The Science of how Living Systems Escape Decay to Equilibrium!

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Abstract

The article discusses how biological systems operate away from equilibrium as open systems, requiring continual input of free energy from the environment to maintain their capacity to do work and self-organize. It also talks about ways in which living cells couple one chemical gradient to another in constructing the many patterns of reactions necessary for life to sustain.

Key Words

Molecular organization, Non-equilibrium, Entropy, steady state, free energy

Introduction

Natural selection, (which is largely accepted as the fundamental law in biology) doesn't account for the irreversibility of evolution, complexity generation and self-organizing behavior of living systems[1]. Therefore, attempts have been made to draw connection between physical laws and biological systems. It has been suggested that the 'driving force' behind biological evolution is rooted in the physical principles of Thermodynamics. Certain features that characterizes self-organizing processes involve spontaneous emergence of new functional structures in open systems, operating far from equilibrium and nonlinearly connected through internal feed -back loop[2]. The following article is a brief commentary on how non-equilibrium processes drive and couple free energies of metabolic pathways to create steady-states featuring continual activity and constancy of composition.

Open Systems and the Paradox of sustained but stable activity

The discussion starts with a first-hand observation that molecular organization leads to greater order and hence decreased entropy, which apparently seems to defy the second law of Thermodynamics (especially, if we consider an irreversible process in an isolated system). This law gives us a measure of entropy- the thermal energy unavailable to do work. or in other words how many ways molecules be arranged (with or without restriction). The logarithm of the number of ways of arrangement is the entropy. Clearly there are a greater number of ways to arrange them (the term "W" is a measure of that) without restriction than with restriction[3]

$[S=k_b \ln W]$, k_b refers to the Boltzmann constant.

However, biological systems are open systems characterized by fluxes of matter and energy. Order can arise till the entropy of the surrounding system increases enough so that the total entropy from the two parts of the system together increases[4]. But before we embark on the specifics, let us briefly discuss the importance of equilibrium (state of least restriction achieved through degenerate energy states) and non-equilibrium systems (created by more restrictions in the occupancy of energy states, and hence higher level of interaction). All living systems are powered by chemical reactions but chemical reactions have the tendency to destroy gradients and achieve a condition of changeless stability[5].The question that naturally arise is how then life sustain itself (because work cannot be extracted from a system in equilibrium, wherein free energy change is zero)? Life thus exhibits a fundamental paradox wherein it displays stability and activity (related to work) within the same system. In ordinary chemical systems (where in mass transfer is generally prohibited) stability at equilibrium and changing concentration of reactions are mutually exclusive process; we are allowed to have either activity or stability but not both at the same time. Life processes are therefore in non-equilibrium. Also, life processes are essentially open systems receiving constant inputs of free energy from concentration gradients outside itself. They may go to a steady state rather than an equilibrium[6]. The question then becomes how does a steady state differ from an equilibrium? In an equilibrium process, the concentration gradient falls to zero whereas a constant concentration gradient is maintained in a steady state process and is not zero. The rate of formation and destruction of species (which is regulated by metabolic

processes outside.) are maintained at a fixed ratio. We may refer to the schematic below (Fig 1) to understand the situation further.
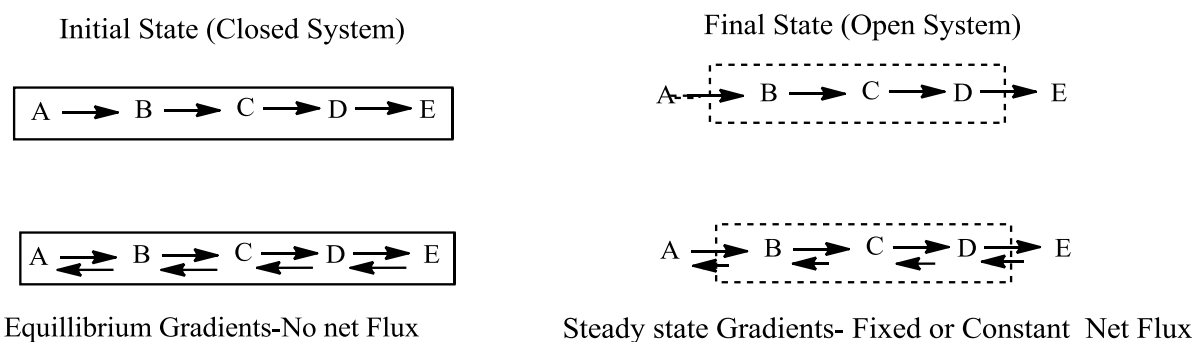
Initial State (Closed System)   Final State (Open System)

A ⟶ B ⟶ C ⟶ D ⟶ E   A⟶ B ⟶ C ⟶ D ⟶ E

A ⇄ B ⇄ C ⇄ D ⇄ E   A ⇄ B ⇄ C ⇄ D ⇄ E

Equillibrium Gradients-No net Flux   Steady state Gradients- Fixed or Constant Net Flux

Figure 1: Difference between equilibrium (left) and Steady state gradients (right)

For a closed system initially **B, C, D** and **E** is produced from **A**. As the concentration of **A** decreases and **B**, **C**, **D** and **E** are produced. A reverse reaction becomes operative till equilibrium is attained. There is no change in concentration of the components as the net flux between any of the components are Zero. Contrary to this for an open system, the back reactions don't build up so far or the equilibrium constant values for the back reactions are not same as the forward reactions. This is dictated by the fact that the source **(A)** and sink **(E)** lies outside the rest of the system and their concentrations are maintained constant by factors in the environment. As **A** converts to **B**, some external factor prevents the concentration of **A** from falling and as **D** is converted to **E**, some external factor limits the concentration rise of **E**. **E** is siphoned off as metabolic pathways are interconnected. This creates a concentration gradient and the system achieves a steady state in which concentrations of **B, C** and **D** remain constant because there is a constant net flux through the system. (Feedback loop-based systems are ubiquitous to biological systems). The living system is thus an assembly of components, **B, C** and **D** forming a link between the source and the sink. They escape tendency to destroy gradients by being an open system by channeling outside energy gradients and living in a steady state rather than settling into an inactivity of equilibrium or in other words an open system achieves stability in steady-state maintaining continuous flow of reactions across a gradient of chemical concentrations[4]. The amount of free energy required to maintain steady-state depends on the extent to which concentration of chemicals are kept removed from equilibrium levels and also the amount of reaction that is allowed to flow across the gradient. In order to maintain the concentration of the species in steady-state,

living systems devised ways to couple one free energy gradient of a reaction to another. Since the quantity of free energy depends on the product of gradient and the amount of charge (matter) flowing across (related to net flux), a large chemical stream with smaller concentration gradient can drive a small chemical stream up a larger gradient, if suitable means can be found to couple one reaction to the other. As an analogy, an electrical step-up transformer can produce a large voltage from a small one provided the current flowing across the high voltage difference is correspondingly smaller than the current across the low-voltage difference. Living cells has developed remarkable means of combining chemical reaction together to utilize free energy of one to drive the other. For example, if aerobic cells (using oxygen) that utilize a powerful downhill reaction (ΔG highly negative) of oxidizing substrates such as glucose, is coupled to another reaction that converts glucose to polysaccharides, the cell would still have an overall downhill system, where a small part of the glucose is oxidized and the remaining used for the uphill polysaccharide synthesis. But for reactions to be added, they must be coupled in a material way through a common intermediary component like (ATP, Adenosine triphosphate) which releases the necessary energy (stored in the chemical bonds) to drive the uphill reaction towards the synthesis of polysaccharides (Fig 2). The role of ATP and ADP (Adenosine diphosphate) is similar to a transmission having gears and rods that connects the engine to the wheel.
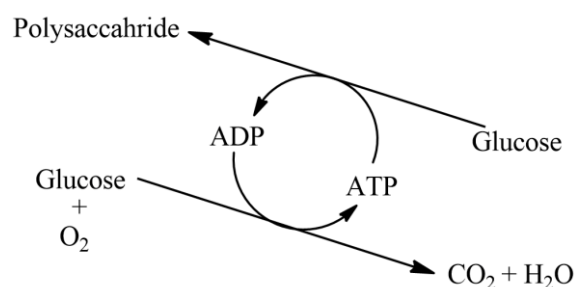

Figure 2: Coupling free energy of metabolic processes

The ultimate gradient is in the environment between the source and the sink and life flows towards the maintenance of this gradient. Life is therefore not the beginning and the end but its maintenance driven by this energy gradient.

Finally, in the words of Fritjof Capra[2] "The more complex the network is, the more complex its pattern of interconnections, the more resilient it will be".

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