

Specific Aims

- How does the organophosphate pesticide (OP) chlorpyrifos (CPF) change serotonin mediated behaviors?
- How do SSRIs (selective serotonin reuptake inhibitors) act synergistically with chlorpyrifos during developmental exposure?
- To what extent do gene expression changes influence changes in serotonin mediated behavior?

Aim 1: Determine mechanism of action of serotonin innervated behaviors and characterize the response resulting from exposure of CPF through the use of established behaviors and a *tph-1* reporter.

Aim 2: Assess synergistic interactions between CPF and the SSRI fluoxetine (Prozac), and investigate what effect these interactions have on both the *tph-1* reporter and behavior, as well as how this can be passed down transgenerationally.

Hypothesis: We hypothesize that CPF will alter serotonin-controlled behaviors and the in the serotonergic system, and this will be seen transgenerationally and is influenced by changes in gene expression and epigenetic mechanisms.

Background: WormLab and Serotonin Biosynthesis

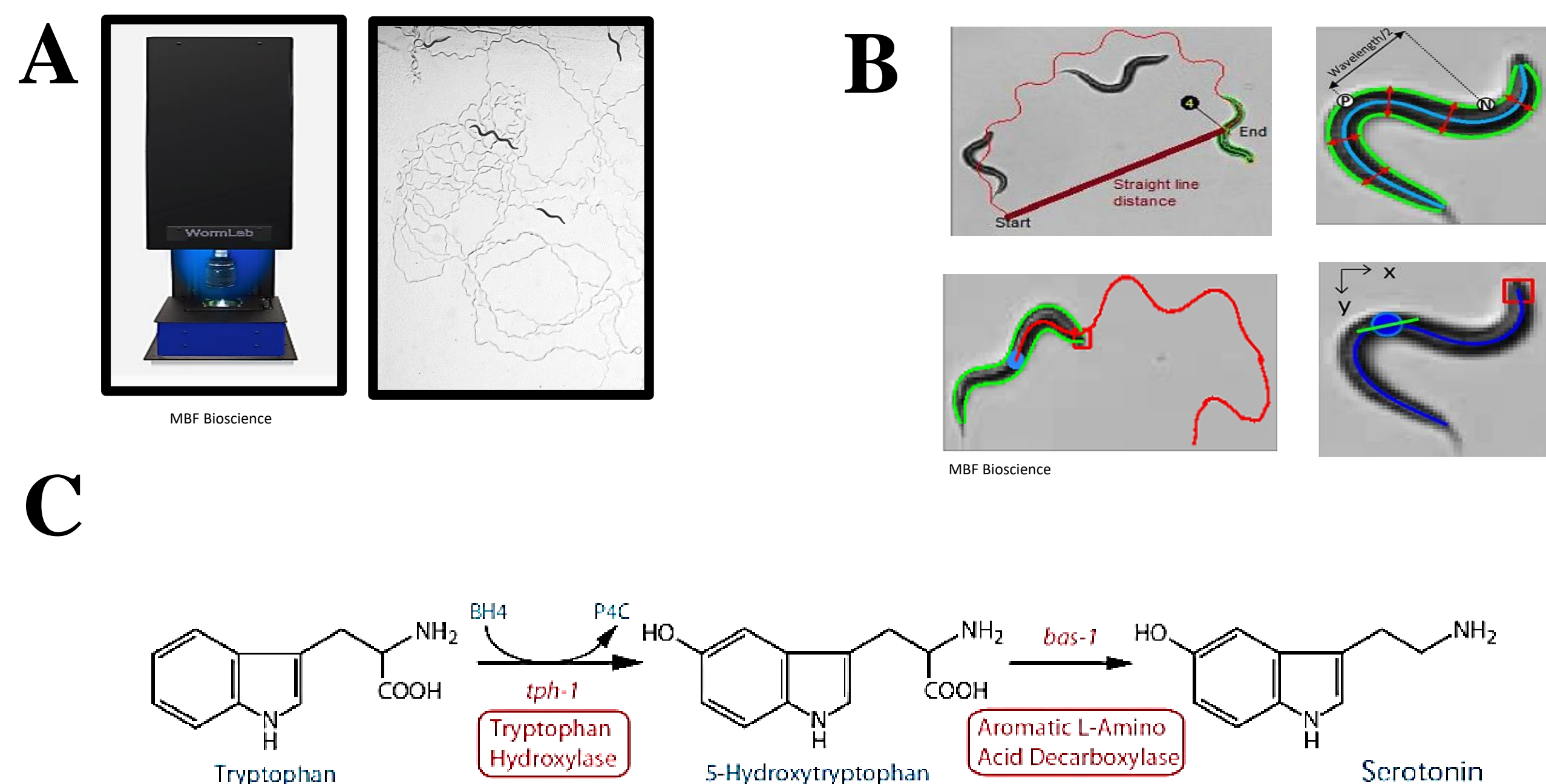
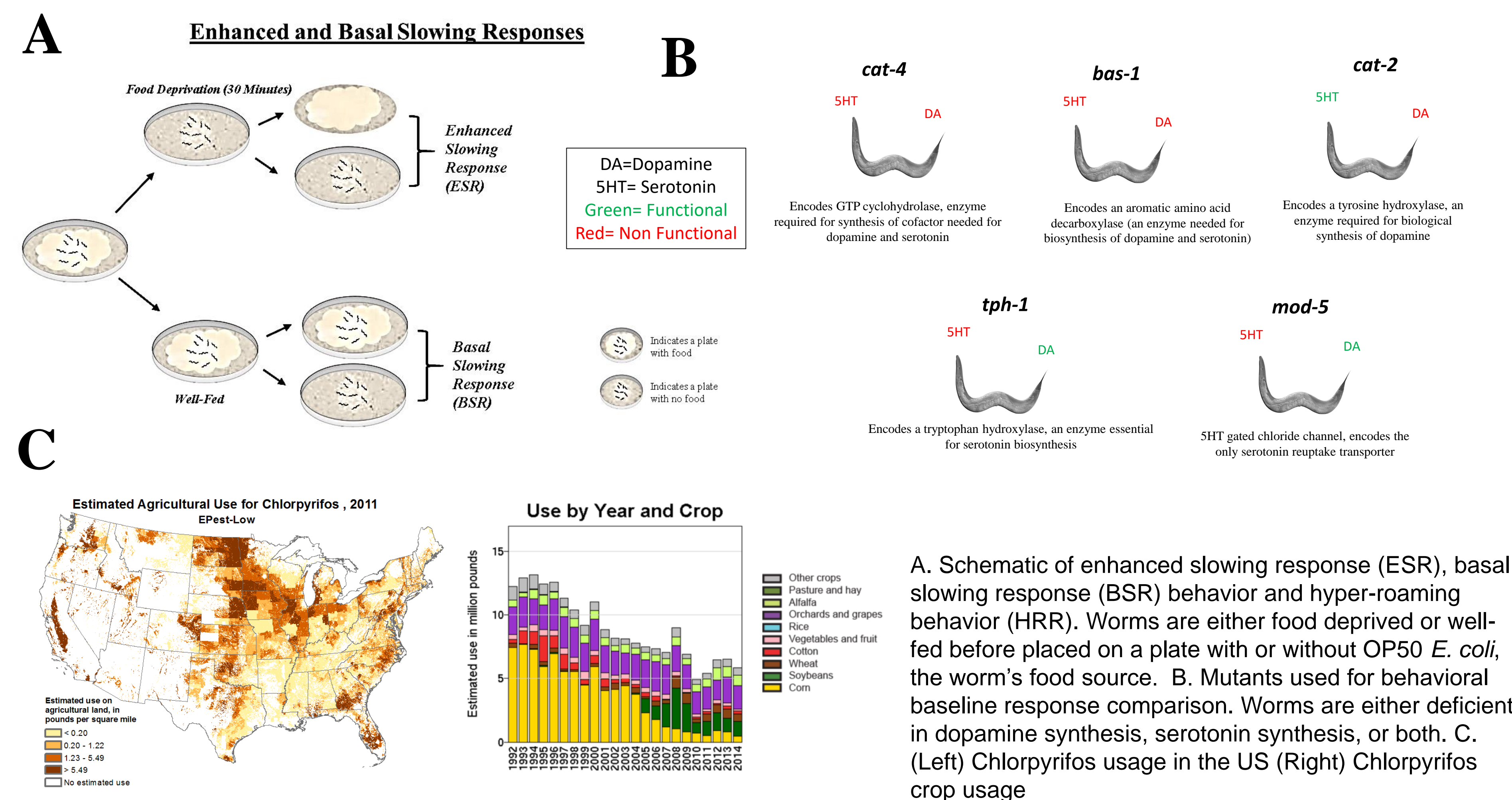


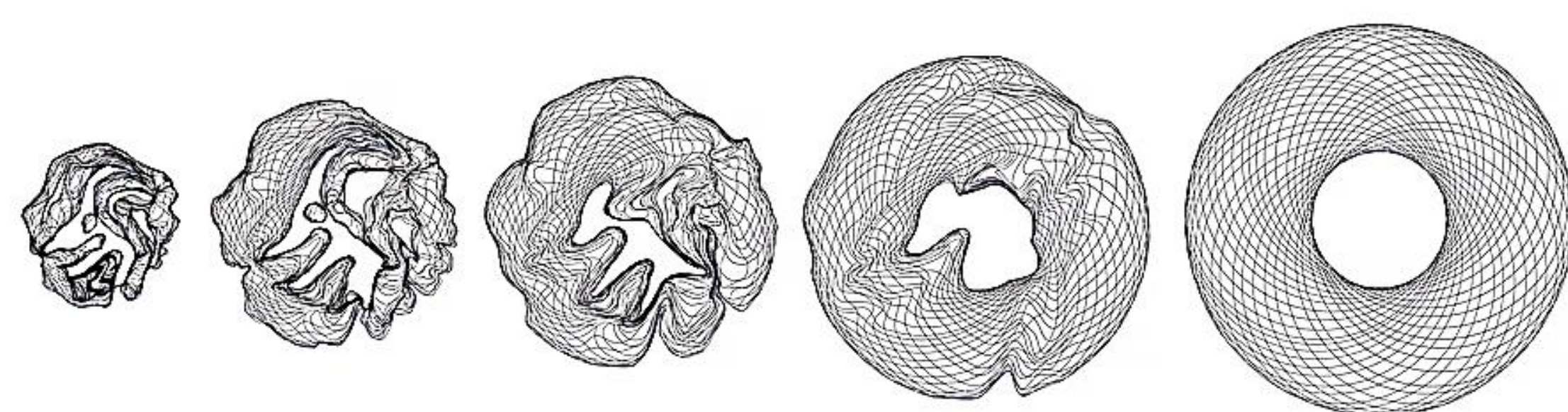
Figure 1. Biosynthesis of Serotonin from Tryptophan

A. (Left) WormLab hardware. Consists of camera, light source, and ambient light blocking hood. Camera records video of worm and companion software tracks worm behavior through algorithm (Right) Visual representation of a WormLab tracking video. B. (Top Left) Visual of WormLab calculation of straight line distance, (Top Right) Wavelength, (Bottom Left) Worm track (Bottom Right) Bending angle. (C) Serotonin biosynthesis, *tph-1* first rate limiting step in serotonin biosynthesis is proposed mechanism of action where *tph-1* is the first rate-limiting step and proposed mechanism of action for CPF.

Methodology: Behavior and Toxicant of Interest



A. Schematic of enhanced slowing response (ESR), basal slowing response (BSR) behavior and hyper-roaming behavior (HRR). Worms are either food deprived or well-fed before placed on a plate with or without OP50 *E. coli*, the worm's food source. B. Mutants used for behavioral baseline response comparison. Worms are either deficient in dopamine synthesis, serotonin synthesis, or both. C. (Left) Chlorpyrifos usage in the US (Right) Chlorpyrifos crop usage

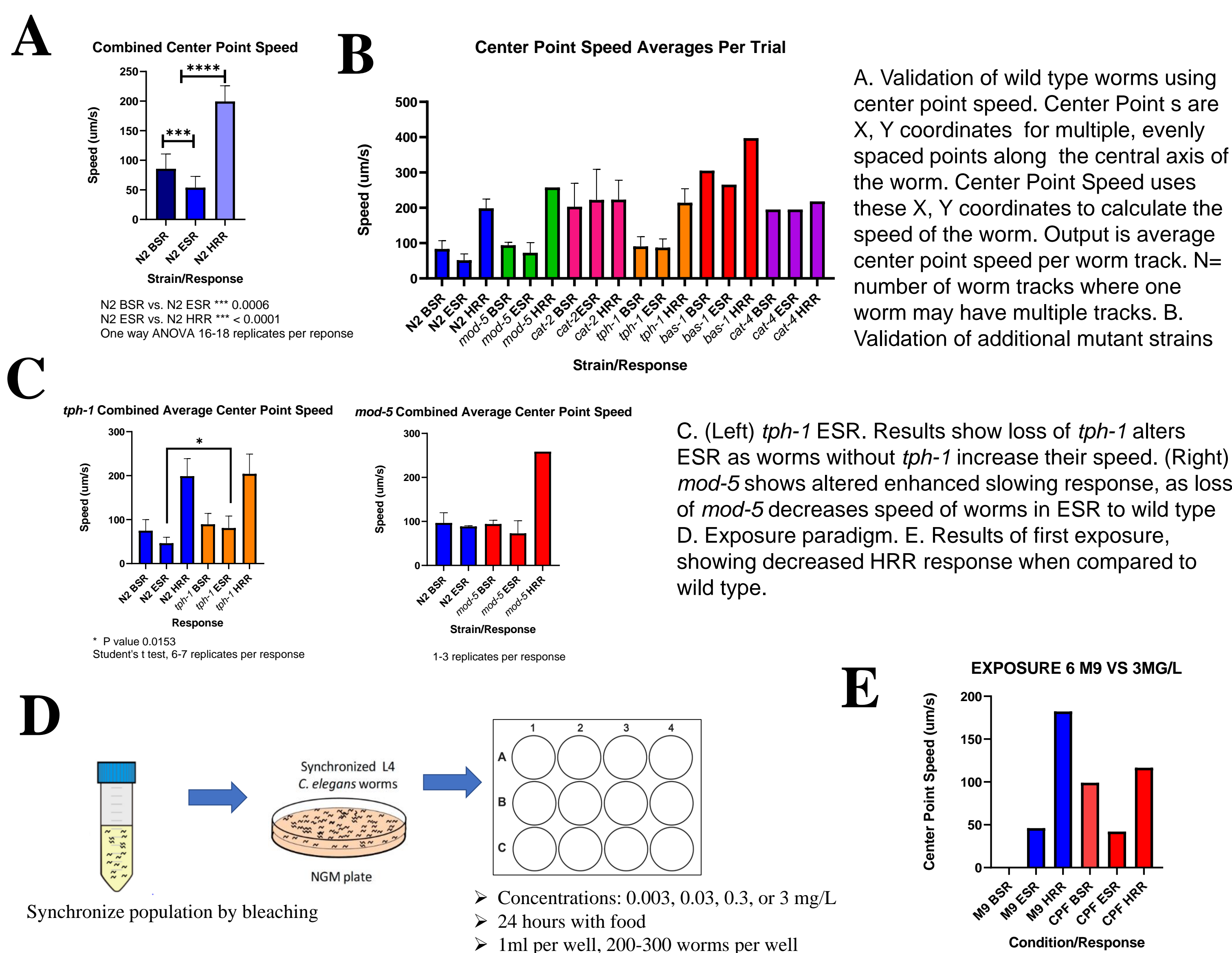


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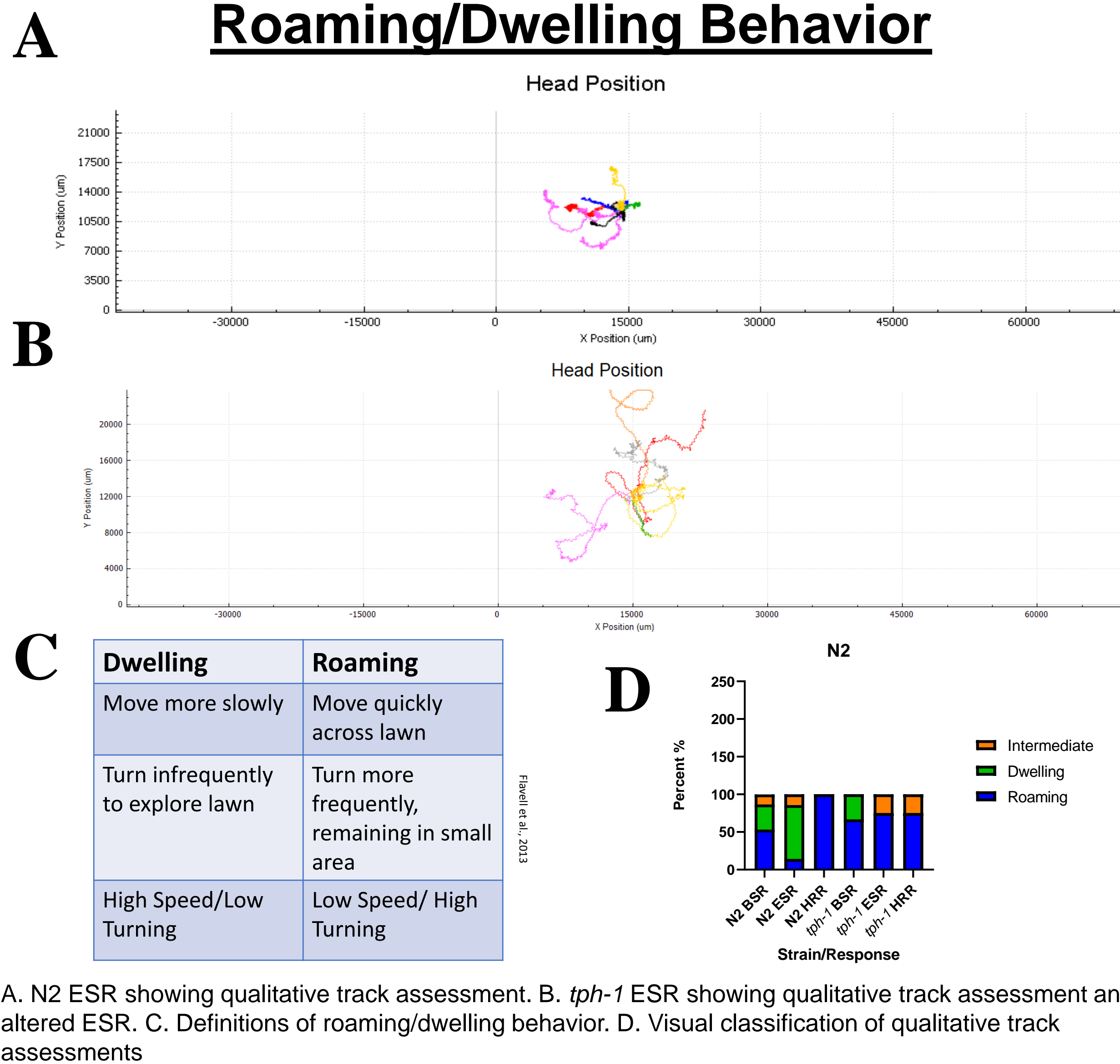
Evaluation of serotonin-modifying toxicants using a standardized tracking and behavioral model in *C. elegans*

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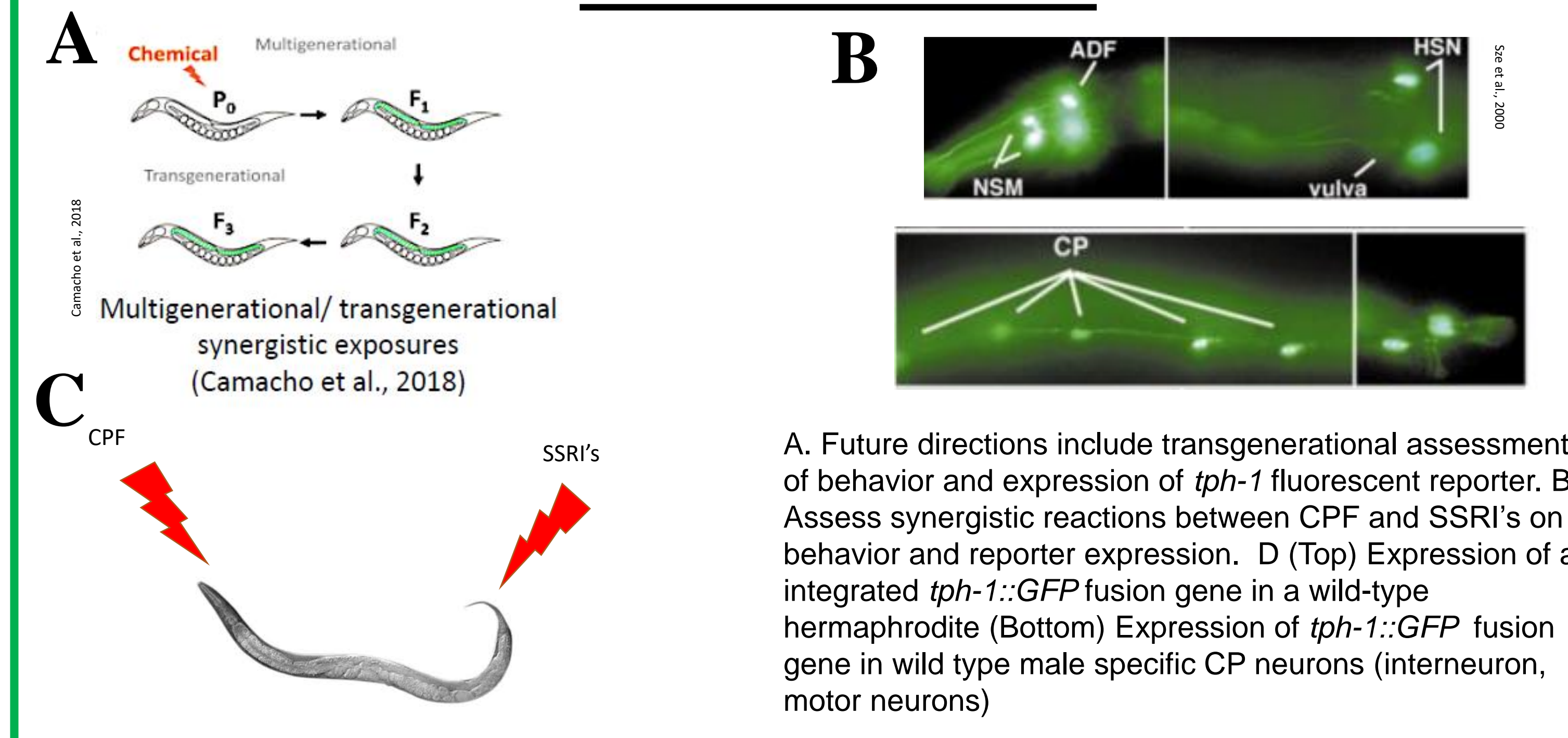
Preliminary Data and Exposure Protocol



Qualitative Track Assessments and Roaming/Dwelling Behavior



Future Directions



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