A Macroscopic Quantum Heat Engine:
Nested Resonant Structures and the Entropic Stability of Life

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ABSTRACT

In search of the life spirit, or energy, that flows through the animal heart to make it beat, theologians, philosophers and scientists have for over two millennia been dissecting the heart down to its most basic structures. Recently, researchers have reached the pinnacle of the anatomists' dream by determining the structure of a cardiac myosin thick filament at roughly twenty angstroms resolution. Yet, dissected down to individual atoms, the energy that flows through the heart is still nowhere to be found. The reason is that there exists in the whole of muscle a form of energy that does not exist in its constituent parts. To identify this energy, we must determine how the billions of randomly moving atoms that make up contractile proteins in muscle scale up to generate the steady unidirectional contraction of muscle. Here, I show that degrees of freedom of small structural elements physically, irreversibly, and discretely collapse to create larger structures with energy landscapes defined by entropic wells quantized by discrete degrees of freedom. The collapse of degrees of freedom across multiple thermal scales results in nested resonant structures from atoms on up to the filamentous structure of muscle, demonstrating that muscle is a quantum heat engine.

INTRODUCTION

Muscle fibers are multi-scale structures (*1*) within which atoms form amino acids that covalently bind to form long peptide chains that fold into secondary, tertiary and quaternary structures of contractile proteins like actin and myosin (*2*–*5*). Ensembles of contractile proteins bind together to form large filamentous complexes (*6*, *7*) arranged within a sarcomere to slide past each other when muscle contracts (*8*). Key to understanding the molecular mechanism of muscle contraction is describing how billions of randomly moving structural elements scale up to create steady unidirectional movement.

Muscle is a binary mechanical system (*9*, *10*) consisting of an ensemble of protein switches, where each switch occurs with a discrete rotation of a structural element (the light chain binding domain, or lever arm) of a single myosin motor (*11*). This switch is induced by actin binding and gated by the release of inorganic phosphate, P, (*12*) and its throw can generate a displacement, *d*, of 10 nm (*13*–*15*). The *N* degrees of freedom of *N* myosin motors create the *N* chemical states of muscle's macromolecular filamentous structure (*10*). The macromolecular energy landscape is an entropic well that describes the potential energy of an entropic spring, and the mechanical work performed in stretching muscle's entropic spring is stored as quantized heat (*10*). I have shown that this model accurately accounts for most energetic, mechanical, and kinetic aspects of muscle contraction (*9*, *10*). It also provides a simple solution to the Gibbs paradox (*16*) and lays the foundation for a novel thermodynamic formulation of chemical kinetics (*17*). Here, I extend this analysis down the thermal scale of atoms.

In general, the *N* degrees of freedom of an ensemble of *N* structural elements physically collapse to create *N* discrete states of a new structure on a new thermal scale. This collapse occurs when thermal energy becomes delocalized among structural elements, at which point these elements are collectively defined as an ensemble structure not as independent structural entities (their degrees of freedom, structural states, mechanical states, thermal fluctuations, etc. are no longer defined). Ensemble structures collapse to create new structures on higher thermal scales, and this process repeats across thermal scales, creating resonant structures nested from atoms to muscle.

The basic mathematical analysis is trivial. The primary challenge is conceptual in that the analysis inverts the way we typically think about how atoms scale up to large structures. Scaling is not a smooth, reversible, mental exercise where the loss of degrees of freedom is a loss of information and the corresponding increase in entropy describes a mental state of not knowing. Instead, here scaling is a physical process where the loss of degrees of freedom physically creates structures on a larger scale, and the associated increase in entropy describes the delocalized thermal energy physically stored as quantized heat within larger structures. When we dissect muscle down to the thermal scale of atoms, while we physically gain degrees of freedom, we physically lose the delocalized energy (i.e., the entropic wells) that defines muscle, its chemical states, and its function.

The results are profound and wide reaching, implying that it is physically impossible to describe molecular mechanisms of muscle contraction; that structural details of proteins serve more as conduits for thermal scaling than functional mechanisms; that muscle is a quantum heat engine; that thermodynamics is quantum mechanics on the energy scale of heat; and that the formation, stability, and function of biological macromolecules is the result of an irreversible physical process energetically driven by entropy, meaning that life is formed and stabilized – not locally against the second law of thermodynamics but – because of it.

RESULTS

Figure 1A illustrates a simple reaction where a structural element equilibrates between one state A and two energetically equivalent states B_1 and B_2 with an equilibrium constant *K* for each reversible transition. If differences between A and B but not between B_1 and B_2 are measurable, the observed equilibrium constant between A and B (B_1 or B_2) is 2K. This sets up a Gibbs-like paradox. That is, as B_1 and B_2 become increasingly similar, the equilibrium constant remains 2*K* up until when B_1 and B_2 become identical at which point the equilibrium constant becomes *K*. The paradox is that a relatively large energy change,

$$k_BT\cdot\ln(2K) - k_BT\cdot\ln(K) = k_BT\cdot\ln(2),$$

is created by an infinitesimally small change in state. The solution to this paradox depends on the nature of the difference between B_1 and B_2.

If B_1 and B_2 are differences within a single degree of freedom, B, they can be treated as substates (part of a rugged landscape) of B that equilibrate with each other (Fig. 1A). These substates can be coarse grained (smoothed, Fig. 1A left to right) to describe an equilibrium between A and B. In this case, as B_1 and B_2 become increasingly similar the shape of the coarse-grained energy well, B, changes smoothly with no discrete energy change when B_1 and B_2 become equivalent. However, if B_1 and B_2 describe two different degrees of freedom, the paradoxical $k_BT\cdot\ln(2)$ remains problematic because degrees of freedom cannot be smoothly coarse-grained away (e.g., the average of two and one degrees of freedom, 1.5, is not defined).

Figure 1B illustrates a particle moving in one of two dimensions (two degrees of freedom) within two potentials, $V_x(x)$ and $V_y(y)$. Starting in a reference state, an infinitesimally small change in energy, δE, can occur with a displacement in either direction, δE_x or δE_y. Because δE_x and δE_y are defined by two discretely different degrees of freedom, even infinitesimally small energy changes cannot be smoothly averaged (coarse-grained) together. Still, muscle's one degree of freedom tells us that two degrees of freedom can collapse into one (Fig, 1B, left to right). While the two states, δE_x and δE_y, are each occupied in one way ($\Omega_x = \Omega_y = 1$) the collapsed state, δE, can be occupied in two ways (δE_x or δE_y, $\Omega = 2$). Thus, according to Boltzmann's equation, $S = k_B\cdot\ln\Omega$, collapsing two degrees of freedom into one results in a discrete increase in entropy

$$\Delta S = k_B\cdot\ln\Omega - k_B\cdot\ln\Omega_x - k_B\cdot\ln\Omega_y = k_B\cdot\ln(2).$$

It follows from the second law of thermodynamics ($dQ = TdS$) that the paradoxical $k_BT\cdot\ln(2)$ is quantized heat, ΔQ, generated when two degrees of freedom collapse into one. If the change in energy, δE_x or δE_y, defined on the thermal scale of x and y approaches zero and only thermal energy, $\frac{1}{2}k_BT$, exists for each degree of freedom, the minimum δE that can be defined on the collapsed thermal scale (Fig. 1B, right) is the heat, $k_BT\cdot\ln(2)$, delocalized between x and y.

The collapse of degrees of freedom is irreversible since the heat it creates cannot be used to recover the degrees of freedom that created it. This results in observational uncertainty, or the inability to define the states of the constituents of a system (their degrees of freedom are no longer defined) on the thermal scale of the system. For example, on the thermal scale of the collapsed state in Fig. 1B, δE_x and δE_y both physically exist with equal probability at a given instant of time within a resonant structure. To determine δE_x and δE_y energy is required to reverse the collapse of degrees of freedom. Clearly, thermal scaling is an irreversible, discrete, physical process not a reversible, smooth, mental exercise.

The Gibbs free energy equation accounts for the increase in entropy, $k_BT\cdot\ln(2)$, with a collapse of two degrees of freedom. Figure 1C revisits the reaction in Fig. 1A only here B_1 and B_2 represent two different degrees of freedom. On the thermal scale of B_1 and B_2 (scale i) the equilibrium constant between state A and B_1 or B_2 is $2K$ because there are two degrees of freedom. The enthalpic difference between states A and B_1 or B_2 is then $\Delta H_i = -k_BT\cdot\ln(2K)$. On the thermal scale of B (scale j), the enthalpic difference between states A and B is $\Delta H_j = -k_BT\cdot\ln(K)$. The difference between ΔH_i and ΔH_j is the paradoxical $k_BT\cdot\ln(2)$, which according to Gibbs is $T\Delta S_j$ where $\Delta S_j = k_B\cdot\ln(2)$ describes the difference between the one way state A can be occupied and the two ways state B can be occupied.

On thermal scale i

$$\Delta G_i = \Delta H_i = -k_BT\cdot\ln(2K) = -k_BT\cdot\ln(K) - k_BT\cdot\ln(2). \qquad \text{Eq. 1}$$

On thermal scale j,

$$\Delta G_j = \Delta H_j - T\Delta S_j = -k_BT\cdot\ln(K) - k_BT\cdot\ln(2), \qquad \text{Eq. 2}$$

where $\Delta H_j = \Delta G_i$ is often referred to as the standard reaction free energy, ΔG°_j.

While mathematically equivalent, these equations describe two physically different systems (i and j). On thermal scale i, $k_BT\cdot\ln(2)$ describes the physical ways that B_1 and B_2 can be occupied (either one or the other state is physically occupied). On thermal scale j, $k_BT\cdot\ln(2)$

describes the a priori ways that B can be occupied (in this case it is always two, independent of the physical occupancy of B_1 and B_2). The latter physically tilts the energy landscape (Fig. 1C, right) to create, on a new thermal scale, a structure B that replaces structures B_1 and B_2 both physically and irreversibly.

Consider a canonical ensemble of N_i structural elements (for simplicity I assume one degree of freedom per structural element) that each change energy by dE_i. The number of ways these N_i elements can as an ensemble change energy by $x_i \cdot dE_i$ is then $\Omega_i = N_i!/[x_i!(N_i - x_i)!]$, where x_i is an incremental change in the energetic state of the ensemble. The total number of states, x_i, is N_i, and the entropy, $S_i(x_i) = k_B \cdot \ln\Omega_i$, of the ensemble in state x_i is

$$S_i(x_i) = k_B \cdot \ln(N_i!/(x_i!(N_i - x_i)!). \qquad \text{Eq. 3}$$

The heat contained by the ensemble in state x_i is then $Q_i(x_i) = TS_i(x_i)$, which is plotted in Fig. 2 for values of N_i of 3, 5, and 20, showing that an ensemble of N_i structural elements collapses into an entropic well that defines the energy landscape (a change in energy with a change in the structural state of the ensemble) of a new structural state.

With a collapse to one degree of freedom, the N_i structural elements irreversibly lose their degrees of freedom and become resonant structures that no longer thermally fluctuate. At the same time, on a new thermal scale, a single structure with one degree of freedom replaces these structural elements (now microstates) and thermally fluctuates about its one degree of freedom within an energy landscape defined by an entropic well (blue double arrow in Fig. 2 indicates $\frac{1}{2}k_BT$ thermal energy). Thermal energy absorbed by this new structure is quantized because the change in heat, Q_i, with a change in structural state, x_i, is quantized by discrete degrees of freedom (Fig. 2). I refer to the difference between the first energy level and the energy minimum as the ground state energy spacing for this structure.

The entropic wells in Fig. 2 resemble entropic funnels in models of protein folding; only here the implication is that protein folding occurs not through a rugged landscape but through nested funnels defined on different thermal scales. For example, secondary structures fold within entropic wells defined by the degrees of freedom of primary structure; tertiary

structures fold within entropic wells defined by the degrees of freedom of secondary structures; etc. The formation of each new entropic well at each new thermal scale is irreversible and stabilized by the increase in entropy associated with collapsed degrees of freedom (Fig. 1). The energy levels of the resulting entropic well are quantized by the discrete number of degrees of freedom that collapse to create it. In muscle, we have shown that resonant structural elements of contractile proteins thermally scale all the way up to muscle's one degree of freedom (*10*), which is to say that muscle is a quantum heat engine that is energetically stabilized – not like a house of cards against entropy but – by entropy.

Thermal scaling requires that all N_i structural elements have similar changes, dE_i, in their ground state energy spacing, which is to say all *Ni* structural elements must have similar numbers of structural states (Fig. 3A). This is analogous to resonant frequencies in a normal model analysis. While the entropic wells in Fig. 3A are created from the number of ways an ensemble of structural elements changes by dE_i, excited states can be created from the number of ways an ensemble of structural elements changes by $2dE_i$, $3dE_i$, etc., (blue lines in Fig. 3A). This is analogous to harmonics in a normal model analysis. For entropic wells created by large N_i, energy levels become less quantized and thermal fluctuations are minimized (Fig. 2) at which point thermal scaling reaches a classical limit.

Histograms of populations of structural elements on scale i with different numbers of states, N_i, are illustrated in Figs. 3B – 3D showing how these populations collapse into new structures on scale j. At one extreme, Fig 3B describes a monatomic gas of *N* molecules with three degrees of freedom. Here, the total, 3^N, degrees of freedom collapse into one degree of freedom, generating $N \cdot k_B T \cdot \ln(3)$ of quantized heat. This heat is not contained within entropic structural wells because there are no bonds between atoms to contain it. Instead, it is contained by the walls of a cylinder and thus is balanced against the pressure, P, and volume, V, of the cylinder as $PV = N \cdot k_B T \cdot \ln(3)$, resembling the ideal gas law [$\ln(3) \cong 1.1$].

As another example, *N* linked structural elements each with two (*N* = 2) structural states (Fig. 3C) collapse into a single entropic well (a polymer) with *N* states. This well describes the potential energy (Fig. 2) of an entropic spring (the energy landscape of muscle's one degree of freedom) (*10*). There are many intermediate resonant structures that must be created between

the thermal scales of atoms and muscle, and Fig. 3D illustrates in general how populations of different structural elements on thermal scale i collapse to form a different set of structures on thermal scale j. It is clear from Fig. 3D that large structures can contain quantized heat if structural elements are incrementally layered across many thermal scales, which is the structural layering that has evolved in most biological systems.

Figure 3E illustrates two different structural states (i.e., chemical states) corresponding to a structure with (P.L) and without (P) a bound ligand on scale i. The two structural elements differ in energy by the binding enthalpy (Fig. 3B), and this difference propagates across all scales (Eqs. 1 and 2). If excited states of the ligand-bound structure (Fig. 3A) overcome the enthalpic difference between chemical states, structural elements from both chemical states can collapse together (Fig. 3E, bottom to top) to create a merged structure on scale j. The resulting activation energy barrier between the two states is a resonant structure defined by thermal energy delocalized among structural elements both with and without bound ligand. While significant effort has been invested into determining the timing of P_i release, actin binding, and the mechanical switch of myosin, the above analysis implies that these sequences of events are not definable. Like in a quantum computer, state transitions occur through entangled tunnels between states (Fig. 3E) not through specific molecular events.

The increase in entropy with increasing thermal scale energetically pulls structures toward their largest thermal scale (minimum degrees of freedom), and only on this scale do changes in structure interact with their surroundings (resonant structures do not have degrees of freedom with which to interact with their surroundings). The macroscopic structure at muscle's one degree of freedom is the macromolecular assembly of actin filaments, myosin filaments, and all associated proteins and molecules in a muscle cell, and the energy landscape for this assembly is described by an entropic well (Eq. 3, Fig. 2) [see (*10*)]. The *N* degrees of freedom that collapse to create this well are *N* myosin motors, which means the macromolecular complex has *N* structural states. The change in energy, *dE*, is the binding enthalpy on scale i for myosin's mechanical switch (i.e., actin-myosin binding and P_i release), which on scale j is the standard reaction free energy, ΔG° (Eqs. 1 and 2). Figure 4 illustrates the

energy landscapes of the myosin switch (MDP to AMD, Fig. 4A) that collapse to form the entropic well of the actin-myosin macromolecular complex (Fig. 4B, black symbols).

As previously described (*10*), the landscape is tilted by ΔG° for each chemical step (Fig. 4B, red symbols). When the system is held at a constant force, *F*, the internal work performed, *Fd*, increases linearly with each chemical step (Fig. 4B, blue symbols) where *d* is the switch displacement (when *F* is less than the isometric force, muscle shortening maintains a constant force). Figure 4C is the sum of the above energetic contributions to the energy landscape. The catalyzed ATPase reaction, *v*, does not affect the landscape, rather it irreversibly transfers myosin motors from AMD to MDP within the landscape (arrow, *v*). If muscle is allowed to shorten, the chemical relaxation back toward an energy minimum performs external work, which diminishes the contribution of ΔG° to the landscape. If muscle is held at a fixed length, the chemical relaxation generates muscle force, *F*, which changes the landscape as illustrated in Fig. 4C. Non-ergodic forces decrease the fraction of F that contributes to the energy landscape.

We have shown that the muscle force-velocity relationship can be derived mathematically from this landscape(*9*). We have also shown that computational models with kinetic rate constants defined by this landscape accurately account for most non-equilibrium behaviors of muscle (force generation, tension transients, and work loops) (*10*). Perturbations to structural elements (mutations, ligand binding, post-translational modifications, etc.) do not mechanistically affect muscle mechanics (they do not affect degrees of freedom); rather they thermally scale up to affect the macromolecular energy landscape.

DISCUSSION

Muscle evolved, not by following the rules of science as we understand them today but, by following the rules of Nature as they have existed for billions of years. It is therefore not a surprise that muscle teaches us new perspectives on science. With the evolution of muscle, Nature found a macroscopic quantum heat engine that we can now energetically dissect to learn about heat quantized by the collapse of degrees of freedom (*10*), a solution to the Gibbs paradox (*16*), the equivalence of thermodynamics and quantum mechanics on thermal scales of heat, a quantum heat interpretation of entropic springs and the ideal gas law, entanglement as

an irreversible increase in entropy with increasing scale, resonant structures that contain quantized heat nested across thermal scales, a thermodynamic formulation of chemical kinetics, and an understanding that life on earth is stabilized – not against the second law of thermodynamics but – because of it.

Two entropically driven processes are described. One is the increase in entropy across thermal scales, which is associated with the collapse of degrees of freedom and drives irreversible physical processes like protein folding. The other is fluctuations within entropic wells defined within thermal scales, which describe either resonant structures that have lost their degrees of freedom or native protein complexes with degrees of freedom that physically interact with their surroundings. Here, I have focused on the energetics of these processes. The kinetics of these processes are determined through a form of normal mode analysis (*18*), where different vibrational modes with different thermal distances occur on different thermal scales. However, here the vibrations are thermal fluctuations not harmonic oscillations, and the "modes" are quantized energy spacings not frequencies. We have shown that this thermodynamic formulation of chemical kinetics accurately describes steady state and transient muscle mechanics, kinetics, and energetics (*9*, *10*).

On the thermal scale of atoms, the largest ground state energy spacing is $k_BT\cdot\ln(2)$, setting an upper limit for the energy that can be absorbed by a resonant structure created when two degrees of freedom collapse into one. Thermal energy is quantized by this spacing; however, quantized light, hv, can also be absorbed by this spacing at a frequency defined by $k_BT\cdot\ln(2) = h\nu$, or $\nu = 200\ cm^{-1}$ at room temperature. This is the highest energy of quantized light that can be absorbed by a structural element as quantized heat. It is commonly assumed that structural elements absorb infrared light because its frequency, ν, matches the frequency of harmonic oscillations of structural elements. Here, structural elements absorb infrared light because its energy, hv, matches the quantum heat spacing of resonant structural elements. This is the bridge from quantized light to quantized heat, which then spans across many thermal scales all the way up to the thermodynamics of muscle's one degree of freedom.

Muscle shines a light on how the world works across all thermal scales within which it evolved and now functions. The collapse of degrees of freedom creates entropic wells within

which proteins fold; stabilizes large aggregate structures; and contracts muscle fibers. Extended to larger scales, it is a reasonable hypothesis that a collapse of degrees of freedom creates entropic wells (i.e., gravitational potentials) that stabilize the aggregation of masses (*19*). All of this follows from a shift in our view of scaling from a smooth, reversible, mental exercise to an irreversible and discrete physical process.

REFERENCES

1. R. C. Woledge, N. A. Curtin, E. Homsher, *Energetic Aspects of Muscle Contraction* (Monogr. Physiol. Society, ed. 41, 1985).
2. H. L. Sweeney, A. Houdusse, J. Robert-Paganin, in *In Myosins*, L. M. Caluccio, Ed. (Springer Nature Switzerland AG, Basel, Switzerland, 2020), pp. 7–19.
3. I. Rayment, W. R. Rypniewski, K. Schmidt-Bäse, R. Smith, D. R. Tomchick, M. M. Benning, D. A. Winkelmann, G. Wesenberg, H. M. Holden, Three-dimensional structure of myosin subfragment-1: A molecular motor. *Science (80-.).* **261**, 50–8 (1993).
4. W. Kabsch, H. G. Mannherz, D. Suck, E. F. Pai, K. C. Holmes, Atomic structure of the actin:DNase I complex. *Nature*. **347**, 37–44 (1990).
5. H. Frauenfelder, S. G. Sligar, P. G. Wolynes, H. Frauenfelder, S. G. Sligar, P. G. Wolynes, The Energy Landscapes and Motions of Proteins. **254**, 1598–1603 (1991).
6. K. C. Holmes, M. a Geeves, The structural basis of muscle contraction. *Philos. Trans. R. Soc. Lond. B. Biol. Sci.* **355**, 419–31 (2000).
7. D. Tamborrini, Z. Wang, T. Wagner, S. Tacke, M. Stabrin, M. Grange, A. L. Kho, M. Rees, P. Bennett, M. Gautel, S. Raunser, Structure of the native myosin filament in the relaxed cardiac sarcomere. *Nature*. **623**, 863–871 (2023).
8. H. E. Huxley, The mechanism of muscular contraction. *'Science*. **164**, 1356–65 (1969).
9. J. E. Baker, D. D. Thomas, A thermodynamic muscle model and a chemical basis for A.V. Hill's muscle equation. *J Muscle Res Cell Motil.* **21**, 335–344 (2000).
10. J. E. Baker, Thermodynamics and Kinetics of a Binary Mechanical System: Mechanisms of Muscle Contraction. *Langmuir*. **38**, 15905–15916 (2022).
11. J. E. Baker, I. Brust-Mascher, S. Ramachandran, L. E. LaConte, D. D. Thomas, A large and distinct rotation of the myosin light chain domain occurs upon muscle contraction. *Proc. Natl. Acad. Sci. U. S. A.* **95**, 2944–9 (1998).
12. J. E. Baker, L. E. W. LaConte, I. Brust-Mascher, D. D. Thomas, Mechanochemical coupling in spin-labeled, active, isometric muscle. *Biophys. J.* **77**, 2657–64 (1999).
13. J. T. Finer, R. M. Simmons, J. A. Spudich, Single myosin molecule mechanics: piconewton

forces and nanometre steps. *Nature*. **368**, 113–119 (1994).

14. J. Molloy, J. Burns, J. Kendrick-Jones, R. Tregear, D. White, Movement and force produced by a single myosin head. *Nature*. **378**, 209–212 (1995).
15. J. E. Baker, C. Brosseau, P. B. Joel, D. M. Warshaw, The biochemical kinetics underlying actin movement generated by one and many skeletal muscle myosin molecules. *Biophys. J.* **82**, 2134–47 (2002).
16. J. E. Baker, Cells solved the Gibbs paradox by learning to contain entropic forces. *Sci. Rep.* **13** (2023), doi:10.1038/s41598-023-43532-w.
17. J. Baker, The Kinetic and Energetic Pull of Chemical Entropy. *BioRxiv* (2023).
18. J. A. Bauer, J. Pavlovíc, V. Bauerová-Hlinková, Normal mode analysis as a routine part of a structural investigation. *Molecules*. **24** (2019), , doi:10.3390/molecules24183293.
19. E. Verlinde, On the origin of gravity and the laws of Newton. *J. High Energy Phys.* **2011** (2011), doi:10.1007/JHEP04(2011)029.

Figure 1. The collapse of two degrees of freedom into one. (A) A three-state kinetic scheme (top) and corresponding energy landscape (bottom) for an equilibrium reaction between states A, B_1, and B_2, where B_1 and B_2 are energetically equivalent states. If B_1 and B_2 are defined within a single degree of freedom they can be coarse-grained together (left to right). (B) A particle thermally fluctuating in two dimensions, x and y, (two degrees of freedom) against a potential V_x and V_y has energy states dE_x and dE_y. When these two dimensions collapse into one (left to right) the particle moves in one dimension against a potential, V, with an energy dE. (C) The kinetic scheme (top) and corresponding energy landscape (bottom) in (A) where B_1 and B_2 are now defined as separate degrees of freedom. The change in enthalpy, ΔH_i, between A and B_1 or B_2 on scale i is the change in free energy, ΔG_j, between states A and B on scale j, where $_{\Delta Sj}$ describes the two ways that the collapsed state, B, can be occupied (B_1 or B_2).

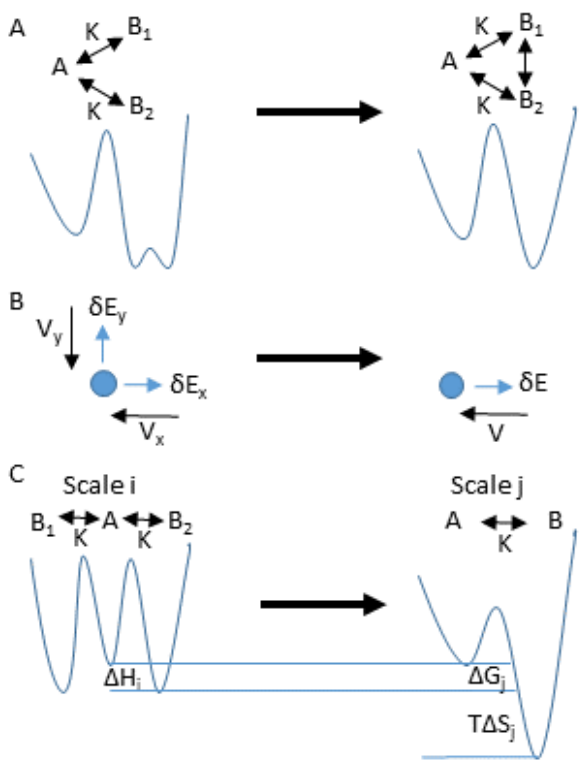

Figure 2. Entropic Wells. (A – C) Equation 3 ($k_BT \cdot \ln\Omega_i$) is plotted versus x_i for N_i = 3, 5, and 20. The blue double arrow is ½k_BT.

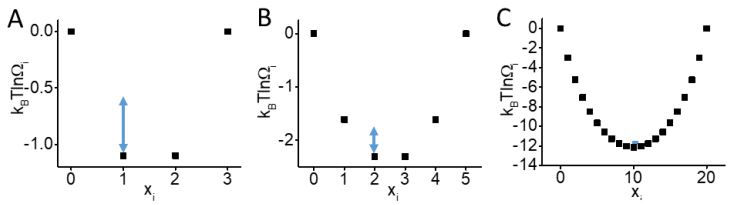

Figure 3. Nested Resonant Structures. (A) Entropic wells (Eq. 3) corresponding to ten ensemble structures on thermal scale i are plotted, five composed of N_i = 10 elements and five composed of N_i = 5 elements. The two sets of five ensemble structures collapse into two new ensemble structure on a higher thermal scale, j (bottom to top) both composed of N_j = 5 elements. The blue lines indicate the excited energy states of wells on scale j created from higher level energy spacings (e.g., 2*dE*, 3*dE*, etc.) on scale i. (B – D) Histograms of hypothetical populations of ensembles of N_i structural elements (x axis) on scale i that collapse (right to left) into ensembles of N_j structural elements (x axis) on scale j. (E) Two sets of ensemble structures (N_i = 10) on scale i, one with ligand bound and the other with no ligand bound are separated energetically by the ligand binding enthalpy, ΔH. An excited state of the ligand bound structures collapse with apo structures to create a resonant tunnel (activation energy barrier) between the ligand bound and apo structures (chemical states).

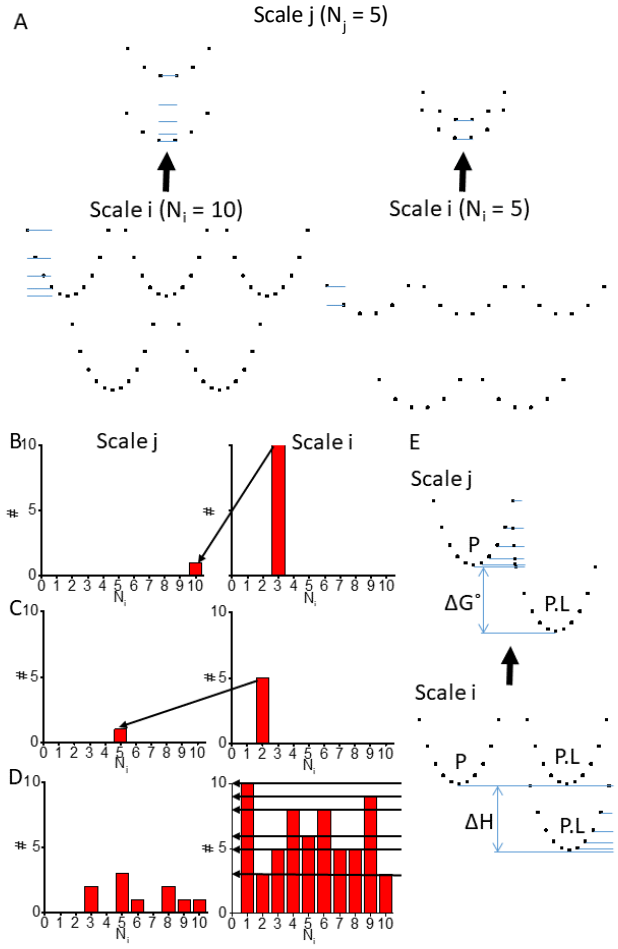
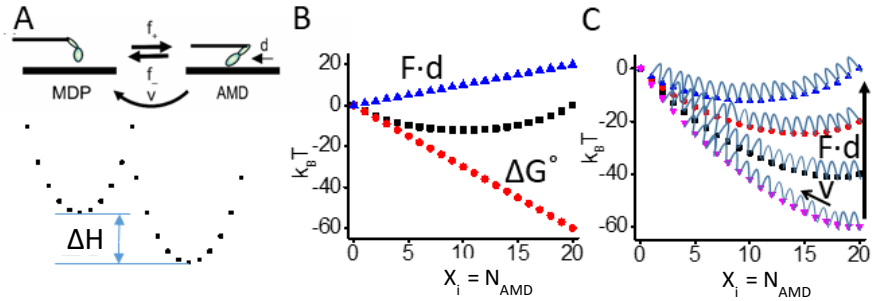
Figure 4. Muscle's one degree of freedom. (A) A myosin motor (M, ovals) is a protein switch induced by actin (A, thick black line) binding and gated by phosphate (P) release with a throw of d. The switch is a reversible intermediate step in the actin-myosin catalyzed ATP hydrolysis reaction, v, with forward and reverse rates, f+ and f-. The entropic wells for the protein switch (energy landscape of chemical reaction) illustrate the enthalpic binding energy, ΔH (bottom) (B) As described in (*10*), the entropic well (Eq. 3) created when N_j = 20 myosin motors collapse into a macromolecular actin-myosin assembly is plotted (black symbols) as a function of the extent of the reaction, x_i, or the number, N_{AMD}, of myosin motors in state AMD. The free energy for the macromolecular complex decreases by ΔG˚ with each net chemical step (red symbols). The internal work performed on the system by a chemical step increases linearly with the extent of the reaction with a slope proportional to muscle force, F (blue symbols). (C) The sum of the energetic contributions to the macromolecular landscape are plotted for different values of F illustrating the activation energy barrier for each step.