A Yeast Pheromone Testbed for Molecular Communication Validation

M. Lestas, E.I. Ehizogie , H. Omar
Frederick University Cyprus

A. Pitsilllides, A. Kirmizis, C. Pitris
University of Cyprus

I.F. Akyildiz
Truva.Inc

***Abstract*—Over the last decade, molecular communications (MC) has become a popular research topic in the field of telecommunications in addition to bioengineering, chemistry, physics and medicine. The focus of MC is primarily on the modeling, characterization, and engineering of information transmission through molecules. Although a very high number of papers have been published on this topic, they have focused mainly on theoretical mathematical models which have been validated mostly by COMSOL simulations. Although some realistic testbeds exist, there is still a need for more realistic testbeds especially at the micro-scale level in order to accurately validate the theoretical findings. This paper aims at filling this gap by providing a new testbed based on the yeast pheromone model. The new testbed uses engineered sender/receiver yeast cells, with pheromones as the communication medium. The main components of the testbed are introduced and some initial results are shown.**

I. Introduction

Within the last decade, MC has received enormous attention. [1], [2]. Despite the research efforts, the development of new testbeds especially in the microscale remains a major challenge. It has been pointed out in the very recent review in [2] that "with only a few experimental demonstration systems reported to date, the Molecular Communications field generally falls short on validation". Through the PheroMolCom project we aim at addressing this significant challenge to develop and characterize a new testbed for molecular communications using tools from synthetic biology, employing yeast cells as transmitters and receivers and pheromones as information carriers. Although prokaryotic systems (bacteria) have been extensively used ([3]), eukaryotic organisms, such as yeast, which provide more complexity in cell-to-cell communications have not been widely employed. Therefore, this paper establishes a novel testbed system which will also offer a framework for expanding and exploring additional molecular communications due to the genetic amenability and wealth of existing fundamental knowledge on this model organism.

At the macroscopic level several testbeds have been proposed [4]. At the microscale, which is more relevant to our system, it has been a common choice to use genetically modified E. coli bacteria as for example in the early work of [3] and much later in [5]. The latter constitutes an example of optical to chemical conversion. Controlled release of the signaling molecules using an electrical interface was considered in [6].

II. Testbed

The main objective is the development of a practical testbed with which to investigate MC. A pheromone based system involving yeast cells will be utilized. The budding yeast Saccharomyces cerevisiae respond to secreted pheromones found in their surroundings to initiate a mating process, which is one of the best understood cell-cell communication and signalling pathways in eukaryotes [7]. Haploid S. cerevisiae cells exist in one of two mating types, MATa or MATα (alpha). Cells of each mating type secrete specific pheromones that they use to detect the proximity of a potential mating partner of the opposite 'sex'. Specifically, MATa cells secrete a-factor pheromone, a 12 amino-acid long peptide, while MATα cells secrete α-factor pheromone, a 13 residue peptide. The secreted pheromones are perceived by cell surface receptors of cells of the opposite mating type. When a haploid yeast cell is stimulated by pheromone secreted by a nearby cell of the opposite mating type, it undergoes a number of changes in order to prepare for mating. These changes include altered expression of a couple hundred genes, cell-cycle arrest, morphological alterations with polarised growth toward the mating partner, and finally fusion of the two partner cells to form a MATa/ MATα diploid cell [8]. The above-described mating process requires secretion of a pheromone from a 'sender' cell, which through diffusion in the media reaches a 'receiver' cell that will induce the pheromone response pathway (Figure 1). Importantly, yeast cells can also respond to synthesized pheromone of the opposite mating type to induce the physiological changes mentioned previously and this feature has been extensively applied in various experimental procedures. Remarkably, this pheromone communication system has been utilised for synthetic quorum sensing [9], signal amplification [10], intercellular and interspecies communication [11] and biological computation [12]. Hence, during this project we plan to exploit this well-studied biological system in order to set-up a molecular sender-receiver communication circuit that will further our understanding on the dissemination of information.

III. System Model

As indicated in the previous section the system comprises of the sender, the receiver and the physical channel. The objective is to design the encoding/decoding and modulation schemes to optimize the communication process. Changes in the signalling pathways may also be pursed due to the genetic amenability of yeast. As an initial step in the modeling procedure we consider nonlinear state space models for the particle production release mechanism and reception mechanism signalling pathway.

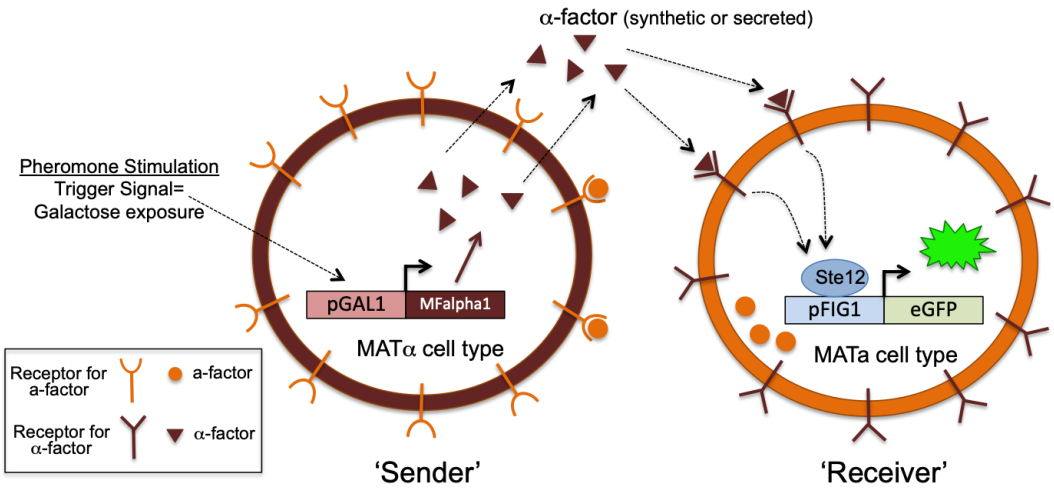

Fig. 1: Schematic of the yeast pheromone sender-receiver communication system.

These have been drawn from [13] and [14]. The former comprises of a 9 state space model which may be reduced to a 5 state model with reasonable representation accuracy. The input of the sender system is the glucose concentration measured in $\%w/V$ (weight per volume) while the output of the system is the $GAL1$ protein concentration measured in mM, which will be suitably modified to secrete pheromone particles. The receiver model comprises of 35 states whose input is the α-factor concentration measured in nM and the output being the complex N, Far1PP–Cdc28 measured in μM.

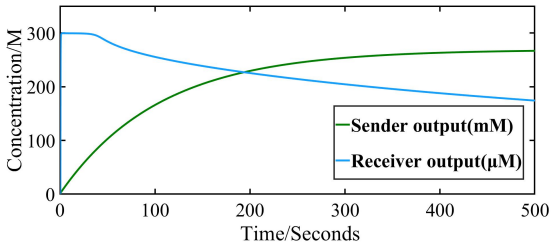

Fig. 2: Sender and receiver responses

In order to investigate the transient properties of the system, we apply step triggering input signals at both the sender and the receiver and we plot the corresponding outputs. The results are shown in Fig. 2 demonstrating convergence within reasonable time. The next step in building a complete simulation model involves mathematically characterizing the diffusion process of the α-factor particles from the sender to the receiver.

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