

Multimodal sensory processing in *Caenorhabditis elegans*

During their lifetime, organisms need to adapt to the environment by evaluating and responding to numerous and diverse external cues. The nervous system senses these cues and integrates them, a process called multisensory integration. Research on sensory integration was initiated by Jean Ayres, an occupational therapist and educational psychologist, in the late 1960s. According to her description, 'sensory integration' is "the neurological process that organises sensation from one's own body and from the environment and makes it possible to use the body effectively with the environment". While sensory integration was at first studied as an important neurological function in humans, later it started being addressed as a necessary neuronal process for organisms to adapt to environmental conditions. Neuronal signals generated by various sensory modalities converge into decision-making centers, which may be distinct neurons or discrete brain regions. Through such integration, the nervous system composes a holistic view of external conditions and computes eventual responses. Simultaneous perception and analysis of heterogeneous cues, such as temperature, humidity, food availability, presence of predators and sex pheromones, are necessary for organisms to understand their environment. These responses are further modulated by neuropeptide and biogenic amine signalling. This ability is dependent on the capacity of the nervous system to integrate and analyse information related to various physical parameters. However, despite the importance of sensory integration for organismal adaptability and survival, the molecular mechanisms that underlie multisensory integration are not fully understood.

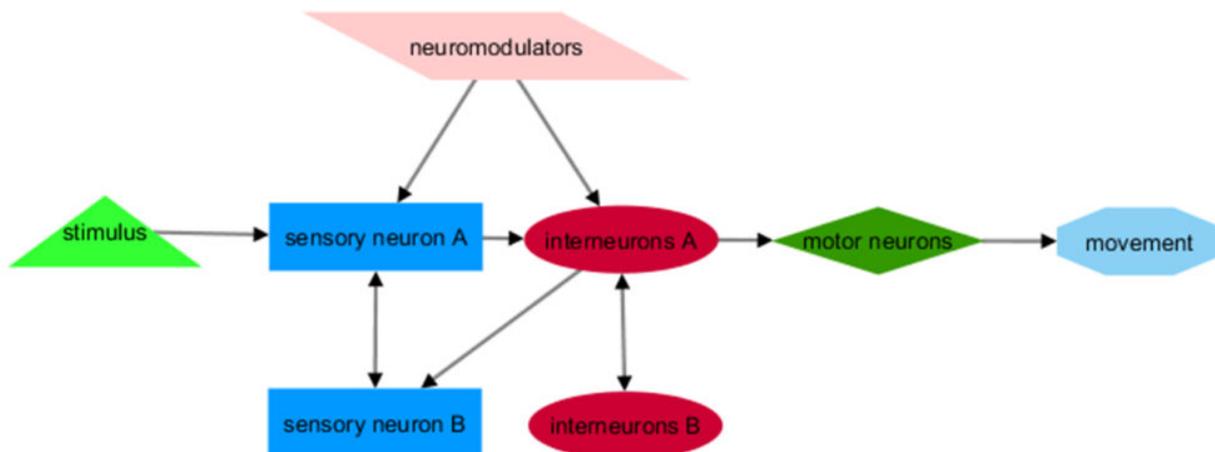


Fig. 1. Schematic diagram of information flow during sensory integration in *C. elegans*. Interneurons concurrently process several external inputs to evaluate environmental conditions and accordingly initiate appropriate motor responses. Sensory neurons are indicated with blue rectangles, interneurons with red ellipses, motor neurons with green diamonds and motor output with light blue octagons. The light green triangle indicates sensory stimuli. Arrows denotes flow of information through synapses or extrasynaptic interactions.

The nematode worm *Caenorhabditis elegans* is amenable to genetic analysis and has a *simple nervous system*, thus, offering a versatile experimental platform for detailed dissection of the molecular pathways that shape behavioural output, triggered by environmental inputs. Indeed, recent sophisticated studies in *C. elegans* have contributed decisively towards elucidating the mechanisms multisensory integration and highlight specific nodal interneurons that function as integration and decision-making centers. Experimental findings indicate that sensory neurons can be uni-modal (specialized for certain modalities) or poly-modal (able to perceive stimuli from various modalities), while others must interact in order to sense external stimuli. In the latter case, combinatorial action of more than one sensory neurons, is a prerequisite for the induction of a proper behavioural response. It has also been suggested that sensory neurons can cross-modulate their activity or interact with each other via neuropeptides to shape a concerted response against external stimuli (Fig. 1). Through such mechanisms sensory neurons enhance their capacity to fine-tune multisensory perception. Subsequently, information derived from sensory neurons is transferred and processed into specific decision-making neuronal centres, which can be distinct neurons or discrete brain regions. Interneurons are neurons that serve as convergence sites for multisensory inputs and functionally resemble coincidence detectors. In some cases, interconnections between sensory neurons and interneurons form distinguishable complex circuits. In these circuits sensory neurons serve as ‘spoke’ neurons while interneurons serve as the ‘hub’ of the circuit. Such mechanisms are suggested to strengthen coincidence responses, facilitate sensory integration and generation of relative behavioural responses.

Apart from external cues, the internal physiological state of organisms also contributes to decision-making. Stress and hunger, for instance, can modulate an organism’s responses to external stimuli. Internal physiological state affects expression and release of neuromodulators, such as biogenic amines and neuropeptides, molecules that can act from distance on nerve cells and can have a general effect on neuronal circuits. Levels of biogenic amines, which are informative for internal metabolic state in animals, can affect sensory integration procedure at different stages and, consequently, relative behavioural responses.

The importance of multimodal sensory processing becomes apparent upon impairment of sensory integration that has been associated with the development of neuropsychiatric pathologies. Converging evidence from research in humans and animal model systems implicates dysfunctional sensory integration in the aetiology of certain neuropsychiatric diseases. Autism spectrum disorders, schizophrenia and attention deficit hyperactivity disorder have been associated with sensory integration impairment. Elucidation of multimodal sensory processing mechanisms will contribute towards deciphering this putative association, and will provide a more comprehensive view of how our nervous system reconstructs the physical world in a coherent and unified representation.

Athanasios Metaxakis¹, **Dionysia Petratou**^{1,2}, **Nektarios Tavernarakis**^{1,2}

¹*Institute of Molecular Biology and Biotechnology, Foundation for Research and Technology*

Hellas, Nikolaou Plastira 100, Heraklion 70013, Crete, Greece

²Department of Basic Sciences, Faculty of Medicine, University of Crete, Heraklion 71110, Crete, Greece

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Metaxakis A, Petratou D, Tavernarakis N

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