M4 Morning session 4: (25 min) Lorenzo Del Moro, Maurizio Magarini and Pasquale Stano On the Evaluation of Observed Semantic Information in Synthetic Cells

There was another paper that I found interesting: **M4 Morning session 4: (25 min) "On the Evaluation of Observed Semantic Information in Synthetic Cells" Lorenzo Del Moro, Maurizio Magarini and Pasquale Stano,** which looks like part of a thesis here - https://www.politesi.polimi.it/bitstream/10589/192552/3/2022_10_Del%20Moro.pdf

They discuss synthetic cells and its co-dependence on environmental changes and at the same time act as drug-delivery agents (remember XenoBots?) using Toxins production to kill Cancer Cells. The work is quite theoretical but convinces to me, to a great extent :)

They evaluate and quantify semantic information in those synthetic cells (when they are in environment and the information, they possess by their surrounding) using KW approach. They propose to quantify the information these synthetic cells have about their environment based on the ideas of KW. (not delved much into KW so far).

The four major roles of the synthetic cells is:

1. Perception and Reception: Looking for chemical activity in the environment. They introduce some energy variables (energy budget) to mimic original membranes that receives signals from surrounding molecules.
2. Broadcast / Internationalization.
3. Toxin production: They control toxin production using synthetic cells. We do not want to produce neither higher level of toxin-molecules far from the Cancer Cells nor a lower level close to them. They maintain some energy budget variables for this as well.
4. Precursor Molecules / Toxin producing materials: It is initialized with a fixed value (or a budget) and gets depleted as Synthetic Cells produce more toxins or degradation. This degradation is important to make the Synthetic Cells die out. And Synthetic Cells do not have a continuous source to produce more toxins or a mechanism, as real world cells do.

When the toxin budget finishes, the internal entropy of the Synthetic Cells increases (I think this is where KW approach comes to play, which measure the amount of information for example as Shannon method does) which further decreases the Synthetic Cells ability to control and function. And hence it has to die out.

They also mentioned about the tradeoff for a Synthetic Cell's trying to self-preserve and goal reachability as there is a fixed toxin budget or pre-cursor molecules.

One another thing I liked is that they propose KW is **not** the optimal to measure the exact information or capture enough complexity necessary for the goal of killing Cancer Cells.

The paragraph discusses a theoretical work related to stored semantic information in the context of synthetic cells. This work is based on the contributions of a person or group represented by the abbreviation "KW." The paragraph suggests that this theoretical work could serve as a foundation for future investigations and practical experiments, spanning various research fields including information theory, molecular communications, and synthetic biology.
The primary focus of the theoretical work, referenced by citations [11, 12], is to delve into an area that may have significant implications for understanding synthetic cells and their relationship with their environment. At its core, the objective of this work is to quantitatively assess the amount of semantic information that a synthetic cell (SC) possesses about its surroundings using the approach established by KW.
A synthetic cell is a human-engineered construct that mimics certain characteristics of natural cells. These synthetic cells are created "from scratch" through a process referred to as a "bottom-up approach." This approach involves the assembly of basic components in order to construct a complex biological system. Despite their similarity to living cells, synthetic cells are not currently classified as living entities; they are more accurately described as molecular machines due to their engineered nature.
One potential application of these bottom-up synthetic cells is in acting as intelligent drug delivery agents. These synthetic cells could be designed to perform the role of delivering drugs in a targeted and responsive manner. This task involves chemical communication and interaction with the environment they are placed in, such as sensing and responding to molecules released by cancerous cells.
The paragraph then mentions that there are three key aspects to consider in the pursuit of evaluating the stored semantic information within these synthetic cells. Unfortunately, the specific aspects are not detailed in this excerpt, but it's implied that these aspects are critical for understanding how synthetic cells can store and process meaningful information about their surroundings.
In summary, the paragraph introduces a theoretical work that explores the concept of stored semantic information in synthetic cells. These artificial cells, while not alive in the traditional sense, are constructed through a bottom-up approach and can potentially serve as sophisticated drug delivery agents. The work aims to quantify the information these synthetic cells possess about their environment based on the ideas put forth by KW, and it suggests that future research could explore this topic further in

various interdisciplinary areas.

The modelling of the SC is such that it has the aim to proportionally respond to that chemicals with a production of a toxin-molecule that kills the CCs. The fact that the amount of released toxin-molecules must be coherent with the chemicals level is worth of note, cause it is possible to associate to that amount of chemicals the proximity to the CCs. Therefore, we do not want to produce neither higher level of toxin-molecules far from the CCs nor a lower level close to them. The paragraph focuses on describing the methodology and modeling approach used to study the interaction between synthetic cells (SCs) and signaling molecules released by cancerous cells (CCs). The main idea is to represent the chemicals, or signaling molecules, released by the CCs using a simplified single state variable called YS, which can take on values from 0 to 5. Each value of YS corresponds to a different level of signaling molecules present in the environment.

- **YS Variable: The variable YS represents the level of signaling molecules. When YS is 0, it signifies that no chemicals are present in the surrounding environment. This could be due to either the degradation of the chemicals over time or the absence of CCs in the vicinity.**
- **Perception and Reception: The synthetic cell (SC) is treated as an autonomous agent that performs four tasks. The first task involves perceiving the level of chemicals in its environment using perfect receptors. The level of signaling perceived by the SC is denoted as XSper. For simplicity, XSper is always equal to the YS value, i.e., XSper ranges from 0 to 5 to match the possible values of YS. If YS is 0, then XSper is also 0, indicating that no chemicals are detected by the SC. In biological terms, XSper represents the receptor on the SC's membrane that senses the signaling molecules.**
- **Internalization / Broadcast: The second task is the internalization of the perceived chemical level. This process is quantified using the state variable XSin, which also ranges from 0 to 5 and is proportional to the XSper value.**
- **Toxin Production:** The third task of the synthetic cell (SC) involves using precursor molecules to synthesize a toxin. This process is quantified using the state variable Xptox, which can take on values from 0 to 8. The toxin is produced with the intention of killing the cancerous cells (CCs) present in the environment. Essentially, the SC uses the precursor molecules to create the toxin, which is then released to target the CCs.
- **Precursor Molecules:** These precursor molecules are the starting materials required for the synthesis of the toxin. The Xptox variable represents the quantity of these precursor molecules available to the synthetic cell. However, there is a key constraint. These precursor molecules have a fixed initial value, and this value decreases over time due to degradation. The degradation happens because the synthetic cells lack specific internal structures that would enable them to generate these precursor molecules continuously.

- **Degradation and Constraints:** The paragraph implies that the reduction in Xptox occurs independently of the presence of the signaling molecules (YS) in the environment. This indicates that the decrease in precursor molecules isn't solely linked to the interaction with the CCs or signaling molecules; rather, it's a natural degradation process. As the Xptox value decreases over time, the synthetic cell's ability to produce the toxin diminishes.
- **System State and Cell Survival:** When the Xptox value reaches 0, a significant consequence follows. The internal entropy of the system increases to a fixed value. In this context, increasing internal entropy signifies disorder or loss of control within the synthetic cell's functioning. This transition indicates that the SC can no longer complete its task effectively. As a result, the synthetic cell is said to "die" since it is no longer capable of carrying out its intended function.

In summary, this part of the paragraph elaborates on the process of toxin production by the synthetic cell to eliminate cancerous cells. It explains the use of precursor molecules represented by Xptox, the degradation of these precursors over time, and the implications of their depletion on the overall functioning and survival of the synthetic cell.

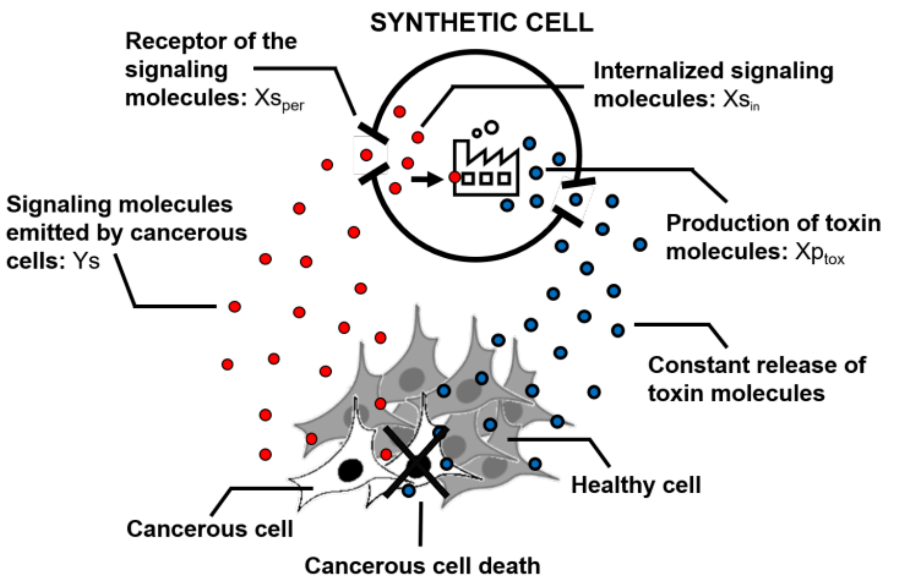

Figure 3.1: Graphical representation of the simulated scenario.

https://www.politesi.polimi.it/bitstream/10589/192552/3/2022_10_Del%20Moro.pdf such that $X = X_{S_{in}} \times X_{S_{per}} \times X_{ptox}$ an the modelled states variable are

$$\begin{aligned} X_{S_{in}} &= \{0, 1, 2, 3, 4, 5\}, \\ X_{S_{per}} &= \{1, 2, 3, 4, 5\}, \\ X_{ptox} &= \{0, 1, 2, 3, 4, 5, 6, 7, 8\}, \\ Y_S &= \{0, 1, 2, 3, 4, 5\}. \end{aligned}$$

This section of the text explores some conceptual observations and clarifications about the nature of the synthetic cell (SC), its goals, and how these aspects relate to the modeling approach. Let's break it down:

- **Autonomous Agent and Exogenously Determined Goal:** The text begins by addressing the nature of the synthetic cell as an autonomous agent. The work draws from the concepts proposed by KW, where an autonomous agent has its own internal processes and decision-making. In the case of the SC, it falls within this category. However, the SC is also engineered with a specific external goal—killing cancerous cells (CCs). The key question that arises is whether this goal is intrinsic to the SC's nature or externally imposed.
- **Intrinsic Goal vs. Externally Imposed Goal:** The discussion delves into the nature of the SC's goals. A synthetic cell inherently strives to maintain itself alive, which can be considered its intrinsic goal. On the other hand, the goal of killing CCs is externally imposed by introducing internal structures that allow the SC to generate and release toxin molecules. The paragraph acknowledges that the goals might not be inherently aligned.
- **Associating Goal Achievement with Viability:** To address the question of whether the SC's intrinsic goal aligns with its externally imposed goal, the authors make an interesting association. They link the macroscopic state in which the SC depletes its precursor molecules with a "dead" state. This means that when the precursors necessary for toxin production run out, the SC stops maintaining itself alive. This intriguing connection implies that achieving the goal of killing CCs becomes inseparable from the goal of self-preservation.
- **Stored Semantic Information and External Goals:** The paragraph presents an alternative perspective. Instead of using the viability function proposed by KW, an objective function is suggested for measuring stored semantic information. This function would be defined as the initial value of syntactic information that causally contributes to the system's goal. This discussion highlights that stored semantic information might not be intrinsic to the SC if the external goal of killing CCs is distinct from the intrinsic goal of self-preservation.
- **Motivation and Research Focus:** The paragraph concludes by clarifying the primary focus of the work. The authors express that their interest lies in understanding the amount of information necessary for effectively killing CCs through the correct release of toxin molecules. They emphasize that

their goal is not to establish whether this amount of information is intrinsic to the SC or not, but rather to assess its utility in achieving the external goal.

In summary, this section delves into the philosophical and conceptual aspects of the SC's goals, both intrinsic and externally imposed. The authors connect the SC's self-preservation and external goal attainment, suggesting that these two might coincide due to the depletion of precursor molecules. They also discuss different approaches to measuring information's role in achieving goals and emphasize their focus on understanding the information necessary for the external goal of killing CCs.

This part of the text discusses the use of negative entropy as a viability function and its relationship to the concept of life and the behavior of synthetic cells (SCs):

- **Negative Entropy as Viability Function:** The text begins by addressing the use of negative entropy as a viability function. Negative entropy, often referred to as negentropy or information entropy, is a concept from thermodynamics and information theory. In the context of the SC, negative entropy is used as a measure of the system's capacity to stay in a thermodynamic out-of-equilibrium state. In this context, "viability" refers to the SC's ability to maintain itself in a state of non-equilibrium, which is required for its functioning.
- **Not Directly Related to Life:** The text clarifies that the adoption of negative entropy as a viability function is not inherently tied to the concept of life. While negative entropy is a key factor in living systems' ability to maintain themselves in non-equilibrium states, the SC under consideration is not classified as a living being. Rather, it is engineered and functions as a molecular machine. The paragraph emphasizes that the utilization of negative entropy is intended to compute the stored semantic information that the SC possesses about its environment. This computation aids in understanding how the SC remains in an out-of-equilibrium state.
- **Stored Semantic Information and Thermodynamic Out-of-Equilibrium:** The paragraph implies that the concept of stored semantic information, which relates to the SC's ability to respond to its environment, is closely linked to its thermodynamic out-of-equilibrium state. The negative entropy reflects the system's ability to resist the tendency to move towards equilibrium, a characteristic that is often seen in living systems but also applies to non-living systems like the SC.
- **Far-From-Equilibrium State and Life:** The text underscores a crucial point: being in a far-from-equilibrium state does not necessarily imply that a system is alive. While living systems are typically characterized by their ability to maintain a non-equilibrium state, the presence of such a state alone doesn't confer life. The paragraph underscores that the SC, despite its ability to stay far from equilibrium using the negative entropy-based viability function, does not possess the full attributes of life. It is not a living organism but a synthetic construct.

In essence, this section highlights the distinction between negative entropy as a measure of viability for maintaining a non-equilibrium state and the concept of life. The SC's utilization of negative entropy allows it to remain in a thermodynamic out-of-equilibrium state, which contributes to its functionality, but the presence of this state alone does not equate to the presence of life.