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ABSTRACT BOOK

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dorsal-ventral orientations can not be recovered. We use a modelling approach to infer beyond what can be directly observed through the data.

The aforementioned problem may be formulated as an optimal control problem for the evolution of a mechanical rod with the control force and torque being interpreted as the reaction force, activated by the worm muscles, from the surrounding fluids [5]. Additionally, we present a new embodied 3D model combining internal body mechanics, muscles and external fluid flow. The model minimises the viscous dissipation of the flow by controlling muscles on the worm's body surface but constrained to match data for the midline velocity. We show the advantages of this model by comparing with our previous rod model as well as laboratory video footage.

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1040V **Neural modulation of systemic stress response requires the insulin like-peptide INS-3** Tania Veuthey[1], Sebastian Giunti[2], Maria Jose De Rosa[1], Mark Alkema[3], Diego Rayes[11]Invertebrate Neurobiology Laboratory, Instituto de Investigaciones Bioquímicas de Bahía Blanca (INIBIBB), [2]invertebrate neurobiology laboratory, Instituto de Investigaciones Bioquímicas de Bahía Blanca (INIBIBB), [3]Department of neurobiology, UMass Chan Medical School

Throughout the animal kingdom, the perpetuation of the flight response leads to reduced ability to cope with environmental challenges, a drastic lifespan reduction, and an increase in disease susceptibility. We showed that, in *C. elegans*, the tyraminergic neuron RIM supplies a state-dependent neural switch between acute flight and long-term environmental stress responses. During the flight-stress response RIM neurons release TA, which stimulates the intestinal adrenergic-like receptor TYRA-3. This leads to DAF-2/Insulin/IGF-1 pathway activation and inhibition of cytoprotective mechanisms in the intestine and other tissues. We hypothesized that TYRA-3 stimulates the release of Insulin-Like Peptides (ILPs) from the intestine that can systemically activate the DAF-2 insulin/IGF1 receptors. We focused on strong agonists ILPs that are expressed in the intestine (INS-3, -4, -6, -32, and DAF-28). We found that *ins-3* mutants are resistant to both heat and oxidative stress, much like *tyra-3* mutants. Moreover, *ins-3* mutants are resistant to the impairment of stress resistance upon exposure to exogenous tyramine. In addition, *ins-3;tyra-3* double mutants are as resistant to environmental stress as single mutants, suggesting that both genes act in the same pathway. Since *ins-3* is expressed in neurons and the intestine, we performed tissue-specific rescue experiments. We found that expression of *ins-3* in the intestine restores stress resistance to wild-type levels. Taken together, our results suggest that intestinal activation of TYRA-3 by the escape neurohormone TA leads to INS-3 release which acts as an endocrine, autocrine, and/or paracrine signal to activate DAF-2 in different tissues.

1041V **Bacterial diets are able to modulate life-history treats in *C. elegans* models of neurodegenerative diseases** Tania Veuthey[1], Andreas Burkovski[21]Invertebrate Neurobiology Laboratory, Instituto de Investigaciones Bioquímicas de Bahía Blanca (INIBIBB), [2]Department of Biology, Friedrich-Alexander-Universität Erlangen-Nürnberg

As life expectancy increase, age-related disorders, such us neurodegenerative diseases (ND), have become more prevalent. Moreover, treatments only attenuate some symptoms, but fail to arrest characteristic neuronal proteotoxicity. Thus, new challenges emerge to science in order to understand molecular basis of these disorders. Lately, the gut-brain axis has gain attention and a close relation between gut microorganism and ND has been proposed. The aim of our work was to evaluate the relevance of the microbiota in the progression of proteotoxic-based disorders, assessing the impact of six non-pathogenic bacterial diets on life-history traits in *C. elegans* models of ND (vs standard OP50). In a first approach, we found 2 bacteria, *Escherichia coli* K12 and *E. coli* HB101, able to improve locomotion in liquid media, in worm's model of Parkinson disease (PD) at adult day 4, versus *E. coli* OP50. Moreover, an age-dependent locomotion improvement, between larva-L4 and adult day 4, was observed in solid media after feeding PD model´s worms with 4 different bacteria versus *E. coli* OP50. We also observed an increase in

the developmental timing of wild-type worms grown in 4 bacteria versus *E. coli* OP50, but more interesting was the accelerated developmental rate selectively found in models of PD and Huntington disease feed with *E. coli* BL21 (DE3). We are currently evaluating aggregate numbers, lifespan and mitochondrial morphology among others. Our results allowed us to identify bacteria with the ability to drive physiological outcomes and improve health status of *C. elegans* models of neurodegenerative diseases.

1042V **Low abundance of propionate promotes α-synuclein-induced neurodegeneration in *C. elegans* through intestine-neuron signaling** chenyin wang[1], Chaogu Zheng[21]School of Biological Sciences, The University of Hong Kong, [2]The University of Hong Kong

Our previous work identified pro-neurodegenerative bacterial genes using the *Caenorhabditis elegans* PD models with neuronal expression of human a-synuclein. Several of those pro-neurodegenerative genes code for proteins involved in the synthesis of vitamin B12 in *E. coli*. We found that depletion of B12 from the *E. coli* diet ameliorated the PD symptoms in *C. elegans,* suggesting that B12 may exacerbate neurodegeneration. Since that dietary B12 is known to breakdown propionate (a short-chain fatty acid) in *C. elegans*, we hypothesize that B12 may promote neurodegeneration by reducing the level of propionate, which has been shown to be neuroprotective in several PD models. We found that propionate supplementation could indeed protect neurons from a-synuclein proteotoxicity. Moreover, transcriptomic analysis found that B12-downregulated genes are also downregulated in PD animals compared to wild-type animals, indicating that dietary B12 and neuronal a-synuclein aggregation target the same genes, both likely through the downregulation of propionate. In fact, our GC-MS analysis found that PD animals indeed have a lower level of propionate than wild-type animals. Propionate serves as a signaling molecule that controls a range of downstream genes, including the transcription factor *nhr-68*, which is significantly downregulated in PD animals compared to the wild type. Interestingly, rescuing *nhr-68* expression in the intestine but not in neurons could rescue neurons from degeneration, suggesting inter-organ signaling between neurons and the intestine. Furthermore, neuronal a-synuclein overexpression induces the activation of mitoUPR markers in the intestine, which contributes to the reprogramming of metabolic genes in the intestine. Overall, our studies suggest that PD animals experience a vitamin B12-like reprogramming of intestinal metabolism due to the low abundance of propionate; this reprogramming leads to reduced energy production in the intestine, which promotes neurodegeneration.

1043V **Turning related neurons RIV, SMB, and SAA gates behavior context dependent processing of mechanosensory stimuli in *C. elegans*** Sandeep Kumar[1], Anuj K. Sharma[2], Andrew M. Leifer[1,21]Princeton Neuroscience Institute, Princeton University, [2]Physics, Princeton University

How does the nervous system integrate external sensory stimuli and the animal's current behavior state to give rise to an appropriate motor response? To answer this question, we investigate the *C. elegans* response to touch because our previous results have shown that worms are less likely to reverse when a gentle touch stimulus is delivered during turns than during forward movement [1].

To probe where in the network behavior context arises, we probed interneurons AIZ, AIB, RIM, AVE, and AVA that are downstream of mechanosensory neurons. We expressed excitatory opsins in these neurons and used a high throughput method [2] to activate each neuron as the animal moved forward or turned and measured the evoked behavioral response. We found that activating neurons AIZ, AIB, RIM, and AVE evoked reversals with a lower probability during turns compared to activation occurring when the animal moved forward. In contrast, activating neuron AVA evoked reversals with similar probability regardless of whether activation occurred when the animal was moving forward or turning. This led us to hypothesize that inhibitory signals during turns are integrated somewhere upstream of neuron AVA.

We next sought to investigate the potential source of this hypothesized inhibition. Wang et al., [3] previously showed and we independently confirmed that inhibition of turning associated neurons RIV, SMB, and SAA increases reversal duration. This led us to hypothesize that these neurons could be the potential source of gating during turns. To test this hypothesis, we simultaneously activated touch neurons and inhibited neurons RIV, SMB, and SAA during turns and found that the probability of evoked reversal is similar to that evoked when the animal moves forward. These findings are consistent with our hypothesis that neurons RIV, SMB, and SAA act as a gate by potentially sending inhibition to the network somewhere upstream of neuron AVA, thus preventing mechanosensory information from traveling downstream in the network.

References:

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