

Hypothesis

Catalysis, evolution and life

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Abstract Living organisms are unique in their ability to generate and replicate ordered systems from disordered components. Generation of order, replication of the individual, and evolution of the species all depend on the successful utilization of external energy derived from chemicals and light. The information for reproduction is encoded in nucleic acids, but evolution depends on a limited variability in replication, and proceeds through the selection of individuals with altered biochemistry. Essentially all biochemistry is catalyzed; therefore, altered biochemistry implies altered or new catalysts. In that sense catalysis is the medium of evolution. We propose that a basic property of enzymes, at least as fundamental as reaction rate enhancement, is to adjust the reaction path by altering and eventually optimizing the reversible interchange of chemical, electrical and mechanical energy among themselves and their reactants.

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1. Introduction

Thermodynamic limits on catalysis are set by the available energy of a reaction and by its dissipation. The available energy (often called high-grade energy) in a chemical reaction [1–3] is the maximum amount of reversible work that can be extracted from it under any circumstances. It is equal to the change of the Helmholtz free energy, $\Delta A = \Delta(U - TS)$, in the reaction. The Gibbs free energy change, ΔG , is almost the same; their difference is $P\Delta V$, which is usually very small. Both free energies are state functions; therefore, they are independent of the path the reaction follows. Nevertheless, the maximum amount of work can be extracted only when the reaction proceeds through fully reversible steps (Carnot cycle). In biological processes, part of the energy is always degraded into heat; otherwise $\Delta G = 0$, and the speed of the reaction would be infinitely slow. The actual work extracted is, then, less than ΔA and part of the available energy – or even all of it – is dissipated. This is indeed the fate of the available energy in most spontaneous processes. Spontaneous exothermic

chemical reactions typically follow a reaction path that maximizes entropy by dissipating the energy in the form of heat, and thus degrading it.

Most previous work on catalysis has been concerned with the acceleration of reaction rates by enzymes. A much more inclusive category of environmental influence on chemical reactions is a change in the reaction mechanism, i.e. a change in the path of the reaction. Accordingly, we will use the term catalysis in the broadest possible sense for any alteration of any detail of a chemical reaction by its environment, provided that the latter stays unchanged at the end of the reaction.

Living organisms (and therefore their enzymes) need to preserve and use the energy generated in exothermic reactions. Evolution selects enzymes based on catalytic rate enhancement as well as the ability to preserve energy in high-grade, usable form. Balancing these two criteria results in the selection of an optimized reaction path in which a significant fraction of energy can be maintained in a high-grade form for subsequent use. We discuss here two of the basic strategies for doing this: (i) manipulating the kinetic outcome of parallel reactions, and (ii) coupling two reactions together for driving a process uphill.

2. Reaction selectors

Organic chemists have long been familiar with the idea of kinetically favored products competing with thermodynamically favored products in a chemical reaction. In Fig. 1, we consider a chemical reaction that has two channels.

Reaction with catalyst 1 lowers the energy barrier between B and D, so that product D accumulates rapidly. In this case the kinetic product, D, has a significantly higher free energy than the thermodynamic product, C. With catalyst 2, both the kinetic and the thermodynamic product is C, and the full reaction energy is dissipated. Examples for kinetic control of this type include the catalytic cleavage of ATP, leading either to ADP and Pi, or to AMP and PPi, or to cAMP and PPi (see, e.g. [4]).

A fundamental property of living systems as well as evolving pre-biotic replicating molecules is that they exploit chemical reactions that already possess both a kinetically preferred pathway and a thermodynamically preferred pathway, and they do this in such a way as to optimize the balance between the two. The optimization process is an evolutionary one, and optimization of the balance can be defined loosely but operationally as changing the propensities of the two pathways rel-

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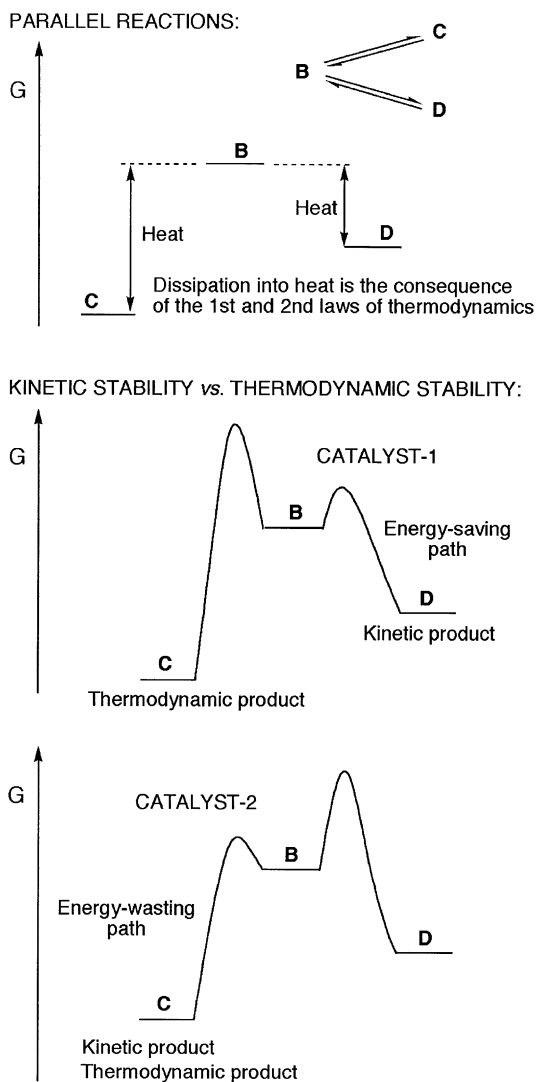


Fig. 1. Reaction selectors. We imagine a chemical reaction with two parallel paths possible. The two products release different amounts of free energy. From the first and second laws of thermodynamics we know that ΔG is dissipated. Catalysts can selectively change the activation energy barrier of the two paths. Catalyst 1 above lowers the barrier for the path that releases a small amount of heat. Catalyst 2 speeds up the other path, dissipating a much higher fraction of energy.

ative to one another in successive rounds of replication and natural selection in a way that maximizes the ability of the system to grow and to replicate itself with reasonable fidelity.

3. Energy converters

Mastering uphill reactions is crucial for life. Specialized enzyme molecules alter the spontaneous course of chemical reactions so that part of the available energy can be used to drive other processes uphill. We will call these enzymes energy converters or ‘Carnot enzymes’. Their tasks include mechanical work, the synthesis of polymers and ‘energetic’ molecules, the control of local entropy in the system (e.g. by various pumps or ‘Maxwell enzymes’), signaling and more. Fig. 2 shows the general scheme of such processes.

Numerous examples show how energy converters work. A

prime example is the case of soluble and membrane-bound pyrophosphatases. Soluble pyrophosphatases convert ΔG to heat (case (a) in Fig. 2). Membrane-bound pyrophosphatases perform reaction (b) in Fig. 2, in which the energy captured by the catalyst is used to pump protons across a membrane. The amount of heat produced by these two types of pyrophosphatases is markedly different [5–9]. We mention one more class here. Studies on heme enzymes [10–12] and on mononuclear ferrous enzymes [13–16] point to a reaction sequence where an energetic oxidizing species is created and stored in the protein for later use with a second substrate. These enzymes couple a strongly exergonic redox reaction (the reduction of dioxygen to water) to drive an endergonic reaction uphill. This is achieved by transiently storing a large fraction of the available high-grade energy from the drive reaction at the iron center that temporarily becomes highly oxidized in the enzyme. All of these proteins are catalysts for the complete reaction cycle as they return to their original state after a turnover.

4. Conclusions

It has always been recognized that enzymes evolve to accelerate the rate of biochemical reactions that benefit an organism. We suggest that an additional selective restraint placed upon enzymes by evolution is the ability to store information and energy in metastable forms that can then be exploited by the organism or pre-biotic replicating molecule. Kinetically favored but thermodynamically less favored reaction products, such as RNA polymers, are perhaps the original and certainly one of the most important examples of this principle. However, this principle may be generalized to include much if not all of metabolic biochemistry, photosynthesis, and bioenergetics.

Evolution becomes possible if there is some imperfection in the process of reproduction. Reproduction requires the capture and processing of available high-grade energy, preventing its degradation to heat. Such ability includes the redirection of the available energy through coupled reactions. By modifying the catalyst, evolution manipulates the amount and disposition of available high-grade energy within the system and,

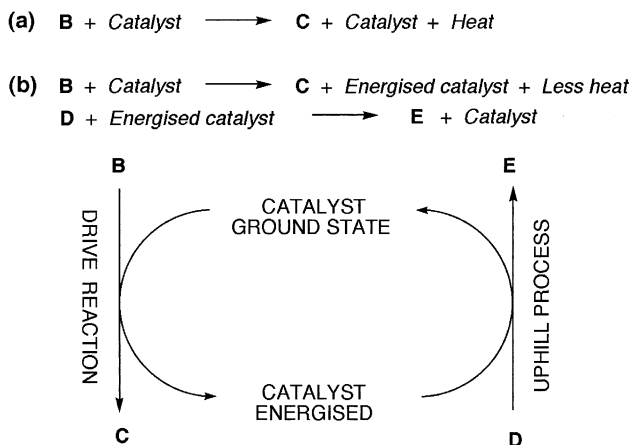


Fig. 2. Energy converters. a: The case where no coupling is possible as ΔG is dissipated as heat. b: Reaction in which the catalyst captures part of ΔG . This feature allows energy transfer by coupling an exergonic reaction to drive an endergonic reaction uphill.

conversely, where, when and how much irreversible entropy is produced during a chemical reaction. By the process of selecting the most appropriate catalysts, evolution produces intricate and elaborate networks of reactions that work harmoniously like a finely tuned orchestra for the maximum benefit of the organism [17].

Living organisms are self-replicating systems, and replication requires energy. Utilization of available energy is, therefore, a prerequisite for self-replication. Any replicating system is also a system with a primitive memory. Life may have started when a catalyst changed the outcome of a spontaneous reaction to be the catalyst itself. That produced a replicating system. The same catalyst could then alter a different reaction, making a network that could evolve.

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