

## Research Paper

# An Energy Balance Concept for Habitability

TORI M. HOEHLER

### ABSTRACT

Habitability can be formulated as a balance between the biological demand for energy and the corresponding potential for meeting that demand by transduction of energy from the environment into biological process. The biological demand for energy is manifest in two requirements, analogous to the voltage and power requirements of an electrical device, which must both be met if life is to be supported. These requirements exhibit discrete (non-zero) minima whose magnitude is set by the biochemistry in question, and they are increased in quantifiable fashion by (i) deviations from biochemically optimal physical and chemical conditions and (ii) energy-expending solutions to problems of resource limitation. The possible rate of energy transduction is constrained by (i) the availability of usable free energy sources in the environment, (ii) limitations on transport of those sources into the cell, (iii) upper limits on the rate at which energy can be stored, transported, and subsequently liberated by biochemical mechanisms (*e.g.*, enzyme saturation effects), and (iv) upper limits imposed by an inability to use “power” and “voltage” at levels that cause material breakdown. A system is habitable when the realized rate of energy transduction equals or exceeds the biological demand for energy. For systems in which water availability is considered a key aspect of habitability (*e.g.*, Mars), the energy balance construct imposes additional, quantitative constraints that may help to prioritize targets in search-for-life missions. Because the biological need for energy is universal, the energy balance construct also helps to constrain habitability in systems (*e.g.*, those envisioned to use solvents other than water) for which little constraint currently exists. **Key Words:** Habitability—Bioenergetics. *Astrobiology* 7, 824–838.

### 1. GENERAL REQUIREMENTS OF HABITABILITY

#### 1.1. Introduction and purpose

**T**HE CONCEPT OF HABITABILITY offers a means by which to constrain the possible distribution of life in any system and thereby provides an important guide for selection of targets in astrobio-

logical exploration. It is important that our sense of habitability be capable of refinement by reference to the example offered by terrestrial life but also that it not be restricted by this reference. Ideally, our concept of habitability should be framed in general terms that are capable of embracing all forms of life. At the same time, our view of terrestrial life has much to gain from a discriminating and detailed view of habitability, which can

do more than simply delineate between “possible” and “not-possible.” Where biochemical specifics are well defined, habitability can define a continuum of states, from thriving to struggling to non-existing. And it can provide an interpretive and predictive framework in which to address the distributions, sizes, and activities of biological populations in reference to their environments, at a metabolism-specific level.

Our present sense of habitability stands at a significant distance from this potential. We currently define habitability in a largely empirical way, relying on “record-holders” in extreme environments to map the boundaries of possibility. This empirical approach, while useful in many respects, inherently focuses on individual physical and chemical parameters in reference to individual organisms. Yet it is both intuitive and suggested by experiment (Lloyd *et al.*, 2005) that simultaneous variations in different environmental parameters yield compound effects on habitability. How, for example, does a change in temperature affect the ability of a particular organism to tolerate extremes of pH? And what can observations of one organism’s limits tell us about the tolerances of a metabolically different organism? To address these issues requires that habitability be understood at a more fundamental level—a level that allows different environmental impacts and different organisms to be considered on a common basis and in quantitative fashion.

This paper describes an energy-based concept of habitability, which offers potential for elucidating and quantifying the underlying connectedness between the various aspects of habitability, for mapping these considerations across different modes of metabolism, and, ultimately, for generalizing to forms of life unlike our own. Broadly, this concept considers the various elements of habitability as terms in a balance between the energetic demands incurred by organisms and the corresponding ability of those organisms to transduce (harvest, store, and reinvest) environmental energy into biological process.

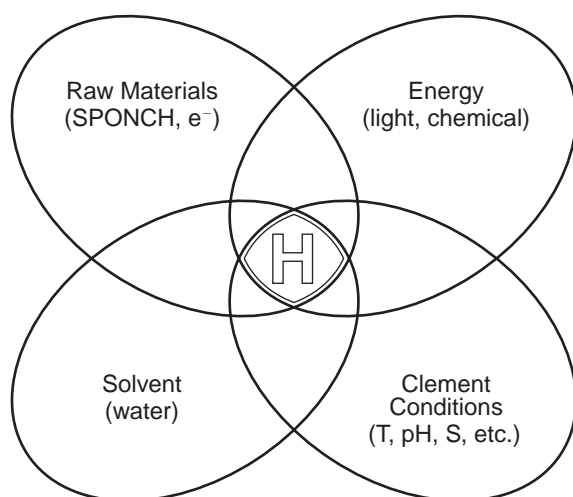
### 1.2. Complexity and the elements of habitability

The fundamental premise of the energetic habitability concept is that (i) life requires a significant level of complexity, order, and organization (hereafter collectively referred to simply as “complexity”) and (ii) energy is required to build and

maintain this complex state. The elements of complexity and energy demand are inherent in most descriptions of life (*e.g.*, von Neumann, 1951; Davies, 1999; Conrad and Neelson, 2001; Cleland and Chyba, 2002; Neelson *et al.*, 2002; Benner *et al.*, 2004; Ruiz-Mirazo *et al.*, 2004) and are abundantly exemplified in terrestrial biology at many levels of organization—molecular (*e.g.*, proteins and genetic molecules), biochemical (*e.g.*, pathways and cycles), genetic (*e.g.*, regulation schemes), structural (cellular, organismal, and community), and even super-organismal (*e.g.*, ecological or social interactions). Importantly, because life is inherently defined by process [life “does something,” as Erwin Schrödinger (1944) noted], this complexity must be functional—for example, via the interaction of complex molecules—rather than static. Habitability, then, derives from the convergence of factors that allow the establishment, persistence, and function of complex forms (whether molecules, cycles, etc.). These factors are

- (i) raw materials;
- (ii) energy with which to assemble those materials into complex forms, and with which to sustain the resultant complexity (see below);
- (iii) a medium (*e.g.*, solvent) that permits the construction and interaction of large, complex molecules, promotes secondary structure and compartmentalization, etc.; and
- (iv) environmental conditions that allow for both the persistence of molecular complexity and the interaction of complex molecules at reasonable rates.

Classically, the intersection of these 4 elements is conceived as delineating habitability (Fig. 1), but the reality is less clearly defined. Certainly, the *complete* absence of any of these elements definitively ensures uninhabitable conditions, but habitability is not necessarily established when all 4 criteria are met. Rather, determining habitability is a matter of degree in these parameters, individually and in combination: how much raw material, in combination with how much energy, allows for the support of life? And how does the picture change as environmental conditions shift or as other metabolisms, or even other biochemistries [see, *e.g.*, Bains (2004) and Benner *et al.* (2004)], are considered? Even the presence of solvent—which, in our own case of liquid water, we tend to view in “+” or “−” terms—is in fact



**FIG. 1. Classical view of habitability.** In this representation, habitability (shaded region) occurs at the intersection of factors that support the creation, maintenance, and function of complexity (with parenthetical terms indicating conditions required by life on Earth). Accurate assessment of habitability requires quantification of the impact of these factors.

a question of degree. (Honey, for example, is a liquid water solution containing abundant energy potential that, under completely clement environmental conditions, is nonetheless rendered largely uninhabitable by virtue of a strongly diminished water activity.) Refinement in our concept of habitability thus requires the definition of a scale, applicable across the various elements of habitability, with which to quantify “degree.” The basis for such a scale derives from the notion that *complexity demands energy* and energy can be grasped in quantitative terms by reference to thermodynamics.

### 1.3. Complexity, energy, and life

In a universe that is marching monotonically toward the most disordered possible (maximum entropy) state, complexity is inherently unstable. Life’s creation of complexity represents a local decrease in entropy that, in keeping with the 2<sup>nd</sup> law of thermodynamics, requires an entropy increase of greater magnitude in the surrounding universe. That is, life must catalyze a positive entropy change in its surroundings. Thus, Schrödinger (1944) noted that the fundamental and obligate activity of life is to feed on the “negative entropy”—the complexity and order—of its surroundings. (As it is defined, entropy cannot

actually be negative, but, in a purely arithmetical sense, an organism could increase the entropy of the surroundings either by contributing “positive entropy” or consuming “negative entropy,” where the latter could be viewed as a measure of “orderliness” (see chapter 6 of Schrödinger’s *What is Life?*). In practice, the complexity and order that can be consumed from the environment seldom correspond exactly to the sort of complexity and order that must be built in the organism. For example, light, which is consumed by some organisms, represents a very different sort of low entropy than that represented in the complex molecules and biochemical pathways of the life that utilizes it. An intermediate step is therefore required to effect the transposition of low entropy from the surroundings into the low entropy of the organism. Our sort of life achieves this—as any form of life would almost certainly have to do—by liberating free energy from the environment and, subsequently, reinvesting that energy into construction of biological complexity from simpler starting materials. Life’s creation and maintenance of complexity thus defines a fundamental and obligate interaction with its environment—the continual harvesting of free energy. (In his notes on chapter 6 of *What is Life?* Schrödinger expresses a preference for framing a more technical discussion in terms of free energy but chooses the “simpler” concept of “negative entropy” for use in the text itself.)

The need for investment of energy to create order from disorder is, it would seem, intuitive and experiential; the need for *continued* investment of energy to *maintain* such a state may not be. For example, it can be correctly asserted that, once established by input of energy, complexity could effectively be safeguarded from decay by imposing conditions in which the thermodynamic drive toward disorder is never actuated (*e.g.*, by freezing to absolute zero). Importantly, however, such conditions would also suspend the interaction of molecules that constitutes the essence of life process. Thus, the very establishment of conditions that allow life to do *anything* also unavoidably enables the destruction of complexity. Energy expenditure is continuously required to offset this destruction.

The laws and relations of chemistry tell us that both the thermodynamic driving force for the destruction of complexity and the rate at which that destruction occurs are functions of environmental conditions (Atkins, 1990). The energy required

for creation of complexity is governed by the same constraints. Thus, specifying a biochemistry and a set of environmental conditions (*e.g.*, temperature, pH, salinity, pressure) quantitatively defines (i) processes and rates by which complexity is destroyed and (ii) the minimum energy expenditure required to offset that destruction and maintain a critical level of complexity. The classical extremes of environment can thus be considered in terms of the added demand they place on biological energy expenditure. Likewise, challenges to complexity imposed by material or solvent limitations have potential to be overcome by quantifiable energy expenditure (with mechanisms for such considered in a subsequent section). Each of the factors that collectively determine habitability—physico-chemical environment, raw materials, energy, and solvent activity—can thus be weighed as terms in an energy balance. Habitability is established when the energetic demands of sustaining complexity are balanced, or more than balanced, by the capacity of a given life form to transduce environmental energy into biological process. The demand and transduction terms are both complex functions of organismal and environmental specifics, with defined boundary conditions. Elaborating the nature of these functions and boundary conditions, first with reference to terrestrial life and subsequently with a brief extrapolation to life unlike our own, occupies the balance of this paper.

## 2. THE BIOLOGICAL ENERGY BALANCE

That energy is essential for life is widely appreciated (*e.g.*, Schrödinger, 1944; Neelson *et al.*, 2002; Benner *et al.*, 2004). And yet, without quantification, this fact is of no practical value in assessing habitability. Energy is available almost ubiquitously in the universe: wherever a single photon strikes, where a molecule vibrates, or where the slightest chemical disequilibrium exists. But how much energy is enough, and what kinds of energy are useful?

### 2.1. Energy demands in terrestrial biology

All known life on Earth is constrained by 2 basic requirements for energy, which can be analogized to the power and voltage requirements of electrical devices (Hoehler, 2004). With respect to both requirements, chemical and biochemical

considerations impose upper limits on the possible rate of biological energy transduction and lower limits on the biological energy demand, thus establishing boundary conditions in the energy balance of habitability.

The analogue to power (energy per unit time) requirements is the maintenance energy (ME), which defines the flux of energy needed to support a unit biomass in a specific metabolic state (Tijhuis *et al.*, 1993; Harder, 1997). Clearly, the synthesis of new biomass (creation of new complexity), as exemplified in growth, requires energy. However, a background activity of energy-consuming processes that are not necessarily related to growth also demands a constant expenditure of energy (Tempest and Neijssel, 1984). And, at absolute minimum, viability requires that the complexity of critical biomolecules be sustained by expenditure of energy (Morita, 1997; Price and Sowers, 2004). The magnitude of energy demand from such processes is shown to increase approximately linearly with increasing biomass—in essence, energy demand scales directly to the “quantity” of complex molecules to be supported (Tijhuis *et al.*, 1993). Thus, in energy-limited systems, a specific energy influx defines a specific biomass at steady state. Human experience readily illustrates this energy-biomass steady state: when energy intake increases (as with a higher-calorie diet), the steady state is re-established with a higher biomass (weight gain); decreased energy intake leads to loss of biomass. However, limits exist on the extent to which decreasing energy intake can be addressed by decreasing biomass. The specific functions performed by a given cell define a complement of necessary biomolecules (informational, structural, and functional) and, therefore, a biomass minimally necessary to accomplish those tasks. These biomass limits define organism-specific maintenance energies that, if not met, render a system uninhabitable to the specified life (Hoehler, 2004). Theoretical considerations suggest that absolute lower limits exist on the quantity of biomass required to constitute a minimally functional organism (Knoll *et al.*, 1999), which implies that discrete lower limits exist for the flux of energy required to support *any* life of the type we know.

The analogue to voltage (energy per unit of energy carrier) requirements is the so-called biological energy quantum (BEQ), which defines the minimum free energy level that can be usefully harnessed by life (Schink, 1997; Schink and Stams,

2002). As with ME, the BEQ constitutes a discrete, non-zero energy level—hence the term “quantum” (which, however, does not reflect a quantum mechanical origin). The BEQ arises because, in the terrestrial version of biochemistry, energy storage and release are channeled through a single molecular currency of energy, ATP. Although the broad spectrum of chemical reactions that comprise terrestrial biochemistry likely exhibits energy demands constituting a near continuum, down to values close to zero, all are nonetheless driven by a single “quantum” of energy (or multiples thereof) that corresponds to the energy released during ATP hydrolysis. Similarly, among the array of possible energy sources in the environment, only those that offer a free energy yield large enough to drive ATP synthesis are biologically useful. The actual mechanism by which environmental energy is typically coupled to ATP synthesis (Mitchell, 1961) allows energy yields as small as one-third to one-fifth of an ATP—but no smaller—to be usefully employed in biological process (Schink and Stams, 2002). This unit of energy corresponds to a discrete minimum voltage requirement: the BEQ.

## 2.2. Ecological and astrobiological implications

Both aspects of energy demand, ME and BEQ, must be simultaneously satisfied by an energy source if the source is to be biologically useful. That each aspect is characterized by discrete minimum requirements implies that some fraction of the energy that is present in the environment may be unavailable for supporting life (Hoehler, 2004). Typically, organisms can access only a small portion of the overall spectrum of available energy sources (*e.g.*, specific chemical combinations or specific wavelengths of light). Energetic habitability is thus applicable at a metabolism-specific level by comparing the energy available to a particular metabolic process against the minimum energy demands of the corresponding organism. When considered at the metabolism-specific level, observational and experimental evidence supports the validity of the energetic habitability concept. For example, anoxic sediments that amply address the habitability requirements of water, raw materials, and clement conditions can be rendered alternately habitable or uninhabitable for methanogenic archaea (as exemplified by the conduct or lack of methane production) solely by fluctuations in the free energy available to

methanogenic metabolism (Hoehler *et al.*, 1994, 2001). To the extent that an environment can be rendered energetically uninhabitable with respect to an individual metabolism, it follows that a total lack of energy sources capable of balancing biological power and voltage requirements would render an environment uninhabitable with respect to any life.

The biological minimum energy requirements are not frequently tested in our surface world but may be among the most important factors that constrain habitability in environments of astrobiological significance. Earth's surface is dominated by abundant energy sources (light, O<sub>2</sub> + organics) that offer voltage and power equivalents in great excess of the biological requirements. However, environments that lack abundant sunlight or abundant products of photosynthesis are often characterized by energy sources whose usefulness is significantly constrained by one, or both, of the biological energy requirements (Hoehler, 2004). In particular, the potential for extant life in the martian subsurface or the euroman ocean may be largely an issue of whether energy is available at needed levels. With respect to the latter, it is noteworthy that energy balance constrains habitability not only with respect to chemical reactions, but also in regard to energy efflux as blackbody radiation from would-be hot vents.

## 2.3. Impact of environmental conditions on energy demand

The remaining elements of habitability—clement conditions, availability of raw materials, and availability of solvent—all influence the magnitude of the biological energy requirements. This energetic connection allows these diverse factors to be quantified on a common basis, as terms in the energetic habitability balance.

The classical extremes of temperature, pH, salinity, and so forth provide perhaps the clearest illustration of a complexity-energy connection to habitability. The biochemical impacts of these various factors, and the mechanisms used to address them, are superficially disparate but fundamentally the same. In each case, the threat to habitability derives from a threat to molecular (and higher level) complexity (Jaenicke, 1981), and in each case the threat demands additional energy expenditure (Krulwich and Ivey, 1990). Detailed consideration of energy expenditure in relation to extremes of salinity, pH, and temper-

ature can be found, respectively, in Oren (1999), Krulwich, (2000), and Jaenicke and Sterner (2002). For the present purposes, the examples of temperature and pH are briefly considered:

(i) Temperature. The impact of temperature on life is clear and quantifiable through reference to basic principles governing the thermodynamics and kinetics of chemical processes (Jaenicke and Sterner, 2002). The thermodynamic driving force associated with a given process, as measured by the Gibbs free energy change,  $\Delta G$ , is given by:  $\Delta G = \Delta H - T\Delta S$  (Gibbs, 1876; Gibbs, 1878). The entropic contribution to this driving force, as measured by the entropy change,  $\Delta S$ , grows linearly with temperature. ( $\Delta H$ , the enthalpy change, is also a function of temperature, but the entropy change dominates the first-order effect of temperature). Reactions that create disorder from order (reactions that destroy complexity) have large positive entropy changes, so that the thermodynamic driving force toward disorder grows almost linearly with temperature (note that more negative  $\Delta G$  values denote more thermodynamically favorable processes). Thus, increasing temperature exerts an increasingly destabilizing influence on complexity (as, for example, essential macromolecules). The rate at which chemical reactions occur is an approximately exponential function of temperature, as described by the Arrhenius equation:  $k = A \cdot \exp(-E_a/RT)$ , where  $k$  is the rate constant for a given reaction,  $A$  and  $E_a$  are positive constants specific to the reaction in question, and  $R$  is the universal gas constant (Atkins, 1990). The collective reactions that define biochemistry are governed by this equation so that overall metabolic rates are exponentially dependent on temperature (Gillooly *et al.*, 2001). The reactions that destroy complexity and otherwise contribute to maintenance energy are similarly temperature dependent. Biological expenditure of energy to rebuild lost complexity and carry out essential cellular functions is, therefore, expected to increase approximately exponentially with temperature. This assertion is supported by measurement of organism-specific maintenance energies (Tijhuis *et al.*, 1993), which exhibit a temperature dependence that can be fit by the Arrhenius equation [ $ME = A \cdot \exp(-E_a/RT)$ ]

(Harder, 1997). Activation energy values ( $E_a = 69.4$  kJ/mol) measured in laboratory experiments correspond to an increase in maintenance energy of more than 5 orders of magnitude over the (roughly) biologically relevant temperature range of  $-20$  to  $120^\circ\text{C}$  (Tijhuis *et al.*, 1993). Measurements in field locales that include low-temperature environments suggest even larger activation energies and, therefore, an even greater temperature dependence in the biological demand for energy (Price and Sowers, 2004). Note that how the temperature effect impacts upon, and is addressed by, organisms depends greatly on their size. At the microscopic scale, it is impossible to maintain a physiologically relevant temperature difference between organism and environment. The effects of temperature thus directly impact biochemistry and cellular process and incur energy demands that are directly calculable by the equations above. Much larger organisms have the potential for regulating internal temperatures (as mammals do) to a point; this strategy also incurs a quantifiable energetic cost, though calculation of such is not as straightforward as for microorganisms.

(ii) pH. Variations in pH from a biochemical ideal (near-neutrality, in the case of most organisms on Earth) can be detrimental to numerous aspects of biochemistry (Krulwich, 1995). Perhaps most critically, high and low pH catalyze hydrolytic cleavage of (essential) information-storing and functional biopolymers—that is, variations in pH speed the rate of destruction of essential complexity. These effects are sufficiently detrimental that all known organisms work actively to regulate intracellular pH within a tolerable range, even in the face of environmental pH that may differ significantly. This strategy is made possible by the presence of a nanometers-thick cell membrane that provides a chemical barrier for separating the intracellular medium from the outside world. The necessity for exchange of materials with the environment, however, means that the membrane must be semi-permeable and, therefore, potentially subject to “leakage” with respect to pH. In such a system, a continuous expenditure of energy is required to maintain the desired intracellular pH, in essence by pumping protons in or out of the cell against an opposing

gradient (Krulwich, 1995; Krulwich *et al.*, 1996; Krulwich, 2000). This is somewhat analogous to the energy expenditure required to air condition an imperfectly insulated house—which grows directly with the difference between interior and exterior temperature. The impact of environmental pH on maintenance energy has yet to be quantified (as it has for temperature), but this should be both calculable and subject to experimental determination. As a first approximation, it can be noted that the added energy expenditure incurred in pH regulation must be minimally necessary to pump protons against a gradient at a rate that balances the unwanted leakage across the semi-permeable membrane. The energy required to pump protons against a gradient is given simply by  $\Delta G = RT \cdot \ln(\{H^+\}_{out}/\{H^+\}_{in})$  or  $\Delta G = -2.3RT \cdot \Delta pH$ , where  $\Delta pH$  is the cellular pH minus the environmental pH (Krulwich, 1995; Krulwich *et al.*, 1996). The rate at which leakage occurs and must be balanced by pumping will be a function of membrane permeability and the environmental concentration of species (*e.g.*, weak acids) capable of carrying  $H^+$  across the membrane in the form of protonated, neutral molecules.

The examples of temperature and pH illustrate distinct differences, at least superficially, in both biochemical impacts and mitigation strategies. One is a physical condition that (at least at the microscopic level) is felt and dealt with intracellularly; the other is a chemical condition that is held at bay across a membrane. Yet these “environment in” and “environment out” issues are fundamentally the same in the threat they pose to biochemical complexity and in their need to be addressed by quantifiable expenditure of energy. The variety of other factors that have been considered as environmental extremes (though not addressed explicitly here) all, in their own way, conform to this complexity-energy pattern.

#### 2.4. Impact of resource limitation on energy demand

The remaining aspects of habitability—the need for raw materials and solvent [in our case, a need for the major biogenic elements (SPONCH), various micronutrients, electrons (re-

ducing power for biosynthesis), and liquid water]—can also be considered as terms in an energy balance.

**2.4.1. Raw materials.** Limitation of raw materials may be manifested in a variety of ways, each of which has potential to be addressed with energetic solutions. Examples of such solutions abound in Earth’s biosphere, and exhaustive discussion thereof is not feasible. Considering a few representative scenarios, however, is illustrative of the potential for assessing the impact of resource limitation in energetic terms.

- (i) Resources may be present locally but in forms that do not readily transit the cell membrane or diffuse through free solution—for example, charged species, very large molecules, or insoluble species. Cross-membrane uptake of small molecules that do not readily transit the cell membrane (ions, for example) can be solved by protein-mediated “active transport” (Broome-Smith *et al.*, 1999). The energy expenditure required for this process is readily quantifiable as a function of the necessary flux of the resource in question, given that each instance of transport is coupled to a “quantized” energy expenditure (a discrete fraction or integer multiples of the ATP hydrolysis energy). Resource extraction from larger or insoluble molecules may be addressed by synthesis and release to the environment of lytic enzymes or chelating agents, respectively. This strategy incurs a cost in energy expenditure (the product of synthesis energy and production/release rate) that, again, can be balanced against an expected rate of return of the sought resource.
- (ii) Resources may be present locally but in thermodynamically or kinetically stable forms that cannot be utilized directly by life. For example, organisms on Earth require nitrogen for protein and nucleic acid synthesis, but the  $N_2$  that is abundantly available in Earth’s surface environments cannot be utilized directly in these syntheses. This problem of resource limitation is solved (in some organisms) by nitrogen fixation—the investment of energy (16–24 ATP) to break the highly stable triple bond of  $N_2$ , thus yielding a form of nitrogen ( $NH_3$ ) that can be used di-

rectly in biosynthesis (Fay and Cox, 1967; Fay, 1992). Here, energy expenditure is a (quantifiable) linear function of the needed influx of biosynthetically useful nitrogen. A second example of resource limitation solved by energy expenditure is oxygenic photosynthesis, in which a need for electrons (to fix CO<sub>2</sub> into more reduced biological molecules) is addressed by extracting them from an abundant, but thermodynamically stable, source—water. The energetic cost of this solution is principally incurred in the voltage requirement: the energy needed to drive water lysis (as measured by the combined energy of the 2 required photons (Overmann and Garcia-Pichel, 2000) is about 40 times greater than the nominal BEQ. A cost in ME is also incurred, however, in the extra energy required to maintain the complex molecular apparatus and organizational/regulatory schemes employed in this process.

- (iii) Resources may be unavailable locally but available elsewhere (where “elsewhere” could define a system of any scale, up to that of the Universe). The only solution to this problem is movement—either of organism to resource or of resource to organism—the energetic cost of which is directly quantifiable in terms of the work required to move a given mass across a given distance at a particular rate while overcoming friction, viscosity, etc. The return on investment of energy is a function of the distribution of needed resources within the system (where the boundaries of the system are defined by the limits of motility). This solution is, of course, the staple of most animals and a wide variety of microorganisms. It also includes perhaps the most extreme example available of a quantifiable energetic investment into habitability: the temporary establishment of a small habitable niche on Earth’s moon. The energy expenditure associated with this creation of habitability was, minimally, the energy output of a Saturn V rocket (though, of course, much more energy investment—into building the capsule, developing the technology, even evolving the brains that conceived the technology—was ultimately required to bring about habitability on the moon). Interestingly (to belabor the point), the energetic cost of establishing sustained

habitability in low-Earth orbit (*e.g.*, by provision of needed resources and regulation of clement environmental conditions on the International Space Station) could quite feasibly be calculated as an organism- or biomass-specific maintenance energy.

**2.4.2. Solvent.** The potential for addressing solvent limitation with quantifiable energy expenditure is somewhat less obvious than in the cited examples of raw material limitation or inclement environmental conditions. A direct parallel exists, of course, in the potential to address solvent limitation with motility, but this option may not be viable for single-celled organisms. For these organisms, it is useful to consider the concept of chemical activities, which allow the issue of environmental solvent limitations to be considered in energetic terms. For example, specifying a required difference in intracellular versus extracellular water activity (defined as the quotient of water vapor pressure over the solution in question and the water vapor pressure over pure water at the same temperature) defines a free-energy change associated with maintaining the trans-membrane difference. The potential for directly addressing solvent limitation by energy expenditure (*e.g.*, by active transport and concentration of solvent within the cell) could then be quantified in reference to the permeability of a membrane with respect to the solvent—in analogy to the energy expenditure required for maintenance of a trans-membrane  $\Delta\text{pH}$ . Alternative strategies—for example, lowering membrane permeability or adjusting/coping with intracellular solvent activity closer to that of the environment—reflect variations on this energy-expending theme, with the appropriate solution constituting a problem of energy balance optimization.

## 2.5. Synopsis of biological energy demand

The biological demand for energy is, thus, a complex function in 2 dimensions—power and voltage—that weighs each of the elements of habitability with reference to biochemical specifics. Each energy dimension is characterized by a discrete lower boundary, even under optimal conditions. These minimum requirements are adjusted upwards by material limitations or deviations from ideal physico-chemical circumstances. The individual impacts of a given envi-



ronmental variable or material limitation on energy demand are, in some cases, well understood and quantified (*e.g.*, temperature), and in others yet to be determined. Yet all are ultimately calculable by reference to thermodynamic and kinetic considerations. The overall function describes the energy expenditure required to support a specified biochemistry in a specified environmental context—the “demand side” of an energy balance that defines habitability.

### 2.6. Constraints on biological energy transduction

Habitability is established when the 2 dimensions of biological energy demand can be simultaneously satisfied. This is ultimately bounded by the potential of the environment to supply energy in appropriate forms at necessary rates and levels [this “supply side” of the energy balance is considered by Shock and Holland (2007)]. Habitability, however, further depends on whether that energy can be transduced (captured, stored, and reinvested into process) at rates and levels that balance energy demand. This is a function of cross-membrane transport rates, enzyme kinetics, and overall efficiency (noting that some energy must be lost in each step of energy transduction to establish a net forward direction of the process) (Hill, 1977). These factors are not considered in detail here, but it is important to note that upper limits exist on the possible rate of biological energy transduction. Two main factors impose upper boundary conditions on energy-transducing potential:

First and foremost, energy influx is useful only when its potential for sustaining complexity through biological transduction outweighs its potential for directly destroying complexity. This is true for both power and voltage, for both light and chemical energy. For example, high frequency (*e.g.*, gamma) radiation can deliver very large units of energy (analogous to high voltage) but is also destructive to the very complexity it would be used to support (Rothschild, 1999). Likewise, light of useful wavelength but of too high an intensity (corresponding to high power) risks breaking down molecular structure. For example, sunlight shining on a leaf at natural levels provides an abundant energy source for building complexity in the associated plant, but the same sunlight focused through a magnifying glass will convert the leaf’s complexity into

(mostly) carbon, carbon dioxide, and water. Analogues exist for chemical energy, particularly in reference to voltage limitations. Most free radicals, for example, would offer very large energy yields but are generally too reactive (including in complexity-destroying reactions) to be useful. Likewise, oxidants with reduction potential much greater than that of O<sub>2</sub> carry too great a risk of doing oxidative damage to the (largely reduced) complement of biomolecules necessary to support life. [Note, for example, that chlorine, ozone, hypochlorite (bleach) and hydrogen peroxide, the first 2 of which have only modestly higher reduction potentials than O<sub>2</sub>, are all used for disinfecting purposes.] Interestingly, for life on Earth, chemical and light energy sources appear to become damaging at roughly the same voltage levels. In the chemical case, O<sub>3</sub> and Cl<sub>2</sub>—the least oxidizing species that still yield oxidative damage—deliver energies of roughly 500 kJ · (mol O<sub>3</sub> or Cl<sub>2</sub>)<sup>-1</sup> relative to oxidation of glucose; light energy becomes damaging (to DNA) at UV wavelengths corresponding to about 460 kJ · (mol photons)<sup>-1</sup> (Rothschild, 1999). Utilization of chemical energy in the form of O<sub>2</sub> respiration comes very close to this apparent upper boundary, but the most energetic photons used in photosynthesis—corresponding to energies of about 260 kJ/mol (Overmann and Garcia-Pichel, 2000)—lie quite far from it.

Biochemical specifics (or technological capabilities, in the case of intelligent life) further constrain the potential rate of energy transduction. The various steps of energy transduction are mediated principally by enzymes, the potential activities of which have practical limits. Rates of enzymatic transformation with respect to substrate abundance are typically described by saturation functions (Michaelis and Menten, 1913). That is, rates asymptotically approach a maximum upper limit that is not exceeded even in the face of continued increases in concentration. The possible rate of enzymatic transformation is, thus, constrained at each step. The quantity of energy that can be processed in a single enzymatic turnover is also constrained for the reasons just described (complexity limitations on voltage intake). In combination, these limitations place an upper boundary on possible power expenditure in biological process. Technological development expands the potential for habitability by revising (upwardly) the limitations on energy-transducing potential. Habitability on the

Moon was essentially enabled by an ability to transduce energy into specific processes at vastly enhanced rates, and it can generally be seen that the sphere of niches in which we can create habitability will grow directly with our energy-transducing potential.

### 2.7. Interpreting energy balance predictions

As a general framework for habitability, the energy balance construct should both capture and draw refinement from the specific case of life on Earth. The ultimate potential in the energy balance approach would be to assess habitability quantitatively for any specified combination of biochemistry and environment using a “first principles” computational approach. We currently stand at a significant distance from the capability to do so. In this regard, reference to life on Earth offers a means of calibrating the energetic habitability scale through measurements of energy demand in various organisms under various conditions. Such calibration will yield predictive models of habitability that can be applied across different metabolic types and with various combinations of physical, chemical, and resource availability factors. It would expectedly also elucidate the more general and fundamental aspects of the relationship between energy and life, as an increasingly broad spectrum of organisms and conditions are considered.

Reference to life on Earth should also be made as a way to ground truth the energy balance concept. Where discrepancies are indicated, such observations can help to “tune” either the framework itself or the way in which we interpret its predictions. Two observations in regard to life on Earth are useful in tuning our interpretations of energy balance predictions. As a preface, it is useful to recall that energy balance defines habitability at an inherently metabolism-specific level because metabolism provides the functional energetic link between organism and environment. That is, metabolic capability determines the specific energy sources within a given environment that can be usefully harnessed by a particular organism. (Habitability for life overall is predicted in this framework simply by defining some overall set of metabolic capabilities as being available to the “super-organism,” life.) With this context, 2 observations yield important insight to the proper interpretation of energy balance predictions:

- (i) Energy balance predicts that an organism should be capable of tolerating wide-ranging excursions in physico-chemical conditions, provided the organism can channel sufficient energy into offsetting the corresponding impact on complexity. Clearly, this is not true in terrestrial biology at the level of individual organisms as, for example, a methanogen plucked from permanently cold sediments would fare poorly if exposed to boiling temperatures, even with an abundant supply of energy. In such a case, biochemical limitations—for example, the relatively narrow range of physico-chemical stability that characterizes many enzymes (Jaenicke and Sterner, 2002)—are encountered before energy balance limitations, which restricts the individual from occupying the entire available range of energetically habitable space (though the organism is still *ultimately* constrained by energy balance). However, in the example of the methanogen, it is also clear that other representatives of the overall metabolic group are quite able to thrive at boiling temperatures (Kurr *et al.*, 1991). This capability is enabled by biochemical changes [*e.g.*, modest rearrangements of proteins that confer conformational stability over a different range of conditions (Jaenicke and Sterner, 2002)] that enable the exploration of differing regions of the overall energetically habitable space. With this in mind, energy balance considerations appear to emplace boundary conditions on habitability for a metabolic group as a whole, rather than for individual organisms—provided evolutionary diversification within the metabolic group has produced representatives suited to the specified conditions.
- (ii) Following from the above, energy balance predicts that metabolisms with potentially greater rates of energy transduction should have representatives that occupy a broader range of physico-chemical niches than metabolisms with lesser rates. Why, then, would aerobic respiration, which offers by far the greatest energy yield per unit of reactant, not give rise to representatives with, *e.g.*, the highest temperature tolerance? Part of the answer, of course, lies in acknowledging that organisms utilizing the highest voltage do not necessarily realize the greatest energy influx,

since local abundance and flux of the resource in question must also be considered. In addition, for the reasons indicated above, expression of tolerance to extremes appears to require evolutionary diversification toward the boundaries imposed by energy balance. For an organism to evolve into a particular niche (*e.g.*, toward a higher temperature tolerance) requires that energy (the fuel of growth and evolution) be consistently available in that niche (a) at levels that satisfy energy balance for growth and (b) over timescales consistent with evolutionary change. Thus, in the example above, O<sub>2</sub> respirers should not be expected to exhibit the highest temperature tolerance because the relative lack of O<sub>2</sub> in Earth's highest temperature settings has provided insufficient energetic fuel for evolution toward that extreme.

It is lastly important to consider that some aspects of biochemical diversification within a specified group may impact directly on energy balance considerations. For example, an organism that created more stable bonds in its biochemistry would be more resilient toward the disordering pressure of high temperature than others. Similarly, the prediction that metabolic rate and maintenance energy will increase exponentially with temperature (see Section 2.3) assumes that the activation energy of the component reactions remains approximately constant, so that, for example, synthesis of enzymes with increasingly high activation energies would mitigate the effect of increasing temperature on ME. Clearly, organisms can and do tune biochemistry to particular ranges of physico-chemical conditions [as in Example (i), above], so it must be allowed that biochemical innovation may cause deviations within a metabolic group from the quantitative predictions of energy balance. However, it is also the case that a certain core fraction of biochemistry (*e.g.*, the composition of genetic molecules and the means of their synthesis, the strength of the amide bond that forms protein backbones, etc.) must be conserved and unchangeable across all groups. For the fraction of biochemistry that is subject to diversification, the obligate coupling to this core set of processes must constrain the possible variations in molecular structures, biochemical pathways, and process rates within limits. Similarly, while diversification may yield

conformational changes in enzymes, to significantly alter the activation energy for catalyzed processes would, in essence, require the evolution of new enzymes using considerably different binding sites—a much more substantial evolutionary change. Hence, there must be limits to the extent of deviation from energy balance prediction through biochemical diversification. The measured exponential temperature dependence of both overall metabolic rate (Gillooly *et al.*, 2001) and maintenance energy (Tijhuis *et al.*, 1993) offers empirical evidence that such deviation is, in fact, quite limited.

## 2.8. Energetic habitability for alternate forms of life

Among the reasons for defining habitability in an energetic sense is the notion that such a concept offers potential to be all-embracing with respect to diverse forms of life. Quantification of energy balance depends on having defined the biochemistry for which habitability is in question (as must ultimately be the case for any discriminating metric of habitability). Yet clearly, for life as yet unknown to us, the biochemistry is altogether *undefined*. Significant insight, if not precise quantification, may nonetheless be gained by identifying the features of biochemistry that are so fundamental as to be obligately common to all life. Reference to such features in terrestrial life allows constraints to be placed on habitability even for undefined life.

**2.8.1. Power and voltage requirements.** I contend that (i) the existence of biological energy requirements is universal, (ii) their form is equivalent to that found in terrestrial biology (*e.g.*, 2-dimensional, with power and voltage requirements), and (iii) they exhibit discrete minima as in our own example. The universal existence of a power requirement, as described in Section 1.3, depends solely on the notion that all life constitutes a disequilibrium state—which *must* be true if life is to *do anything* (Schrödinger, 1944). The power requirement will, likewise, exhibit a discrete minimum in all cases if minimal function of life requires (i) some minimal complement of molecules not at equilibrium and (ii) a minimum non-zero temperature. These would, again, seem to be an absolute requirement of life as it has classically been defined. Whether the magnitude of

the power requirement is similar to that of terrestrial organisms depends on whether the level of minimally required complexity and the susceptibility of critical molecules to breakdown are comparable.

A discrete voltage requirement likely also exists for all life. The investment of energy into biological process necessarily occurs in discrete chemical events (*e.g.*, individual steps in a reaction pathway). From among these events, some must be absolutely essential to proper function of the life in question. The most energy-demanding of these critical events defines a unit of energy investment without which life is not possible. This unit corresponds to the discrete minimum voltage requirement. Subdivision of the unit voltage is conceivable, as with the molecular mechanisms that subdivide the ATP synthesis energy by one-third to one-fifth (Stock *et al.*, 1999), but the degree of subdivision must certainly be limited to small factors (and clearly cannot be infinite). Enzymes that coordinate reaction of more than a handful of species per "turnover" are essentially unknown (Silverman, 2002), perhaps because this would require enzymes of unmanageable size and complexity. The potential for subdivision by non-enzymatic (purely chemical) mechanisms is even smaller, since the probability of simultaneous collision (as required in such mechanisms) drops very rapidly with the number of species involved. To what extent the magnitude of the voltage requirements of unknown life may be similar to that of terrestrial organisms depends on (i) the magnitude of energy demand associated with the "critical steps" that define unit voltages and (ii) the extent to which these unit voltages may be subdivided. The lengthy discussion required to address these points adequately (and the issues of magnitude associated with power requirements) is left for consideration in future work.

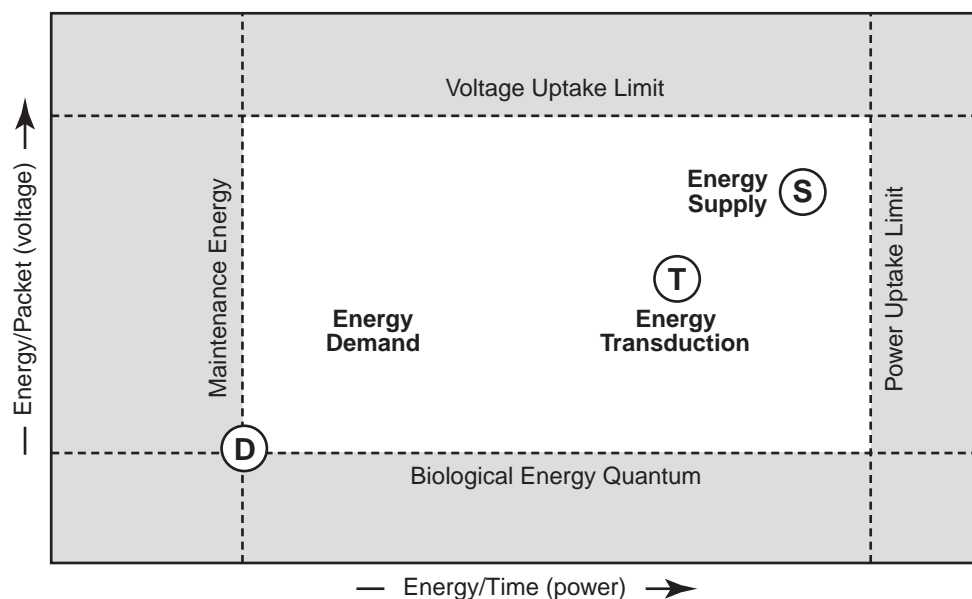
**2.8.2. Environmental Context.** The impacts of resource limitation and physico-chemical variability on energy balance, as described in Sections 2.3 and 2.4, derive from fundamental aspects of chemistry and physics rather than from specific attributes of terrestrial biology. Regardless of the biochemistry in question, energy demand will always increase as a result of increasing temperature or damaging radiation; deviations from ideal pH, salinity, or chemical environment; and employment of strategies to address deficiencies in

material resources or solvent. It is, of course, impossible to define the ideal chemical environment for an unknown biochemistry, so the limits of habitability with respect to such parameters as pH cannot be evaluated without first making assumptions about the nature of that biochemistry. The response of power demand to temperature is, however, absolute and predictable: energy demand will expectedly exhibit an (Arrhenius-like) exponential dependence on temperature regardless of the particular biochemical form.

### 3. SUMMARY

Habitability is defined here as the convergence of elements necessary to permit the construction, maintenance, and function of complex entities (molecules, pathways, structures, etc.). These elements are raw materials, energy, solvent, and element conditions. All can be weighed as terms in a biological energy balance that determines habitability. When the demand for expenditure of energy in biological process is balanced, or more than balanced, by the transduction of energy from the environment, habitability is established. The biological demand for energy is 2-dimensional, with discrete power and voltage requirements that must be met simultaneously. Variations from ideal environmental conditions or limitations in material resources or solvents yield quantifiable increases in one or both requirements. Transduction of environmental energy into biological process is maximally limited by both biochemical aspects of the transduction process (*e.g.*, enzyme kinetics and efficiency) and environmental energy availability. Either factor can prove limiting in a given situation. Biological access to energy is also limited to power and voltage levels that are not inherently destructive to complexity. Combined, these factors describe a bounded energy balance that defines habitability (Fig. 2). Via this energy balance, habitability is defined at an inherently metabolism-specific level, since metabolism provides the functional means by which environmental energy supply is harnessed and put to use in biological process.

Quantification of the energy balance requires knowledge of the specific biochemistry for which habitability is to be assessed, as must be true for any discerning predictor of habitability. Nonetheless, identification of aspects of the energy bal-



**FIG. 2. Habitability as an energy balance.** In this representation, habitability occurs when the potential for transduction of environmental energy into biological process (T) outweighs the biological demand for energy (D). The demand for energy is a 2-dimensional (power and voltage) function that encompasses biochemical specifics, physicochemical conditions, and material or solvent limitations. Upper limits on energy uptake are imposed when supplies reach power or voltage levels that are more directly destructive to complexity than their corresponding constructive potential. The 2 dimensions of energy demand, along with these uptake limits, impose boundary conditions on energetic habitability, with stippled regions representing energetically uninhabitable space. Transduction rate is maximally constrained by environmental energy supply (S) or by saturation of the energy-transducing complex, either of which may prove limiting in a given situation.

ance that derive not from biochemical specifics but from fundamental chemical properties, or that must be common to all biology, allows constraints to be placed on habitability even for undefined forms of life. It is argued here that all life must be characterized by discrete energy requirements of the sort found in terrestrial biology (power and voltage) and, further, that the impacts of various environmental factors on energy balance will be consistent qualitatively, if not quantitatively, across all forms of life.

The appeal to energetic considerations yields a broad-based concept of habitability that can ultimately be applicable for (i) weighing the various contributors to habitability on a common scale, (ii) assessing habitability on a metabolism-specific basis, (iii) incorporating empirical data relating to specific organisms and specific aspects of habitability into predictive models that are applicable across metabolic groups and to combinations of environmental variables, (iv) incorporating observations of habitability in terrestrial systems into a framework capable of embracing alternative biochemical models, and (v) predicting habitability for any defined biochemistry via computational methods. For systems in which

water availability is envisioned to constrain habitability (*e.g.*, Mars), this approach offers additional, quantitative layers of constraint that may aid in prioritizing targets for future astrobiological missions. For systems envisioned to host non-water-based life, this approach offers constraints where virtually none presently exist.

## ACKNOWLEDGMENTS

Formulation of this concept has benefited from discussions with numerous individuals during several years. In particular, I would like to thank Andrew Pohorille for consistently insightful and stimulating conversations. This work was supported by the NASA Exobiology and Astrobiology programs.

## ABBREVIATIONS

BEQ, biological energy quantum; ME, maintenance energy; SPONCH, sulfur, phosphorous, oxygen, nitrogen, carbon, and hydrogen.

## REFERENCES

- Atkins, P.W. (1990) *Physical Chemistry*, Oxford University Press, Oxford.
- Bains, W. (2004) Many chemistries could be used to build living systems. *Astrobiology* 4, 137–167.
- Benner, S.A., Ricardo, A., and Carrigan, M.A. (2004) Is there a common chemical model for life in the universe? *Curr. Opin. Chem. Biol.* 8, 672–689.
- Broome-Smith, J.K., Baumberg, S., Stirling, C.J., and Ward, F.B., editors. (1999) *Transport of Molecules across Microbial Membranes, Society for General Microbiology Symposium No. 58*, Cambridge University Press, Cambridge.
- Cleland, C.E. and Chyba, C. (2002) Defining life. *Orig. Life Evol. Biosph.* 32, 387–393.
- Conrad, P.G. and Nealson, K.H. (2001) A non-Earthcentric approach to life detection. *Astrobiology* 1, 15–24.
- Davies, P.L. (1999) *The Fifth Miracle: the Search for the Origin and Meaning of Life*. Simon and Schuster, New York.
- Fay, P. (1992) Oxygen relations of nitrogen fixation in cyanobacteria. *Microbiol. Rev.* 56, 340–373.
- Fay, P. and Cox, R.P. (1967) Oxygen inhibition of nitrogen fixation in cell-free preparations of blue-green algae. *Biochim. Biophys. Acta* 143, 562–569.
- Gibbs, J.W. (1876) On the equilibrium of heterogeneous substances (part one). *Transactions of the Connecticut Academy of Arts and Sciences* 3, 108–248.
- Gibbs, J.W. (1878) On the equilibrium of heterogeneous substances (part two). *Transactions of the Connecticut Academy of Arts and Sciences* 3, 343–524.
- Gillooly, J.F., Brown, J.H., West, G.B., Savage, V.M., and Charnov, E.L. (2001) Effects of size and temperature on metabolic rate. *Science* 293, 2248–2251.
- Harder, J. (1997) Species-independent maintenance energy and natural population sizes. *FEMS Microbiol. Ecol.* 23, 39–44.
- Hill, T.L. (1977) *Free Energy Transduction in Biology*, Academic, New York.
- Hoehler, T.M. (2004) Biological energy requirements as quantitative boundary conditions for life in the subsurface. *Geobiology* 2, 205–215.
- Hoehler, T.M., Alperin, M.J., Albert, D.B., and Martens, C.S. (1994) Field and laboratory studies of methane oxidation in an anoxic marine sediment: evidence for a methanogen-sulfate reducer consortium. *Global Biogeochem. Cycles* 8, 451–463.
- Hoehler, T.M., Alperin, M.J., Albert, D.B., and Martens, C.S. (2001) Apparent minimum free energy requirements for methanogenic archaea and sulfate-reducing bacteria in an anoxic marine sediment. *FEMS Microbiol. Ecol.* 38, 33–41.
- Jaenicke, R. (1981) Enzymes under extremes of physical conditions. *Annu. Rev. Biophys. Bioeng.* 10, 1–67.
- Jaenicke, R. and Sterner, R. (2002) Life at high temperatures. In *The Prokaryotes*, edited by M. Dworkin, Springer, New York, pp. 167–209.
- Knoll, A., Osborn, M.J., Baross, J.A., Berg, H.C., Pace, N.R., and Sogin, M. (1999) *Size Limits of Very Small Microorganisms: Proceedings of a Workshop*, National Research Council, National Academy Press, Washington, DC.
- Krulwich, T.A. (1995) Alkaliphiles: “basic” molecular problems of pH tolerance and bioenergetics. *Mol. Microbiol.* 15, 403–410.
- Krulwich, T.A. (2000) Alkaliphilic prokaryotes. In *The Prokaryotes*, edited by M. Dworkin, Springer, New York, pp. 283–308.
- Krulwich, T.A. and Ivey, D.M. (1990) Bioenergetics in extreme environments. In *Bacterial Energetics*, edited by I. Funsalus, J. Sokatch, N. Orston, and T.A. Krulwich, Academic Press, Orlando.
- Krulwich, T.A., Ito, M., Gilmour, R., Sturr, M.G., Guffanti, A.A., and Hicks, D.B. (1996) Energetic problems of extremely alkaliphilic aerobes. *Biochim. Biophys. Acta* 1275, 21–26.
- Kurr, M., Huber, R., König, H., Jannasch, H.W., Fricke, H., Trincone, A., Kristjansson, J.K., and Stetter, K.O. (1991) *Methanopyrus kandleri*, gen. and sp. nov. represents a novel group of hyperthermophilic methanogens, growing at 110°C. *Arch. Microbiol.* 156, 239–247.
- Lloyd, K.G., Edgcomb, V., Molyneaux, S.J., Böer, S., Wirsén, C.O., Atkins, M.S., and Teske, A. (2005) Effects of dissolved sulfide, pH, and temperature on growth and survival of marine hyperthermophilic Archaea. *Appl. Environ. Microbiol.* 71, 6383–6387.
- Michaelis, L. and Menten, M. (1913) Die Kinetik der Invertinwirkung. *Biochem. Z.* 49, 333–369.
- Mitchell, P. (1961) Coupling of phosphorylation to electron and hydrogen transfer by a chemiosmotic type of mechanism. *Nature* 191, 144–148.
- Morita, R. (1997) *Bacteria in Oligotrophic Environments*, Chapman & Hall, Norwell, MA.
- Nealson, K.H., Tsapin, A., and Storrie-Lombardi, M. (2002) Searching for life in the universe: unconventional methods for an unconventional problem. *Int. Microbiol.* 5, 223–230.
- Oren, A. (1999) Bioenergetic aspects of halophilism. *Microbiol. Mol. Biol. Rev.* 63, 334–348.
- Overmann, J. and Garcia-Pichel, F. (2000) The phototrophic way of life. In *The Prokaryotes: An Evolving Electronic Resource for the Microbiological Community*, edited by M. Dworkin, S. Falkow, E. Rosenberg, K.-H. Schleifer, E. Stackebrandt, Springer-Verlag, New York.
- Price, B. and Sowers, T. (2004) Temperature dependence of metabolic rates for microbial growth, maintenance, and survival. *Proc. Natl. Acad. Sci. U.S.A.* 101, 4631–4636.
- Rothschild, L.J. (1999) Microbes and radiation. In *Origin, Evolution, and Versatility of Microorganisms*, edited by J. Seckbach, Kluwer, Dordrecht, pp. 551–562.
- Ruiz-Mirazo, K., Pereto, J., and Moreno, A. (2004) A universal definition of life: autonomy and open-ended evolution. *Orig. Life Evol. Biosph.* 34, 323–346.
- Schink, B. (1997) Energetics of syntrophic cooperation in methanogenic degradation. *Microbiol. Mol. Biol. Rev.* 61, 262–280.
- Schink, B. and Stams, A.J.M. (2002) Syntrophism among prokaryotes. In *The Prokaryotes: An Evolving Electronic Resource for the Microbiological Community*, edited by M. Dworkin, S. Falkow, E. Rosenberg, K.-H. Schleifer, E. Stackebrandt, Springer-Verlag, New York.

- Schrödinger, E. (1944) *What is Life? The Physical Aspect of the Living Cell*, Cambridge University Press, Cambridge.
- Shock, E.L. and Holland, M.E. (2007) Quantitative habitability. *Astrobiology* 7(6), 839–851.
- Silverman, R.B. (2002) *The Organic Chemistry of Enzyme-Catalyzed Reactions*, Academic Press, London.
- Stock, D., Leslie, A.G.W., and Walker, J.E. (1999) Molecular architecture of the rotary motor in ATP synthase. *Science* 286, 1700–1705.
- Tempest, D.W. and Neijssel, O.M. (1984) The status of  $Y_{atp}$  and maintenance energy as biologically interpretable phenomena. *Annu. Rev. Microbiol.* 38, 459–486.
- Tijhuis, L., van Loosdrecht, M.C.M., and Heijnen, J.J. (1993) A thermodynamically based correlation for maintenance Gibbs energy requirements in aerobic and anaerobic chemotrophic growth. *Biotechnol. Bioeng.* 42, 509–519.
- von Neumann, J. (1951) The general and logical theory of automata. In *Cerebral Mechanisms in Behavior, The Hixon Symposium*, edited by L.A. Jeffress, John Wiley & Sons, New York, pp. 1–31.

Address reprint requests to:  
Tori M. Hoehler  
NASA Ames Research Center  
Moffett Field, CA 94035

E-mail: [tori.m.hoehler@nasa.gov](mailto:tori.m.hoehler@nasa.gov)

**This article has been cited by:**

1. Tori M. Hoehler , Jan P. Amend , Everett L. Shock . 2007. A “Follow the Energy” Approach for AstrobiologyA “Follow the Energy” Approach for Astrobiology. *Astrobiology* 7:6, 819-823. [[Citation](#)] [[PDF](#)] [[PDF Plus](#)]