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Challenges of Biomimetic Infochemical Communication☆

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Abstract

The natural world abounds with chemical information. Animals rely on chemical communication for behaviors as diverse as finding mates, locating food sources, or avoiding predators. Insects, in particular, are capable of incredibly precise chemocommunication using low-power signaling and processing systems. Most species rely on several compounds to convey specific information, establishing a diverse palette for chemical communication. This complex form of information exchange mediated by chemicals represents an unexplored form of communication and labeling technology that has yet to be exploited. In an attempt to mimic chemocommunication in the insect world, we have developed a new class of technology based on the infochemical communication of moths. We describe how this new class of technology could be realized by combining the latest advances and convergence of expertise in the fields of pheromone biochemistry, entomology, genetics, biophysics, materials science and neuroscience. The principles of signal biosynthesis and molecular detection in olfactory receptors and the central nervous system of insects are discussed. We then describe the technological aspects of implementing a microsystem capable of producing biosynthetic compounds as well as the development of a detector unit comprising a biological cell coating expressing specific ligand receptors and coupled to an acousto-electric transducer.

Keywords: biosynthesis; olfactory receptor; biosensor; neuromorphic modelling; neuroengineering; robotics; source localization

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1. Chemical Communication: Inspiration from Biology

Chemical communication is the ubiquitous language of nature. Chemical messages are utilized by virtually all living organisms to locate food, avoid predators, find mates, or mediate metabolic functions. Words are made of molecules, and sentences can be formed from specific combinations of compounds blended in a spatiotemporal fashion. The persistence and complexity of chemical signals create a highly specific and long-lasting form of communication. With a dictionary bounded only by the limits of biochemistry, such signals establish an incredibly diverse and fascinating mechanism to transmit information over space and time.

Pheromones are species-specific chemicals that mediate a number of complex behaviors. Insects, in particular, utilize a staggering number of pheromones. In fact, the molecular composition of sex attractants have been elucidated for over 1600 species [1]. Most insect pheromones are multicomponent blends of geometric or optical isomers in specific ratios [2]. Many of these attractants are synthesized *de novo* from biosynthetic precursors within the insect itself. Chemical

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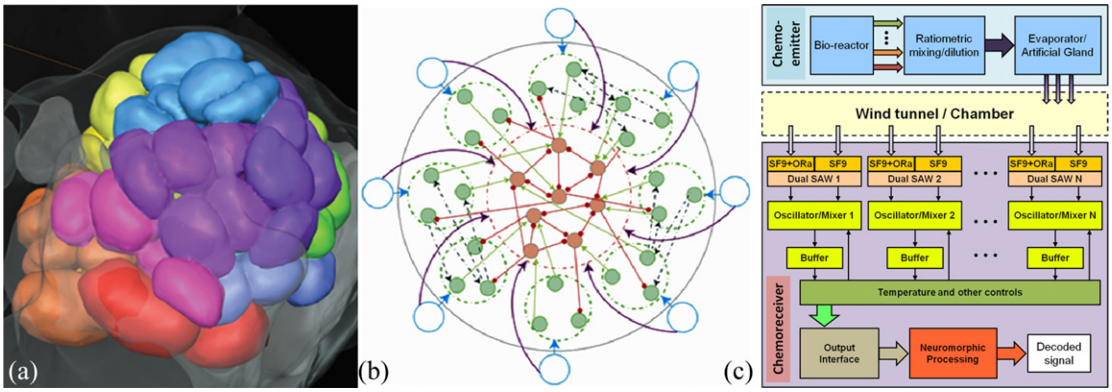

Fig. 1. (a) 3-D reconstruction of a moth antennal lobe showing dense spherical synaptic regions (glomeruli; adapted from [7]); (b) computational schematic of the antennal lobe showing sensory neuron input (blue), projection neuron output (green) and interneuron connectivity (orange); (c) schematic block diagram of a possible biosynthetic infochemical communication system based on a micromachined bioreactor and "artificial gland" chemoemitter, and a chemoreceiver consisting of olfactory receptor-expressing SF9 cells coupled to surface acoustic wave sensors with subsequent neuromorphic processing architecture.

diversity is established through highly sophisticated biosynthetic pathways that alter the variety and order of enzymatic activity to establish different carbon chain lengths, functional groups, and levels of saturation [1]. An understanding of such pathways provides an efficient means to produce an astonishing variety of chemical "sentences", each with specific ratiometric quantities and qualities.

In concert with this chemical symphony, insects have evolved a highly sensitive and specific olfactory system. Insects can detect just a few hundred molecules of odor, making them up to 10 orders of magnitude more sensitive than the human nose. Olfactory detection in insects begins at the antennae. Odorant molecules bind to specific receptor proteins located on the surface of sensory neurons, which are then transmitted to the central nervous system as electrical potentials. Within the brain, these sensor signals are first sent to a region known as the antennal lobe, which is analogous to the mammalian olfactory bulb. Here, the signal from many different receptor types is filtered and processed for further integration with learning, memory, and motor centers. This highly specialized system housed in a tiny, low power biological platform provides immense opportunities to understand the fundamental mechanisms by which high bandwidth chemical information can be detected (Fig. 1).

2. Biological Challenges of Infochemical Communication

Insect chemocommunication provides a remarkable template from which to develop a novel communication system based on chemical information. For specific signals such as sex pheromones, the process can be envisioned in three steps: the signal, the sensor, and the brain. Each of these tasks requires an interdisciplinary exchange between biochemistry, molecular biology, neuroscience, and behavioral ecology. Our biological inspiration for this new form of technology is the Egyptian armyworm, *Spodoptera littoralis*. This moth is an attractive model for infochemical communication due to its intricate chemically-mediated mating behavior. Female *S. littoralis* release a complex signal of 6 monoene and conjugated and non-conjugated diene acetates to attract male conspecifics. To replicate the biosynthetis artificially, we first reviewed the enzymatic routes required to produce this blend [2]. A diacylglycerol acyl transferase from *Acinetobacter sp.* (a wax ester synthase) was identified as a suitable enzyme to convert the alcohol precursor of the major pheromone component into the corresponding acetate. Electrophysiological tests using male antennae revealed the efficacy of enzymatic conversion.

To harness the specificity of the receptor neuron sensors found in the male antennae, we heterologously-expressed olfactory receptor proteins in SF9 cells (from *Spodoptera fugiperda* ovarian tissue). This allowed us to isolate the biological detectors for coupling with an artificial sensor system (see below). In parallel, we assessed the ratiometric coding of the first olfactory processing center of the moth brain, the antennal lobe. We found that the moth brain uses a highly combinatorial, non-linear process for coding complex blends. By unraveling network processing, we found that each neuron utilizes several different spatiotemporal elements to represent the blend electrically. These elements were mathematically represented in a computational model of the antennal lobe that was then used to establish the neuromorphic processors of the artificial system. In this fashion, we were able to biomimetically replicate the complex mating behavior of *S. littoralis* in an artificial communication system.

3. Technological aspects of implementing chemical sensing in mobile systems

Another important aspect of infochemical communication is the ability to track airborne chemical information back to a stationary source (i.e. "source localization"). The technological challenges associated with implementing a mobile chemical sensing and tracking system that mimics *S. littoralis* are considerable. For example, the odor released by the sex glands of the female moth is on the order of nanograms per minute. Sex pheromones also have generally low volatility, so their concentrations in air are parts per billion or less. Yet, the male insect is able to detect the specific odor plume of its mate over great distances [1]. This requires two additional demands on our artificial infochemical system: first, a high sensitivity to the odor signals, and secondly the ability to detect these signals rapidly in odor plumes.

In order to mimic infochemical communication, we require four component parts: an artificial odor source (or artificial gland) that releases the odor blend at a constant flux or rate; a wind tunnel in which air transports the odor blend along a plume at constant velocity; a "chemoreceiver" that can detect the odor blends, and finally a mobile robot that can move intelligently up the plume and towards the odor source. The most technologically challenging aspect is probably the chemoreceiver, which must detect low concentrations of odor blends in less than one second while coping with wind velocities of meters per second. Ideally, source localization should take place in roughly a minute. Most chemical sensors today respond on the order of seconds of tens of seconds [3]. However we have shown that using ultra-thin polymer based sensors can reduce the response time to well below one second [4] based upon a diffusion-rate limited process. Thus, the combination of thin polymers on high frequency SAW resonator sensors can lead to sub-second response times as shown by our tests in wind tunnels. Consequently, we believe that a new generation of fast, chemoreceiver based mobile systems is possible to mimic insect infochemical communication and behavior.

4. Technological challenges of infochemical communication

The technological implementation of an artificial infochemical communication system includes the fabrication of both a "chemoemitter", a microsystem capable of producing and releasing a precise mix of biosynthetic compounds (i.e. pheromones), and a "chemoreceiver", a sensor system capable of detecting the biosynthetic ligands and decoding ratiometrically-encoded information. In the chemoemitter, each biological process of the pheromone production pathway is implemented in microreactor modules [5]. Combining these modules enables the production of diverse blends of pheromone compounds. Each microreactor module facilitates the immobilization of key enzymes whilst preserving catalytic activity, and provides accurate control of the concentration and residence time of the reactants and end-products. Ratiometric encoding is achieved by programming the concentration ratios of the compounds, and the synthesized pheromone blends are released into the environment by controlled thermal volatilization from a micromachined evaporator [5].

The chemoreceiver comprises a ligand-specific cell coating (see above) coupled to an acousto-electric transducer, and a subsequent neuromorphic processing architecture. Pheromone detection is achieved by monitoring the ligand binding-related changes between the cell coating and the surface acoustic waves generated by the acousto-electric transducer. The design of the sensors is based on the dual bio-SAW concept [6] where only one side of the dual pair is functionalized while the other side serves as a reference enabling a differential output that ameliorates environmental variation. By employing an array of sensors coated with SF9 cells expressing different ligand-specific olfactory receptors, a simplified artificial antenna can be constructed. The output signals of these biological microsensors are processed, and ratio recovery and blend recognition are obtained by implementing a biophysically constrained neuromorphic model mimicking the ratiometric processing in the antennal lobe of moths.

5. A Vision for the future: ORchestra

Our development of an infochemical communication system has lead to several breakthroughs - and avenues for future development. In particular, we envision a future where both signal and detection are realized in microscale. There is a tremendous need for more effective chemical and biological sensors in a variety of commercial, medical, and technical applications. Our concept, based upon the integration of biological detectors with micromachined emission and processing technology, is known as ORchestra. Such a system will be capable of releasing molecular levels of volatile blends at precise temporal scales. With an entire olfactory repertoire present on a single cell, ORchestra will be capable of unprecedented millisecond response to complex chemical signals using multifluorescent detection of receptor/ligand binding. This system will also be able to process high-bandwidth chemical input with biologically-based sensor fusion principles. The combination of highly sensitive biological detection with recent advances in MEMS technology provides a powerful tool for small-scale, yet high-throughput chemical detection. We believe that such communication technology sets the agenda for biosensing in the European Union.

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