Poster Presentation prepared for

GATHERINGS IN BIOSEMIOTICS 2020

Molecular Information as an Agency of Biophysical Causality in Living Systems.

Even though ‘information’ is recognized to play an essential role in the life of living systems many questions remain unanswered.

Walker and Davies codify their perspective in the following words, “Although it is notoriously hard to identify precisely what makes life so distinctive and remarkable there is general agreement that its informational aspect is one key property, and perhaps the key property.”[1]

How does information act?

In retrospect, the research to find the answer, raises the awareness that incomprehension is a form of blindness.

The observation.

The primary biofunction of the living state is the phenomenon of life. By observation, in the presence of nutrition, the living state within cells is spontaneous. This is perhaps among the most remarkable facts of life. The living state is an entirely lawful state, present within the constraints of the laws of thermodynamics and kinetics.

The spontaneity of a chemical reaction is known to be a fact of chemical physics that satisfies two conditions, one kinetic and the other thermodynamic. Therefore the spontaneity of the molecular processes at the basis of life must be acts of biophysics.

It is here posited that since the living state is a state prescribed by and through molecular information then the prescribed molecular information must have specific thermodynamic and kinetic properties that are the primary cause of the spontaneity of living state within the context of the cell. The secondary cause is the availability of ATP.

Three Concepts.

In order to understand how life works three concepts must be investigated, namely, information, thermodynamics and kinetics.

Measuring Information.

1. **Shannon’s Theory of Information.**

We live in what has been described as ‘the information age’. Shannon’s theory of information arose in the context of the development of the technical means of mass communication. This enormous field is presently dominated by digital technology. Shannon’s theory of information is specifically directed toward ‘signal detection’; the recognition of a signal in a background of

[1] Walker and Davies. The algorithmic origins of life. *J. R. Soc. Interface* 2013 10, 20120869

noise. The Shannon signal is recognized by its improbability. The signal is not entropic, on the contrary it is negentropic and it is recognized by the fact of its negentropicity.

The signal is recognized as ‘information’. Therefore ‘information’ is a name for the physical presence of negentropy.

Language also gives insight into our understanding of phenomena. The word ‘information’ is somehow visual, containing the word ‘form’ and where a signal has form. On the other hand the word ‘negentropy’ is a physical word containing the word ‘entropy’ that is a physical quantity. Negentropy recognizes the absence of entropy and therefore the presence of information.

The Shannon information paradigm has been applied to the quantification of the replication and expression of nuclear DNA.

DNA expression

Consider the operation of the genome through the lens of Shannon information. Megabits of specific information expressed out of the nucleus dynamically configure the cell’s proteome and determine its specialized biofunctions.

“Production of DNA in the nucleus takes place even in cells that are not replicating. A typical mammalian cell polymerizes approximately 200 million nucleotides of DNA a minute into nuclear RNA. Only 5% ends up in the cytoplasm, coding for protein synthesis. It has been estimated that of the order of 700,000 bits (700kB) of genetic information are transmitted from the nucleus to the cytoplasm every second.”[2]

This translates to the transmission of 42MB per minute or 1.12GB per hour from the average mammalian cell nucleus to the cytoplasm. The average mammalian nucleus therefore produces 22.4GB of genetic information per hour of which 1.12GB is transmitted to the cytoplasm.

These observations quantify the generation and flow of information in terms of Shannon information, that is in terms of bits. It therefore measures genetic information in terms of the ‘symbolic information’ of nucleotides and nucleotide sequences.

What Shannon information does not consider are the biophysical characteristics of molecules that are intrinsic to their biofunction. Nonetheless it remains a valuable form of information even though it measures neither intrinsic nor relative negentropy.

2. Brillouin’s Negentropy Principle of Information.

Remarkably the connection between information and thermodynamics was made by Leon Brillouin in 1953 only a few months after the publication of the structure of DNA[3]. Brillouin formulated the Negentropy Principle of Information wherein he recognised that information has the thermodynamic property of negentropy. By observing the forms and structures of nucleotides, nucleotide sequences, amino acids and proteins we recognise the presence of information.

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[2] Paul C.W. Davies, Elisabeth Rieper, Jack A. Tuszynski. Self-organization and entropy reduction in a living cell BioSystems 111 (2013) 1– 10.

[3] Leon Brillouin. The negentropy Principle of Information. Journal of Applied Physics 24(9):1152-1163 October 1953.

The Negentropy Principle of Information states that where entropy decreases information is created and conversely where entropy increases information is lost.[4] Information and entropy are in fact opposing physical forces. In the cell biosemiotic molecular information confronts entropy in so far as it constrains specific, and therefore non-random, outcomes.

The second law of thermodynamics recognises that the power and force of entropy tends to spontaneously opposes information and specific order in favour of randomness and greater degrees of freedom.

Through his Principle, Brillouin shows that molecular information has thermodynamic significance and therefore thermodynamic power. In practice biomolecular information becomes a causal agency through its inherent biophysical property of negentropy.

Causal Information.

The question arises as to how information ***causes*** life. How does it act? How does information become a causal agency? The answers to these questions are known.

The ***spontaneity*** of any physical transformation has two conditions; the first is ***thermodynamic,*** the second ***kinetic***.

A reaction or transformation can only proceed if it is both thermodynamically and kinetically permitted to do so. These may be described separately as the **thermodynamic condition** and the **kinetic condition**. The word ‘condition’ is here interchangeable with ‘constrain’ because the condition is the constraint and vica-versa.

The Thermodynamic Condition; Gibbs Function and the direction of spontaneous change.

Between 1875 and 1878 Willard Gibbs published a 300 page treatise in two parts, “On the equilibrium of Heterogeneous Substances” that developed a thermodynamic treatment of systems involving more than one phase, where a phase refers to a state of matter such as a solid, liquid or gas. In his treatise there are over 700 mathematical equations that deal with quantifying the complexities of the thermodynamics of transformation.

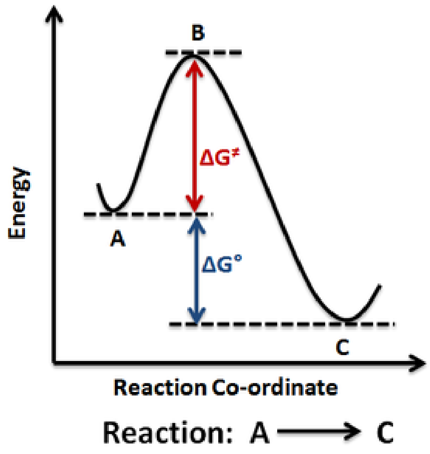
Gibbs brought together the state functions of enthalpy (H) and entropy (S) into a universal equation, known as the Gibbs Equation, that allows calculation of the spontaneity or non-spontaneity of a given transformation based on measured changes in these two state functions.

delta G = delta H – T. delta S

This equation is of supreme importance in physical chemistry. In words it states that the overall change in the Gibbs free energy (delta G) is equal to the change in Enthalpy (delta H) minus the change in Entropy (delta S) multiplied by the temperature T.

Consider the reaction A → C. Here A is called the reactant and C the product. By considering the enthalpy and entropy of the product and of the reactant the changes in these quantities can be calculated.

[4] Leon Brillouin. The negentropy Principle of Information. Journal of Applied Physics 24(9):1152-1163 October 1953.



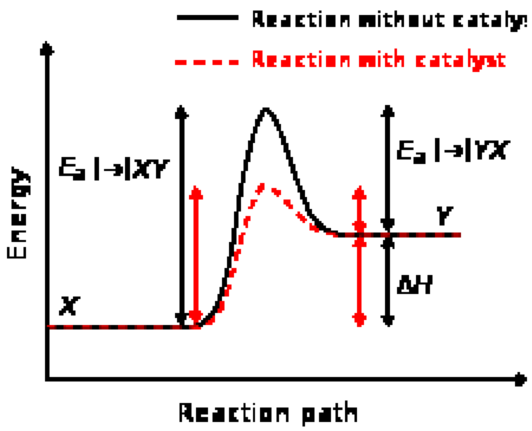
This is called a Reaction Coordinate Diagram of a simple A→C reaction via an intermediate state B. It considers the overall Gibbs free energy change (lower delta G) and the Activation Energy of the reaction (upper delta G).

Through this equation the thermodynamic allowedness or disallowedness of a given transformation may be calculated; that is whether a given transformation is thermodynamically allowed or not. (A negative value of delta G indicates an overall increase in entropy.) It shows that the direction of spontaneous change is favored by loss of information and gain of entropy. This is the essential thermodynamic condition of all chemical reactions and transformations.

The Kinetic Condition.

Kinetics is about speed and speed is about time. In chemistry the speed of a reaction or transformation is called its rate. In a single step transformation there is only one step and therefore only one rate. Where more than one step is associated with a specific transformation the overall rate is determined by the slowest step.

The second essential condition for a reaction or transformation to take place is kinetic because in order for a chemical reaction to happen it must be kinetically permitted to do so. The kinetic barrier to permissibility is called the 'activation energy'. The rate or speed of a chemical reaction or transformation is determined by the activation energy of the rate determining step.



This diagram shows the reaction path for the reaction X → Y. It shows the Activation Energies required in each direction Ea. In addition it show how catalysts function, that is by lowering the activation energy.

The Thermodynamics of Reaction Kinetics.

Kinetics and thermodynamics are connected through the activation energy of the rate determining step.

For example a catalyst is an agent that has the power to lower the activation energy of the rate determining step, thereby accelerating the rate of transformation. In biology, protein catalysts are called enzymes and proteins are not the only biological catalysts.

Since we are considering the spontaneity of life our focus is on the thermodynamics and kinetics of biological reactions.

Operation of the Negentropy Principle of Information.

The information of biosemiotic molecules acts kinetically through the activation energy of prescribed reactions. The negentropy of biosemiotic molecules lowers the activation energy of specific reactions or transformations. By dramatically lowering activation energies specific reactions are constrained to take place.

Thus information determines outcomes through kinetics. Therefore negentropy determines direction.

Enzymatic rate acceleration.

A protein enzyme accelerates the rate of a specific reaction. The molecule that an enzyme acts upon is called the substrate. Any realistic understanding of the unique reality within the cell must take into account true kinetic observations such as the following.

> "Consider an enzyme, for example. If its substrate molecule is present at a concentration of 0.5mM, which is only one substrate molecule for every 10,000 water molecules, the enzyme's active site will randomly collide with about 500,000 molecules of substrate per second. And a typical globular protein will be spinning to and fro, turning about various axes at rates corresponding to a million rotations per second."[5]

The speeds quoted here are beyond visualization.

What makes the active site unique is that it is specific for its given substrate. The catalytic acceleration happens because there is little or no activation energy required. The information of the entire enzyme, and specifically of the active site, and the information of the substrate, are cooperatively complicit in the kinetic spontaneity of reaction.

We can gain a glimpse into the nature of living state when we realize that within it, all reactions and transformations are catalyzed by biomolecular information. This includes all reactions

[5] The Cell as a Collection of Protein Machines: Preparing the Next Generation of Molecular Biologists Bruce Alberts President, National Academy of Sciences Cell, Vol. 92, 291–294, February 6, 1998.

involving DNA, RNA and the myriad of reactions catalyzed by protein enzymes. Signalation processes are also biosemiotic and function at catalytic speeds.

Transportation through pores is catalytically accelerated for specific molecules and ions because of the molecular informational characteristics of both the pore and the molecule or ion of passage.

Two distinct points.

The negentropy of biological molecules does not change the thermodynamics of an overall reaction. It only influences the kinetics of a reaction through the activation energy of the rate determining step. In practice it does this by limiting degrees of freedom. In other words the 'information' of biological molecules becomes deterministic through its inherent negentropy that determines the spontaneity of direction.

In biological systems the thermodynamic condition of spontaneity is ensured by the specific intervention of ATP.

Therefore the process of life is directed through the specific negentropy of biological molecules within the context of the cell where ATP furnishes site-specific thermodynamic fuel.

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