

A Biophysical Model of Chemical Sensing

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Short Abstract — Molecular sensing is the primary function of olfactory sensory neurons. Utilizing a combinatorial strategy, a relatively small number of receptors located on the surface of these cells is able to detect and distinguish among an enormous repertoire of odors. Inspired by the principles of olfaction, arrays of receptors with overlapping specificities have been proposed as a means to create sensitive, inexpensive chemosensory assays. In this work, we describe a biophysical model that will guide the design of combinatorial receptor arrays and provide a theoretical framework for understanding how multiple ligands are discriminated simultaneously and quantitatively.

Keywords — chemical sensing, olfaction, receptors, Bayesian analysis, nested sampling

I. INTRODUCTION

Olfactory systems are remarkable in their ability to detect and discriminate thousands of odorant molecules varying in both size and shape, and often occurring in just trace amounts in the environment [1,2]. This incredible range and sensitivity are achieved through a combinatorial receptor coding scheme [3] whereby an individual odor molecule is recognized by more than one receptor and most receptors recognize several odors. Identification of an odorant molecule depends on which receptors are activated and to what extent.

Many chemosensory technologies have been advanced as 'artificial' noses, based on their use of combinatorial arrays of receptors as sensors [4]. Despite ongoing interest in such olfactory-mimetic chemical detection, there is no consensus as to how to optimize the design of a given receptor array. Our model provides a theoretical framework for understanding and predicting the success of a putative set of receptors, allowing for selection of the 'best' binding affinities, efficacies, and other properties that determine array performance.

II. BACKGROUND

In previous work [5], Ault *et al.* demonstrated that G protein-coupled receptors (GPCRs) can be engineered to change their relative responses to chemical ligands, and subsequently, how receptors with variable responses to a given set of ligands can be applied in a combinatorial manner to discriminate among closely related molecules. For example, the UDP-glucose receptor can be modified to respond preferentially to UDP-galactose, a stereoisomer of

UDP-glucose, and then pairwise application of the engineered receptors makes it possible to differentiate between pure solutions of the two ligands.

These experiments lead naturally to a number of questions: Given the success of engineered receptors in discriminating among pure solutions of ligands, how well would they perform with mixtures? Can all ligands present in a mixture be identified, and with what accuracy can their concentrations be determined? How many receptors are necessary to recognize and quantify a mixture containing N ligands? Does the presence of an antagonist completely distort the picture or can information be recovered with proper analysis?

III. METHODS AND RESULTS

In order to answer these questions, we looked at mixtures of 1-4 ligands for four different receptors. Using a Bayesian nested sampling algorithm [6], we were able to show that the identity and relative concentrations of ligands present in binary, tertiary, and quaternary mixtures can be successfully determined with the aid of our model. These inferences improve with an increase in the number of receptors present in the array, confirming that a combinatorial strategy is an effective method of chemical detection. In addition, we probed the theoretical limits of combinatorial receptor arrays and discovered a linear relationship between the number of receptors and the number of simultaneously discriminated ligands. These results will guide optimal array design and allow us to check the limits of discriminatory powers of arrays based on naturally occurring as well as engineered receptors.

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