Using Game Theory for Real-Time Behavioral Dynamics in Microscopic Populations with Noisy Signaling

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Abstract—This article introduces the application of game theory to understand noisy real-time signaling and the resulting behavioral dynamics in microscopic populations such as bacteria and other cells. It presents a bridge between the fields of molecular communication and microscopic game theory. Molecular communication uses conventional communication engineering theory and techniques to study and design systems that use chemical molecules as information carriers. Microscopic game theory models interactions within and between populations of cells and microorganisms. Integrating these two fields provides unique opportunities to understand and control microscopic populations that have imperfect signal propagation. Two case studies, namely bacteria resource sharing and tumor cell signaling, are presented as examples to demonstrate the potential of this approach.

I. INTRODUCTION

For decades, communication engineers have applied mathematics and signal processing to design and understand communication networks. Wired and wireless networks have permeated into our everyday lives by connecting humanity and making it easier for us to receive and share information. By controlling the end-to-end communication process, engineers have built and continue to design systems that are fast, efficient, and reliable. However, communication system design is not exclusive to engineers. Nature has also evolved many strategies for living things to signal each other and share information.

While it is common knowledge that many species (including ourselves) have natural methods to communicate, some of us may not appreciate the extensiveness and complexity of communication in the microscopic domain, nor the important role it plays, in both our evolution and our everyday health. Signals are being regularly transmitted within and between individual cells and microorganisms. These signals may not be sending packets of data in the conventional communication sense, but nevertheless they enable conventional communication applications such as sensing, coordination, and control. Thus, we can adapt conventional communication engineering theory and techniques to study these signaling mechanisms and understand how they work.

An emerging research field in this direction is molecular communication, which considers the use of chemical molecules as information carriers and where traditional communication engineering does not directly apply; see [1]. The growth of this field has been primarily driven by two factors. The first is the ubiquitous use of molecules by cells and microorganisms. The second is the incredible potential to use molecules in new devices and networks where traditional communication designs are not suitable, such as for fighting neurological diseases or for sending messages within microfluidic chips.

An engineer typically expects that a transmitter and a receiver will function as designed. However, unlike modern wireless networks and other communication systems, engineers have less top-down control over systems that include cells and microorganisms. Reasons for this include the limited intelligence of individual cells and the presence of distinct sources of noise. The strength of noise sources, including molecular diffusion and chemical reaction kinetics, are often time-varying and signal-dependent (e.g., see Fig. 1). These characteristics lead to the following problems:

1) If we want to send a signal to a natural microorganism, such as an individual bacterium, then we are constrained to using (noisy) signaling mechanisms that can propagate in microorganism environments and which they would understand.

2) Even if signals were correctly received and detected, we may not be able to guarantee that an individual microorganism behaves as we expect. Microorganisms do not typically live in isolation but in diverse environments where there can be many species (e.g., see Fig. 2). Often, these organisms are sharing signals that influence their behavior, yet they will have imperfect knowledge about each other.

An individual microorganism is not a rational thinker, but it would have evolved to optimize its response to noisy environmental signals. Thus, understanding and controlling microscopic populations requires more than “simply” applying communication theory principles. We must also account for the real-time behavioral dynamics of the population, i.e., the individuals’ behavioral responses to repeated interactions, which is the subject of this article.

The need to predict and control behavioral dynamics suggests the application of game theory [3]. Game theory is a tool for understanding the interactions between rational players whose actions are influenced by their perceived gains. Unlike conventional optimization, game theory models how players adjust their behavior in response to the behavior (or anticipated
**Time [s]**

| Number of Molecules |
|--------------------|
| 0                  |
| 5                  |
| 10                 |
| 15                 |
| 20                 |
| 25                 |
| 30                 |

**Expected Signal**

0
0.02
0.04
0.06
0.08
0.1
0.12
0.14
0.16
0.18

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**Fig. 1: Noisiness of a diffusion wave.** Even in a stable uniform environment without obstacles or chemical reactions, molecular diffusion is a noisy process. The distribution of molecules observed versus time at some distance from an instantaneous point release of molecules is shown. The color bar on the right is the legend for the distribution values, which add up to 1 for each sampling time. The observed diffusion signal has a variance that is proportional to the time-varying strength of the expected signal (solid white line).

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**Fig. 2: Signaling in a diverse microscopic environment.** Microscopic environments can be home to many different species of cells, including animal cells (Type A) and bacterial cells (Types B and C). Even within an individual species, different phenotypes (variations) express different observable traits (e.g., different shades of cell type B). It is common for cells of the same species to communicate with each other (arrows with solid lines), but cross-species communication is also very common, whether intended or not (arrows with dashed lines). Many examples are reviewed in [2].

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**Example of a simple game.** The *Prisoner’s Dilemma* is a classical game theory example that can also be applied to natural microbial environments (see [4]). The players, Alice (A) and Bob (B), are apprehended after a crime and are isolated from each other. Each is offered freedom if they confess and testify against the other player; the other player will receive 20 years in prison. If both confess, they receive 15 years each. If neither confesses, they will be convicted of a lesser offense and receive 1 year each. The reward for players (A, B) can be expressed as follows:

|                  | B confesses | B doesn’t confess |
|------------------|-------------|-------------------|
| A confesses      | (−15, −15)  | (0, −20)          |
| A doesn’t confess| (−20, 0)    | (−1, −1)          |

Regardless of B’s strategy, A can always improve her outcome by confessing: if B confesses, A can improve from −20 to −15; if not, A can improve from −1 to 0. The same is true for B with respect to A’s strategy. Thus, the strategy where both players confess is a strict Nash equilibrium (NE), and this is the only such equilibrium in the game. The “dilemma” is that the NE (both confess) is far from the global optimum (neither confesses).

While structurally simple, the prisoner’s dilemma captures the problem of “cheating”, i.e., acting in self interest when the global optimum requires cooperation. A related problem is the *Tragedy of the Commons*, in which there is a global incentive to conserve a shared resource, but an individual incentive to overuse it. There are many examples of this in biology, including microscopic populations, e.g., the proliferation of tumor cells (the “cheaters”) at the expense of healthy cells (the “cooperators”); see [5].

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**Box 1: The Prisoner’s Dilemma as an example of a mathematical game.**

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In Box 1, game theoretic models are usually described in terms of strategies and decisions, but they are also applicable (and arguably more so) to microbial populations, even though they are not “rational” beings; see [4]. This is precisely because their behaviors are driven by evolution and responses to external signals.

This article serves as a tutorial for applying game theory to behavioral dynamics in microscopic environments with noisy signaling. We propose combining the ideas of game theory for microorganisms with the communication engineering approach from molecular communication. The existing applications of game theory have generally focused on evolution and not accounted for the imperfect propagation of physical signals. Studies of molecular communication have focused on stochastic signal propagation but have not considered behavioral dynamics. This article seeks to bridge this gap and demonstrate that unique insights and engineering opportunities can result.

Our ultimate objective is to design systems that use chemical signaling, where we can predict and control behavior between...
autonomous devices. If we can understand the system as a game, then we can ask how to modify the game in order to achieve a desired result. For example, we could seek how to maintain a healthy system state, how to mitigate disease, or how to efficiently allocate resources for effective signaling. Two specific examples that we describe in this article as case studies are resource sharing by bacteria and signaling by cancer cells. Related work, which did not consider the control of behavioral dynamics, includes [6], where bacteria could form links with other bacteria and share resources, and [7], where two transmitters either compete or cooperate when sending molecules to a common receiver. Cooperation between bacteria for carrying information is also considered in work including [8].

The remainder of this article is as follows. First, we present an introduction to game theory, where we describe how games are classified and how they have been formulated for biological systems. Next, we focus on existing examples of games and game-theoretic analysis in microbial systems, which demonstrate the complexity of on-going competition and cooperation in microscopic environments. Finally, we highlight the significance of noisy signaling to microscopic behavioral dynamics through case studies of bacteria resource sharing (based on our previous work in [9]) and cancer cell signaling.

II. GAME THEORY BACKGROUND

Game theory provides a formal analytical framework with a set of mathematical tools to model and analyze situations of interactive decision making. These situations are the “games”, and the decision of each participant (i.e., each “player”) affects the outcomes for all participants. Game theory can be used to predict each player’s behavior and how it alters its decisions to achieve its goals. Over the past 60 years, game theory has made a revolutionary impact on a wide range of fields including theoretical economics, computer networks, political science, military scenarios, and biology. Example games include the negotiation of sales between vendors and buyers, resource access in mobile telephone networks, and military tactics in war [10]. Game theory has such wide applicability because it is an abstract toolbox for any situation of interactive decision making.

Although the modern formal mathematics for games were developed for the field of economics, the game-theoretic analysis of biological systems has a long history. The earliest such game was the study of Sex Ratios by Darwin, which considered the number of males and females in a given species. Since a male’s contribution to reproduction is only during mating, intuition suggests that an optimal ratio is having fewer males than females. However, Darwin used a game-theoretic argument that was popularized by Fisher in [11] to show that the stable distribution of sexes in an individual’s offspring is to have an equal number of each sex. Any deviation from this behavior, where there are more children of one gender, can be shown to be best countered by producing more children of the other gender. So, most species that use sexual reproduction have evolved to produce male and female offspring in roughly equal numbers, even in species where only a small proportion of males get all of the female partners.

As presented in [3] Ch. 4], other “classical” games also apply in biology. These include the Hawk-Dove game, which is used to understand the use of aggression within and between populations, the War of Attrition, where individuals compete by waiting to receive a reward, and even the Prisoner’s dilemma (see Box. [1], where individuals have an incentive to cheat instead of cooperate with the rest of the population. Each of these game types can have many variations. More formally, there are many different methods for classifying games. In the following, we briefly describe the components of a game and highlight some distinguishing game properties. We draw particular attention to properties that are relevant to microscopic systems.

A. Defining a Game

Every game has the following components:

1) Players are the individual participants, and there must be at least two. A player does not need to be aware that it is participating, but it must be able to make decisions, at least in the sense that it behaves in response to the conditions of the external environment. Furthermore, its decisions must have an impact on what happens to other players. Thus, microorganisms qualify as players, even though they are not rational decision-makers.

2) Strategies are the choices of decisions that players can make. For biological systems, individual players are usually treated in aggregate and we describe the distribution of strategies in a population, e.g., how many cooperate and how many are cheating. If particular strategies can only be evolved and not decided within an individual’s lifetime, then it is common to consider how the strategy distribution evolves and whether it converges to what is called an Evolutionarily Stable Strategy (ESS). In fact, most existing work in biological game theory is concerned with determining and analyzing ESSs; see [3], [4], [10]. For example, a balanced gender ratio in the Sex Ratios game is an ESS. By contrast, we are interested in the dynamics of real-time behavior (i.e., which an individual can change) in response to noisy signaling.

3) Payoffs are the net rewards that players receive as the outcome of the game. Although payoffs can be as intangible as whether a player feels good or ashamed about their behavior, payoffs in biology are usually measured in more concrete terms, such as survival or the number of offspring. For example, Fisher used the number of grandchildren as the payoff in the Sex Ratios game. The key requirement for a game is that a player’s payoff must depend on the strategies chosen by the other players.

If a game has only two players (or types of players) that directly interact with each other, and each player has a finite number of strategies, then an easy way to describe the game is with a payoff table (for example, see Box. [1]). In a payoff table, the row corresponds to the strategy of one player and the column corresponds to the strategy of the other player.
Each element lists the payoffs to the two players when the corresponding strategies are chosen. In a more general sense, a player’s payoff is a function of each player’s strategy.

B. Game Properties

Now that we have described the components of a game, we can discuss the properties of these components and those that are most applicable to microscopic systems.

Regarding players, a game will have some number of players and the players will have some information about each other. Traditionally, games are often modeled as having 2 players with perfect information, but these 2 players could be drawn at random from a larger population. The motivation for this idea is that no more than 2 players will encounter each other at the same time, and players are intelligent enough to observe what the other player is doing. In biology, 2-player games are suitable for actual physical encounters between pairs of members from two populations, such as in the Hawk-Dove game. However, when the actions of a player affect what happens to every other player, it is more appropriate to consider the entire population simultaneously, such as in the multi-player Prisoner’s dilemma where a cheater’s behavior affects all the other players. We are interested in large populations of interdependent microorganisms, so multi-player games will generally be more relevant. Furthermore, due to the limited intelligence of the individual players and the impact of information uncertainty due to noisy signaling, we are interested in players that have imperfect information about each other.

Regarding strategies, a game has players who may or may not inherently cooperate, and they may make decisions once or repeatedly. Games in microscopic systems are inherently non-cooperative, since the players are unable to “agree” a priori to coordinate their behavior (however, cooperation can still occur as a response to external signaling and be preserved via evolution over generations of “successful” cooperators). These games are also dynamic, because the strategic interactions occur repeatedly and it is possible that a player could modify its strategy over time in response to what it is has “learned” via signaling, or a strategy could evolve over generations of players. For example, the formation of bacterial colonies, where bacteria decide whether to form links with other bacteria, was treated as a dynamic non-cooperative game in [6].

Regarding payoffs, it is important to note that we are interested in nonzero sum games, i.e., games where the net sum of all player payoffs is not zero (unlike zero sum games such as Rock Paper Scissors, which always have a “loser” if there is a “winner”). This means that it is possible for all players to be winners (i.e., have positive net payoffs), or even for all players to be losers. For example, all bacteria in a population could “win” if they reach a quorum and successfully form a biofilm, or they could all “lose” by dying.

C. Game Solutions

As we discussed previously, the typical “solution” in a biological game is the Evolutionarily Stable Strategy (ESS). An ESS might not be a global optimum for the total payoff, but it is a strategy distribution that remains stable. Even if mutant strategies introduce deviations from the ESS, the distribution will return to the ESS. However, we are interested in applying game theory to the dynamics of signaling when individuals can alter their behaviors, so the notion of the ESS is less relevant. Instead, we find it more appropriate to consider the notion of the Nash Equilibrium (NE), which is a state where no individual player can improve its own payoff by changing its strategy. The “dilemma” of the 2-player Prisoner’s dilemma (see Box. [1]) is that the game’s NE is for each player to confess, even though the global optimum is for neither player to confess. We are interested in how we could guide microbial populations towards a particular NE or how we could convert a desired system state into a NE. For example, we could seek to promote the growth of healthy bacteria by encouraging cooperation or to prevent the formation of harmful biofilms.

III. MICROSCOPIC SYSTEM DYNAMICS

We have established the components and properties of games, so now we briefly discuss examples of game theoretic applications and analysis in microscopic systems. These examples demonstrate progress in understanding the complex and dynamic interactions within and between microbial populations, and enable us to draw inspiration to control the behavioral dynamics of such populations when they rely on noisy signaling.

A. Game Theory in Microscopic Systems

Generally, microbial environments are both diverse and dynamic; they are often home to multiple species, including bacteria and animal cells, and their populations can migrate and evolve both spatially and temporally. [4] reviewed games where the players are cells that compete or cooperate with each other. Examples include the following:

- **Metabolic games** – There are different metabolic pathways for breaking down sugars, including respiration and fermentation, which have different effective rates and different efficiencies (e.g., fermentation is faster but less efficient). We can view a cell’s pathway as its strategy, and it is even possible for a cell to switch pathways or use multiple pathways simultaneously. Game theory has been applied to understand why different pathways have evolved and how different pathways can be maintained within a stable population.

- **Cross-feeding** – Multiple species can cooperate to break down resources in a process known as cross-feeding. This can occur sequentially in stages, where a waste product from one species is consumed by another species, or reciprocally, where different species benefit by exchanging nutrients. Game theory has been used to explain how cross-feeding could have evolved to maximize resource consumption, for example by making each segment of the population evolve to specialize in one stage of degradation.

- **Tumor Growth** – A recent area of research uses game theory to understand the growth and progression of malignant tumors. Games have modeled competition between
healthy and tumor cells, and between different types of tumor cells.

Additional examples in [4] include how different variations of the same species take turns dominating a population, and how cells send information with pheromones. Importantly, a common refrain in [4] is that non-uniform spatial distributions lead to system stability by providing suitable local interactions. This feature suggests that molecular communication analysis (which considers signal propagation between local individuals) is relevant for microscopic populations.

B. Quorum Sensing

On the topic of signaling, a common mechanism for real-time coordination amongst bacteria is quorum sensing (QS). In QS, each bacterium both releases and detects signaling molecules to estimate the population density. When the density is sufficient, the bacteria initiate collaborative actions, such as biofilm formation. These actions require more effort from each bacterium but can lead to a greater payoff for the community (i.e., a higher chance of survival). Furthermore, the study of QS has applications beyond bacteria. For example, [12] drew analogies between QS and the behavior of malignant tissues (i.e., cancer).

[2] described many non-trivial signaling and behavioral dynamics associated with QS, including the use of multiple types of molecules, crosstalk between different species (see Fig. 2), and eavesdropping by cells that do not release signaling molecules. There are opportunities to model these scenarios as games, and also to draw inspiration from communication engineering concepts such as network security and dealing with interference. Work that has analyzed signaling between bacteria as a game includes [6], [13]. [13] presented a model that accounts for the cost to generate signaling molecules and the cost of cooperating. [6] studied the formation of links between pairs of bacteria and whether a colony of connected bacteria could form. However, existing analysis does not tend to model physical molecular signals and their stochastic signaling dynamics.

IV. SAMPLE APPLICATIONS OF GAME THEORY AND MOLECULAR COMMUNICATION TO MICROORGANISMS

We complete this article with two practical case studies that integrate game theory and molecular communication to control behavioral dynamics in microscopic populations. The first case study considers cooperation within a bacterial population for sharing a common resource, as we proposed in [9]. The second case study considers signals from tumor cells and their interactions with healthy tissue and the immune system. The two studies demonstrate the breadth of potential for integrating stochastic signal propagation with game theory. Game theory enables us to model complex interdependent behavior, and molecular communication analysis enables us to describe the imperfect local information due to stochastic signal propagation.

A. Case Study 1: Bacteria Resource Sharing

Inspired by QS, we consider a resource sharing game where bacteria consume a common resource (e.g., food) and they could work together to access the resource. For example, the bacteria could cooperate to coordinate an attack on a larger organism or to optimize nutrient extraction via cross-feeding (see [4]). In QS, each bacterium estimates the size of the population. We are interested in how the uncertainty in the population size (due to diffusion noise) affects the bacteria’s behavior. If we can assume that all bacteria behave in their own interest, then any individual bacterium would only commit the additional resources necessary for cooperation if it would benefit from doing so, or if it “believes” that it would benefit.

We consider some (realistic) constraints to keep the model and its analysis simple, as we studied in [9] and summarize in Fig. 3. We assume that the amount of resource available is finite and fixed. As the cooperating segment of the population grows, the gain in resource extraction efficiency decreases, so there are diminishing returns for cooperation. We also assume that the system has mechanisms in place to deter cheating, such that the resource extraction efficiency of non-cooperators decreases when cooperation increases. Cheater control mechanisms could include blocking cheaters from the resource or releasing selective toxins; see [5] for more examples. Finally, to implement real-time QS, every bacterium estimates the size of the population and the number of cooperators, where the detection probability decreases with the distance separating two bacteria. Furthermore, cooperating bacteria can be misclassified as non-cooperating (and vice versa).

A game emerges by allowing each bacterium to change its behavior after it has estimated the population distribution and assessed the expected payoff for cooperation. By running multiple rounds, we can track the changes in the population over time and understand the population’s sensitivity to the system parameters. In particular, we demonstrated in [9] (and show in Fig. 3) that uncertainty in the size and behavior of the rest of the population can overcome a lack of explicit coordination and lead to cooperation. This suggests that we could manipulate a microbial system towards a desired NE, in spite of (or even perhaps due to) unreliable signaling.

Future work with our model can include studying more diverse populations with more complex payoff structures, adding more detail to the estimation processes, and tracking the evolution of strategies over generations of the population. Nevertheless, this simple model is sufficient to demonstrate the potential for integrating game theory and molecular communication analysis in bacterial signaling. Applications of this model might lead to improved strategies for combating antibiotic resistance or improving the health of essential bacterial communities.

B. Case Study 2: Tumor Cell Signaling

Our next case study considers a more diverse environment that includes cancer cells, healthy cells, and immune system cells. Cancerous tumors are groups of cells that undergo abnormal growth and can invade surrounding tissue. They
The immune system relies on local signals to determine behaviors, such as the regulation of adaptive immune responses, and the use of immunotherapy. The immune system relies on local signals to determine behavior, such as the regulation of adaptive immune cells, to promote or inhibit tumor growth. Even if immunity were developed, the adapted T cells need to locate the tumor cells in order to identify and attack them, and can eventually metastasize and spread throughout the body, at which stage they are very difficult to treat.

As we previously noted, there are similarities in behavior between communities of bacteria and cancer cells in a tumor. We see that bacteria cannot do better with cooperation until there are at least 6 cooperators. In b), we plot the average number of cooperators in a 100-round game as a function of the probability of mis-classifying a selfish bacterium as cooperative (false alarm). If all bacteria are initially cooperative, then they remain in a cooperative NE. However, if they are all initially selfish, then they stay in a selfish NE unless the false alarm probability is sufficiently high. Plots are adapted from [9].

There are also complex behavioral dynamics between cancer cells and the immune system; see [14]. The immune system is intended to provide both adaptive and innate protection against external threats. However, epidemiological studies have demonstrated that patients with compromised adaptive immunity are at a reduced risk for some types of cancers, and environmental conditions can actually prompt innate immune cells to promote tumor growth.

While there is existing literature describing tumor development with evolutionary game theory, as reviewed in [4], there are opportunities to develop real-time models that account for signaling between individual cells. In particular, we are inspired by agent-based modeling (ABM), which is a simulation approach that considers the interactions between individual cells (or “agents”). The agents in ABM respond to a set of rules and make decisions that lead to particular behaviors, so it has similarities with game theoretic modeling. The review in [15] demonstrates that ABM has already been successfully applied to support wet lab experiments in cancer biology, immunology, and other areas.

Let us briefly discuss a couple of examples of games that we could consider for tumor signaling:

1) We could model tumor cells as players that compare the payoff between keeping the diffusion rate high (which keeps nutrient levels high but makes the cells more susceptible to detection by the immune system) or signaling the surrounding healthy tissue to reduce the diffusion rate (which reduces the ambient nutrient levels but decreases the chance of detection). This game can include noisy signaling amongst the tumor cells and with the surrounding tissue (see Fig. 4), and help us understand and mitigate the conditions where healthy tissue supporting the tumor is an attainable NE.

2) We could model the competition between cancer cells, immune system cells, and the use of immunotherapy. The immune system relies on local signals to determine behavior, such as the regulation of adaptive immune cells, to promote or inhibit tumor growth. Even if immunity were developed, the adapted T cells need to locate the tumor cells in order to identify and attack them, and

Fig. 3: Bacteria resource sharing game from [9]. Each bacterium in a population of size 20 can either cooperate or behave selfishly. In a), we plot the payoff to every player (bacterium) as a function of the total number of cooperators.

Fig. 4: Signaling by tumor cells. Cancer tumor cells (grey) are capable of manipulating nearby healthy tissue cells (white) to produce infrastructure that protects the tumor and shields it from detection by the immune system. The signaling by the tumor to the tissue (represented by arrows with dashed lines) results in an environment that has similarities to that achieved by bacteria communities that create biofilms; see [12].

![Fig. 3: Bacteria resource sharing game from [9]. Each bacterium in a population of size 20 can either cooperate or behave selfishly. In a), we plot the payoff to every player (bacterium) as a function of the total number of cooperators.](image1)

![Fig. 4: Signaling by tumor cells. Cancer tumor cells (grey) are capable of manipulating nearby healthy tissue cells (white) to produce infrastructure that protects the tumor and shields it from detection by the immune system. The signaling by the tumor to the tissue (represented by arrows with dashed lines) results in an environment that has similarities to that achieved by bacteria communities that create biofilms; see [12].](image2)
these can also be noisy processes. The “baseline” case can be compared with that achieved via immunotherapy, where the adaptive immune system is modified with the intention to improve immunity against a particular target, but this could also lead to negative consequences such as tumor growth; see [14].

These two games use signaling and decision-making at the cellular level to gain insight into cancer development and treatment. Integrating game theory and stochastic signaling with the ABM approach can help us understand and possibly manipulate the competitive dynamics between cancer and the healthy body at a physical scale that accounts for the actions taken by individual cells and groups of cells.

V. CONCLUSIONS

In this article we identified opportunities to integrate game theoretic modeling with noisy signaling for real-time behavioral dynamics in microscopic environments. Game theory applies a framework with strategies and payoffs to understand interactive decision making, and extensive work has applied this framework to microscopic systems. Nevertheless, molecular communication engineering has developed tools for the study of stochastic phenomena at this scale and which can be applied to introduce noise and uncertainty to decision-making processes. We presented bacteria resource sharing and tumor cell signaling as two sample scenarios whose analysis and understanding could benefit from this integrated approach and eventually lead to control. We anticipate that many other microscopic scenarios could also benefit.

REFERENCES

[1] N. Farsad, H. B. Yilmaz, A. Eckford, C.-B. Chae, and W. Guo, “A comprehensive survey of recent advancements in molecular communication,” IEEE Commun. Surv. Tutorials, vol. 18, no. 3, pp. 1887–1919, 2016.
[2] S. Atkinson and P. Williams, “Quorum sensing and social networking in the microbial world,” J. R. Soc. Interface, vol. 6, no. 40, pp. 959–978, Nov. 2009.
[3] M. Broom and J. Rychtar, Game-Theoretical Models in Biology. CRC Press, 2013.
[4] S. Hummert, K. Bohl, D. Basanta, A. Deutsch, S. Werner, G. Theißen, A. Schroeter, and S. Schuster, “Evolutionary game theory: Cells as players,” Mol. BioSyst., vol. 10, no. 12, pp. 3044–3065, Aug. 2014.
[5] M. Travisano and G. J. Velicer, “Strategies of microbial cheater control,” Trends Microbiol., vol. 12, no. 2, pp. 72–78, Feb. 2004.
[6] L. Canzian, K. Zhao, G. C. L. Wong, and M. van der Schaar, “A dynamic network formation model for understanding bacterial self-organization into micro-colonies,” IEEE Trans. Mol. Biol. Multi-Scale Commun., vol. 1, no. 1, pp. 76–89, Mar. 2015.
[7] C. Koca and O. B. Akan, “Anarchy vs. cooperation on internet of molecular things,” IEEE Internet Things J., vol. 4, no. 5, pp. 1445–1453, Oct. 2017.
[8] B. D. Unluturk, S. Balasubramaniam, and I. Akyildiz, “The impact of social behavior on the attenuation and delay of bacterial nanonetworks,” IEEE Trans. Nanobioscience, vol. 15, no. 8, pp. 959–969, Dec. 2016.
[9] A. Noel, Y. Fang, N. Yang, D. Makrakis, and A. W. Eckford, “Effect of local population uncertainty on cooperation in bacteria,” in 2017 IEEE ITW, to be presented., pp. 1–5.
[10] M. Maschler, E. Solan, and S. Zamir, Game Theory. Cambridge: Cambridge University Press, 2013.
[11] R. A. Fisher, The Genetical Theory of Natural Selection. 1930.
[12] A. Noel, L. Estévez-Salmerón, S. Oh, D. Liao, B. M. Emerson, T. D. Tlsty, and R. H. Austin, “An analogy between the evolution of drug resistance in bacterial communities and malignant tissues,” Nat. Rev. Cancer, vol. 11, no. 5, pp. 375–382, May 2011.
[13] S. P. Brown and R. A. Johnstone, “Cooperation in the dark: Signalling and collective action in quorum-sensing bacteria,” Proc. R. Soc. London B Biol. Sci., vol. 268, no. 1470, pp. 961–965, May 2001.
[14] K. E. de Visser, A. Eichten, and L. M. Coussens, “Paradoxical roles of the immune system during cancer development,” Nat. Rev. Cancer, vol. 6, no. 1, pp. 24–37, Jan. 2006.
[15] B. C. Thorne, A. M. Bailey, and S. M. Peirce, “Combining experiments with multi-cell agent-based modeling to study biological tissue patterning,” Brief. Bioinform., vol. 8, no. 4, pp. 245–257, Mar. 2007.