to switch from local to global foraging strategies, while others perform an alternative strategy.

The disparity between individual versus average temporal behavior is common in chemistry[6]. Individual molecules defined by the same reaction kinetics can stochastically produce long or short dwell times, not because one molecule is inherently faster than the other, but because they are stochastically sampling from the same time distribution. The variance in individual worm reorientations is very similar to this. The saturating exponential curve emerges from the average of trajectories that do not necessarily conform to this curve individually. However, even those that produce abrupt switches in reorientation rates could still emerge from a simple exponential decay strategy. Since reorientations occur stochastically, the abrupt changes in reorientation rates could simply be the result of stochastic sampling of an underlying decay phenomenon[7].

We tested this hypothesis by modeling a stochastic sampling of decay with the Gillespie algorithm, a common strategy used to model the kinetics of individual molecules[8]. With this strategy, the time between events is modeled by randomly sampling from the exponential time distributions defined by the reaction rates. In our approach, we fit the exponential curve in Eq. 2 to the population average, and then used these parameters

to model 1,000 individual worms. The time between reorientations of a simulated worm was governed by an exponentially decaying probability curve (Eq. 1).

When plotted along with the experimental data, the *in silico* worms produced a distribution of linear regression parameters comparable to the experimental worms (Fig. 1F). The simulation was able to produce individual trajectories that demonstrated switching behavior, despite the lack of a switching mechanism in the model (Fig. 1F). Furthermore, our model demonstrated a continuum of switching to non-switching behavior that was observed in experimental results (Fig 1F). The model deviated slightly from the experimental data for traces with late inflection points. The model does not predict increases in reorientations at later times, whereas this is occasionally observed experimentally (Fig. 1F). We are not certain why this occurred in this experimental dataset. We can only speculate, but one possibility is that these experiments were performed with groups of 10-15 animals, so encounters with pheromone tracks could have potentially altered behavior[9].

This exception aside, modeling worm foraging behavior with a simple exponential decay of reorientations was sufficient to capture most experimentally observed trajectories, both switch and non-switch-like. These findings show that apparent switches between local and global search behavior can result from stochastic sampling of an underlying continuous strategy. Crucially, this model does not rely on any abrupt decisions between two different search strategies; all apparent decisions are simply the result of stochastic sampling.

The lack of a decision simplifies the dispersal strategy for *C. elegans*. Rather than relying on the accumulation of evidence to make a decision, the worm relies on a decaying signal in the absence of food that drives the reorientation rate. This strategy increases the diffusion constant of the worm, and ensures a more efficient search strategy to find food[3]. The physical basis of the decay kinetics can come from multiple sources. The loss of sensory stimuli alters metabotropic glutamate signaling from sensory neurons which in turn modify the kinetics of the motor network[4]. Altered ionotropic glutamate signaling and dopamine release also influence foraging kinetics[10], as well as neuropeptides[11]. Further work will be needed to reveal how the kinetics of reorientations emerges explicitly from underlying signaling kinetics.

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Supplementary Material:

Data availability:
Experimental data were curated from Lopez *et al*[4].

Source Code availability:
Analysis was performed using custom written code in MATLAB which can be found in this repository: https://github.com/GordusLab/Margolis_foraging

Author Contributions:
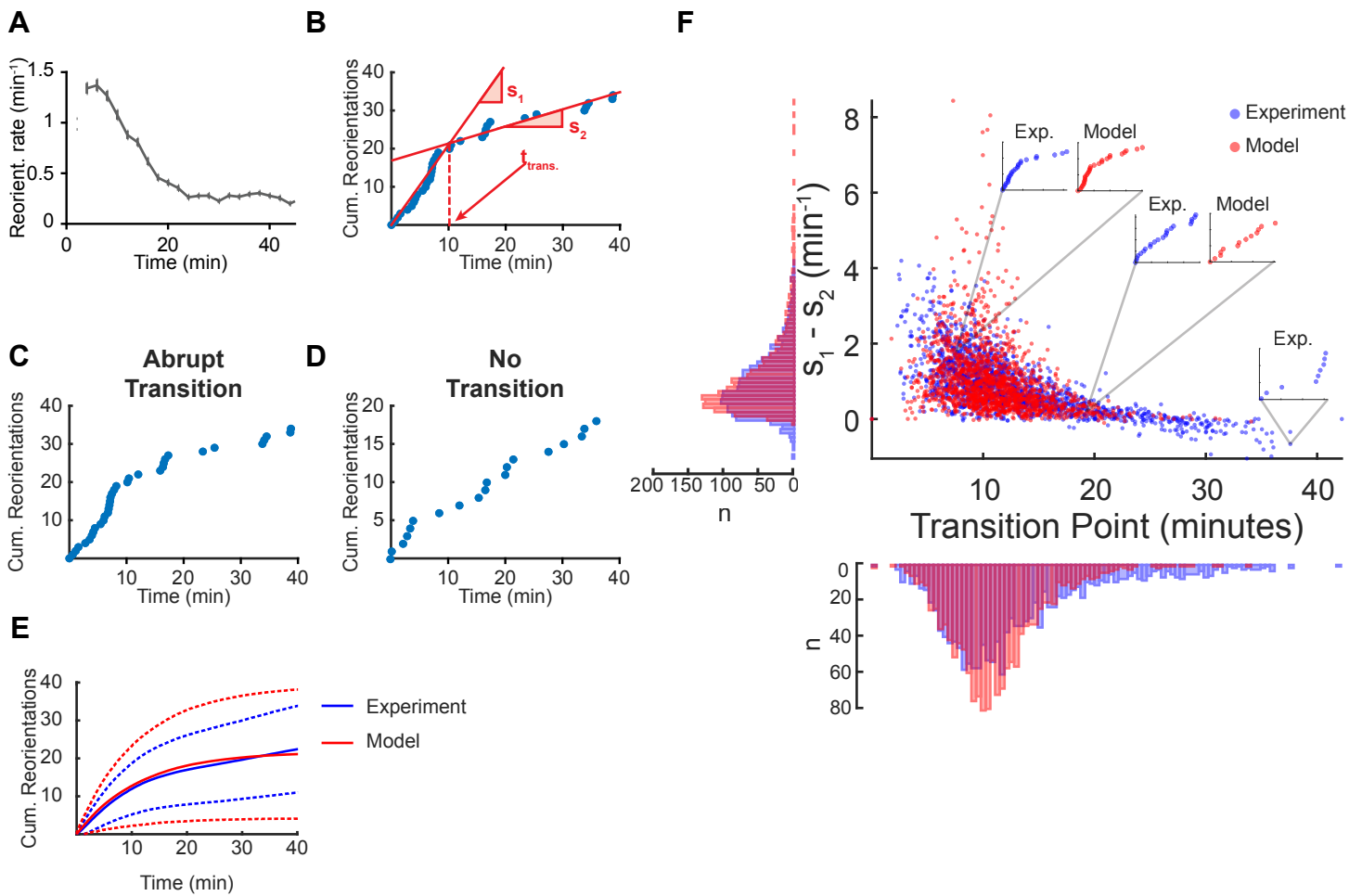A.M. and A.G. conceived the research plan, analyzed the data, and wrote the paper.

Figure 1: Foraging kinetics of C. elegans

A. Average experimental population reorientation rate, sampled every 2 minutes (adapted from López et. al.).

B. Abrupt transitions were identified by performing two linear regressions on observed reorientation curves. Transition times were defined by the intersection of the regressions.

C. An example of an experimental abrupt reorientation transition.

D. An example of an experimental reorientation curve that lacked an abrupt reorientation transition.

E. Average experimental and model reorientation curves. Model parameters: α = 1.6 min⁻¹, γ = 0.19 min⁻¹. Dashed lines are one standard deviation above and below the average.

F. Distribution of slope differences and transition times from regressions fit to the experimental and modeled data. Insets are individual examples of experimental and modeled reorientation curves.