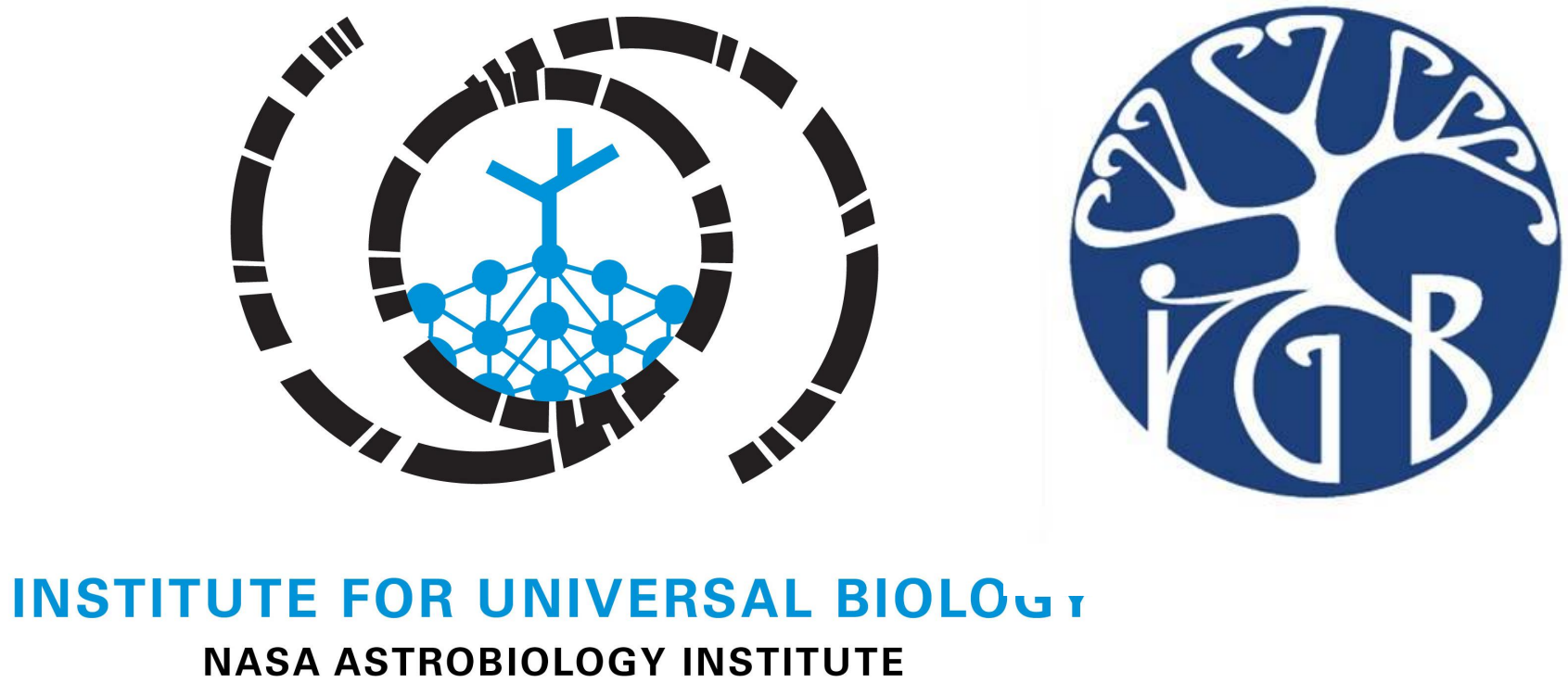
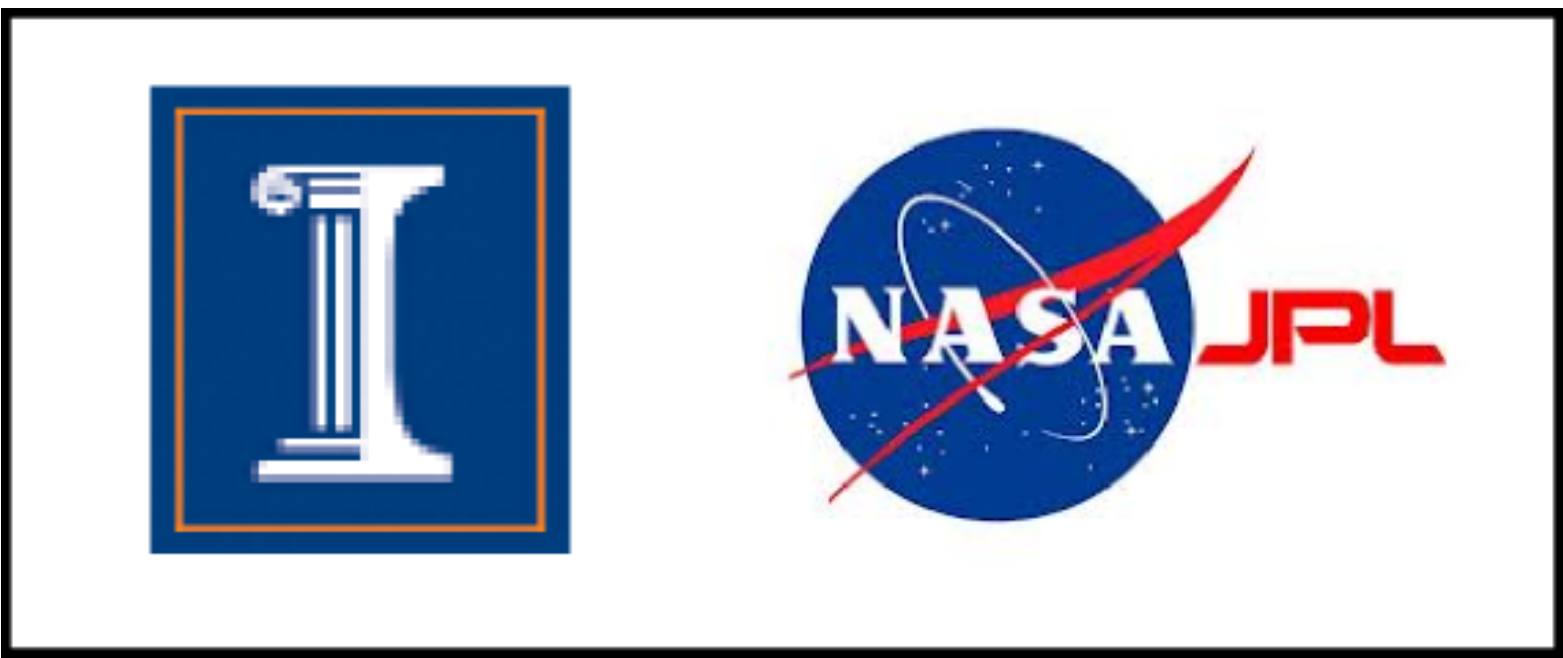


# Fluctuation relations, bioenergetics and the emergence of life

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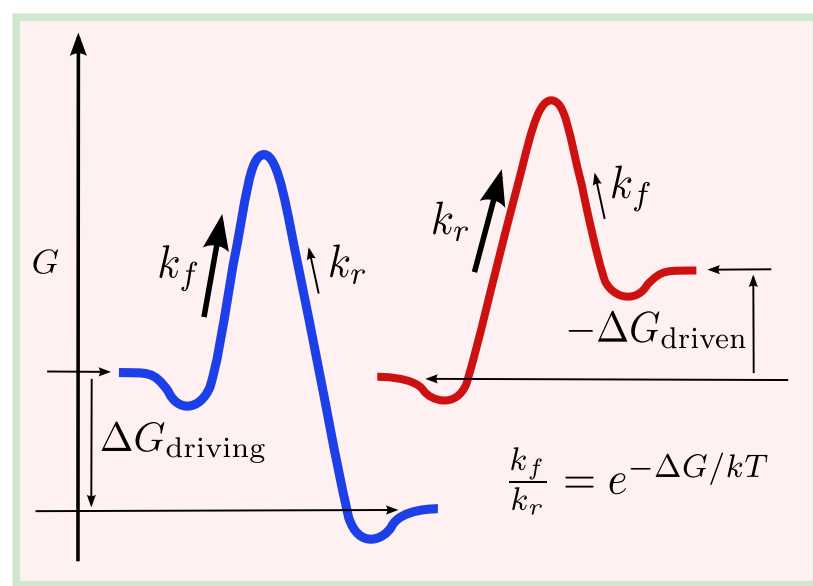
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## 1 Life's problem: the need to force many reactions to run up-hill (often very far).

Only possible solution: trap chance *fluctuations* that run against the 2nd law and pay for the crime later (but quickly).

At the individual event level, all chemical reactions are "fluctuation driven" (see figure) and proceed in both forward (entropy-increasing) and reverse (entropy-decreasing) directions; the 2nd law merely demanding that in a spontaneous reaction the entropy-increasing ("exergonic") events statistically predominate. How then can a reaction be forced to run "up-hill" – to have, that is, its entropy-decreasing "fluctuation" events predominate? The only possibility is to have that reaction 'coupled to' another, larger one, that is running down-hill. But how does 'coupling' actually work in this fluctuation driven world?



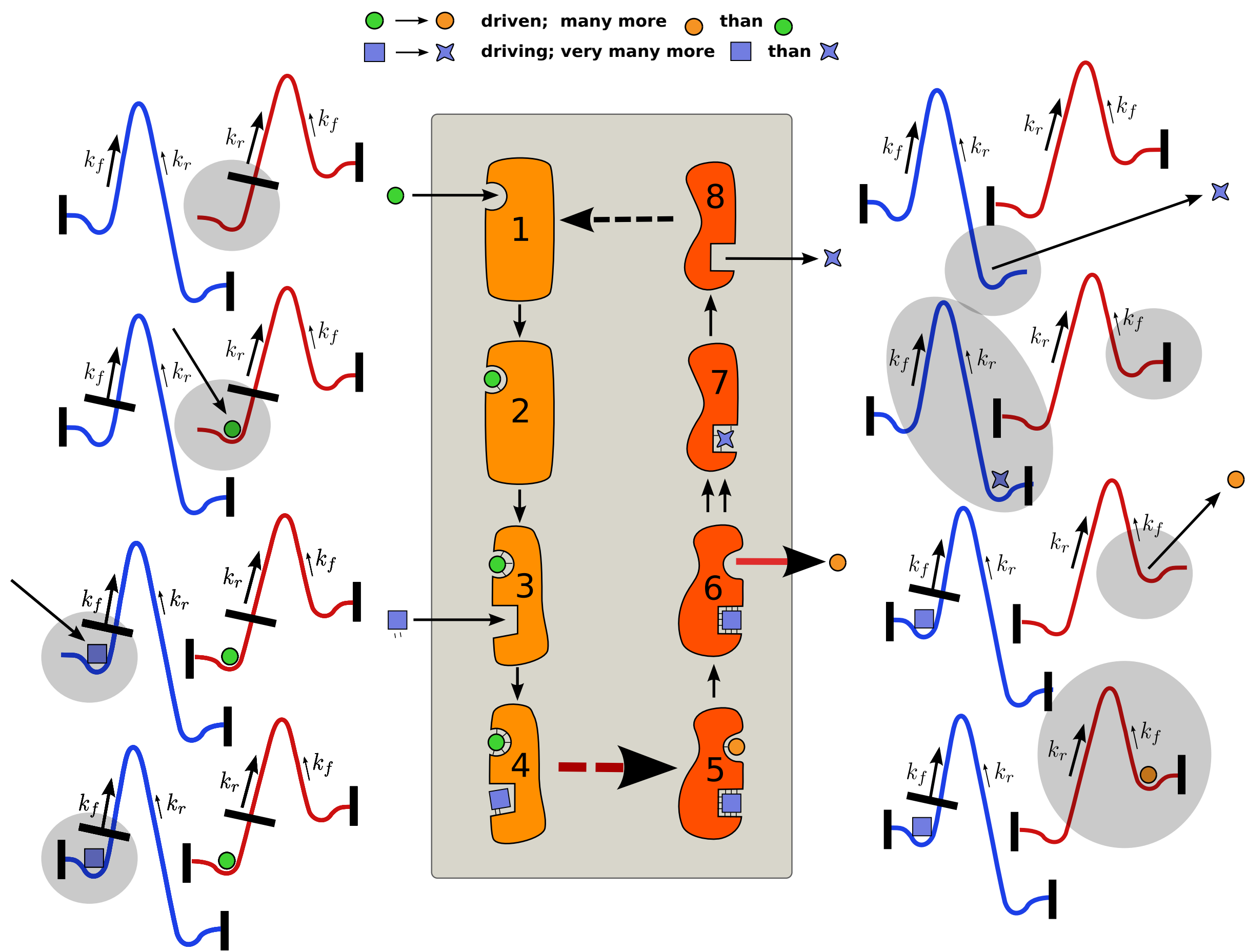
How could the blue (forward) reaction cause the red (backward) one? Forward and reverse events are both caused by Brownian fluctuations that raise either the reactants or the products to the transition state; their different rates reflecting only how much more likely the needed fluctuation is in one case than the other.  $\Delta G$  does NOT cause the reaction – it is merely a measure of the 'fluctuation' directional bias:  $k_f/k_r = \exp(-\Delta G/k_B T)$ ; an example "fluctuation relation".

But how can one legally permit only a reaction's 'reverse' fluctuations?

**Fluctuation relations:** An open system thermostated by a bath will undergo 'fluctuation' exchanges of energy and material with the bath which both increase and decrease the system's entropy; the former being exponentially more probable (in the magnitude of the entropy change) than the latter[1][2]:

$$\frac{p(\Delta S)}{p(-\Delta S)} = \exp(\Delta S/k_B)$$

## 2 Disequilibria conversion requires a dual-process, cross-controlled, chameleon enzyme; i.e. an 'engine'



## 3 Nitrogenase: an example from real life

Duval et al. 2013, PNAS 110/41, 16414-15419. *Electron transfer precedes ATP hydrolysis during nitrogenase catalysis*

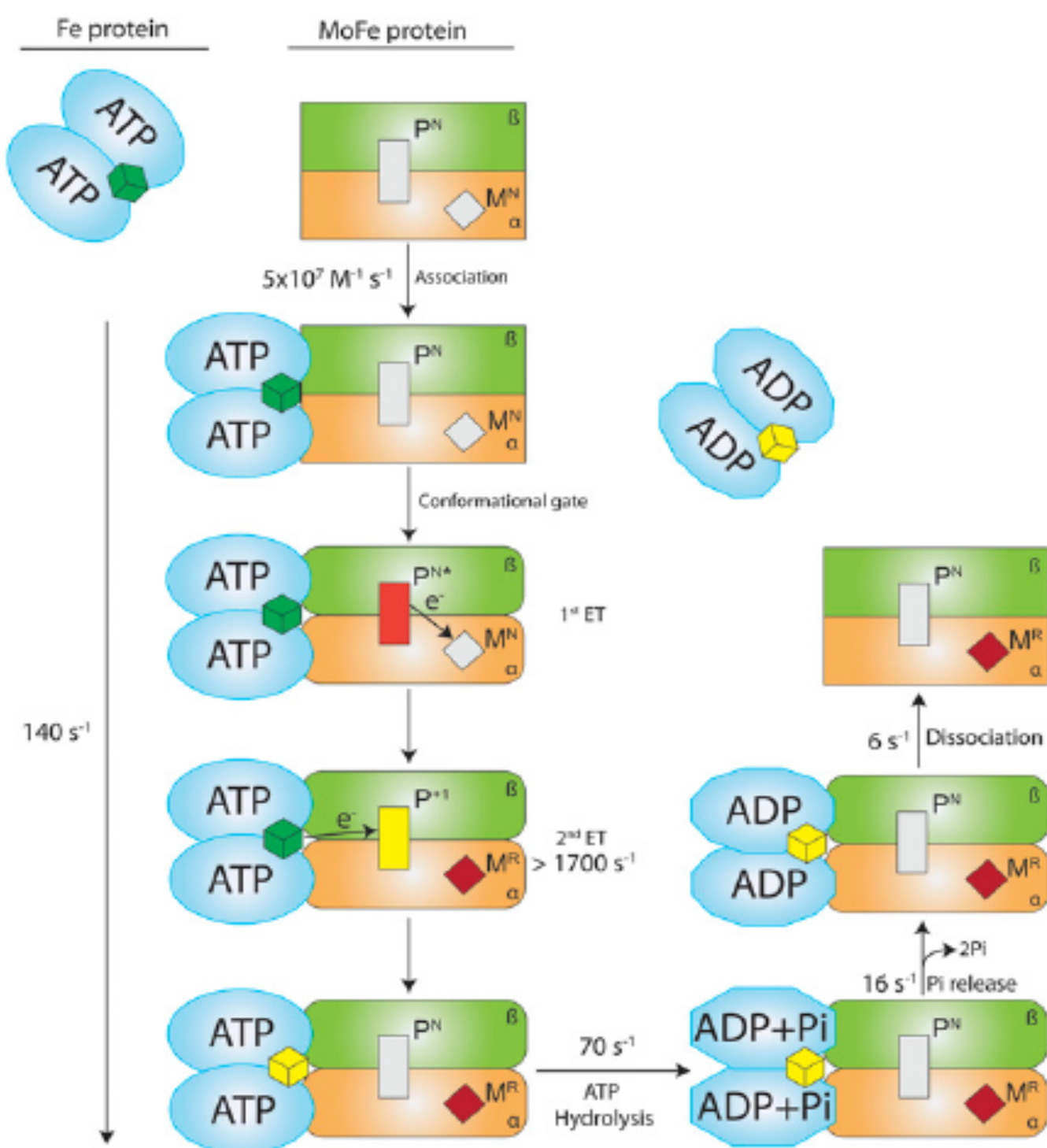


Fig. 4. Model of nitrogenase order of events. Shown is the Fe protein (blue ovals) with the [4Fe-4S] cluster in the 1+ (dark green cube) or 2+ (yellow cube) oxidation state. The MoFe protein (α-subunit orange and β-subunit green) with the P cluster (rectangle, gray PN, red activated PN\*, and yellow P+1 state) and the M cluster (diamond, gray MN and maroon MR state). The reaction sequence starts at top left with the association of the Fe protein with the MoFe protein and ends at top right with the dissociation of the oxidized Fe protein from the reduced MoFe protein. First-order rate constant ( $k, s^{-1}$ ) values for 25°C are shown. Conformational changes in the Fe protein and MoFe protein are denoted by changes in shape of the ovals or rectangles.

Eight sequential single electron (plus  $H^+$ ) reduction cycles, each driven by the 'after-the-fact' and simultaneous hydrolysis of two ATP's, achieve the reduction of one  $N_2$  to two  $NH_3$  molecules.

## 5 A green rust ramjet reducing nitrate to ammonia?

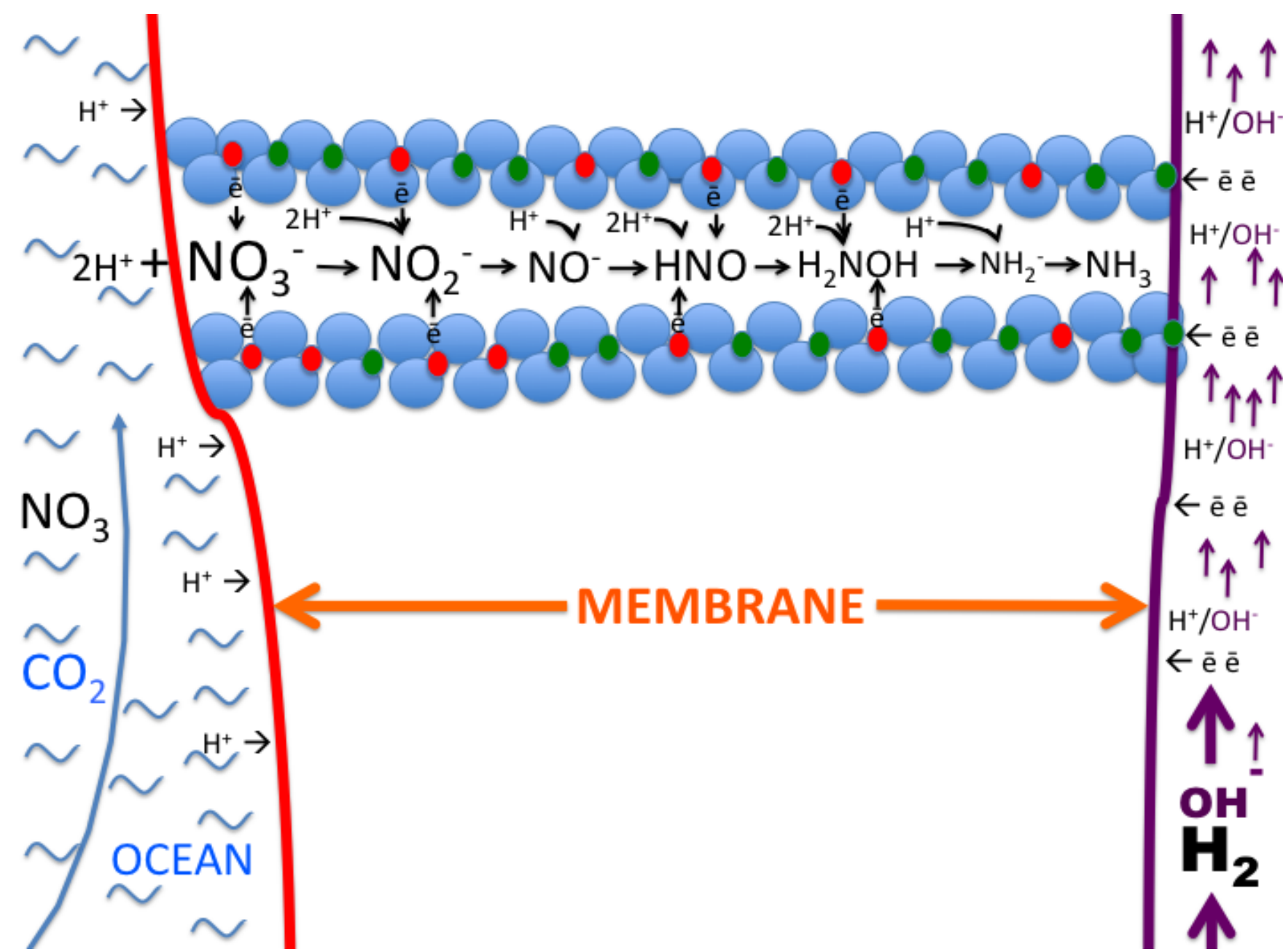
### Figure Caption

Steep redox, pH and nitrate gradients imposed across the green rust membranes of the alkaline hydrothermal mound from left(ocean) to right(vent), along with a continuous supply of hydrothermal hydrogen in the vent effluents, drive nitrate reduction. Hydrogen in the vent effluent is presumed to be oxidized by a 'protohydrogenase' which we might assume to be an iron-nickel sulfide precipitate (on the vent-side margin, not shown); the resultant electrons would be conducted ocean-ward along the iron atoms comprising the green rust (brucite-type) layers drawn by the strong (probably  $\geq 400mV$ ) voltage gradient while the released protons would be driven into the vent interior by that same gradient to be spent on the abundant hydroxyl molecules of the alkaline vent fluids. Proton flow into the interlayer from the Hadean Ocean (left), is driven by the transmembrane difference in proton chemical potential between the acidulous exterior and the alkaline interior. Nitrate in the Ocean, entering the margins of the gallery from the ocean side oxidizes the green rust causing a repulsion of the opposing ferric iron atoms, thereby giving access to the nitrate anion. This nitrate oxidizes adjacent ferrous iron atoms and is thereby concomitantly reduced to nitrite. Being of the same charge, the nitrite too, is partially immobilized. The negatively charged nitrogen-bearing anions are charge-trapped at the green rust 'inlets'. It is only when they are reduced and hydrogenated can the grip of the positively-charged interlayers be relaxed and the ammonia or ammonium ion may then be driven in the interior by the nitrate gradient.

## 4 Can minerals in the right context perform like miracles of disequilibria conversion?

A green rust 'ramjet' reducing nitrate to ammonia?

It is known that this reduction takes place in 'batch mode'[3].



The precipitate mounds formed at alkaline hydrothermal vents acting in the Hadean, would have included double layer hydroxide minerals such as 'green rust'. These act as semi-permeable membranes separating an oxidized and mildly acidic ocean (left) from the strongly alkaline and reduced vent effluents (right), thereby forming strong proton and redox gradients spanning the membranes. See figure caption in the next panel.

## 6 Concluding points

- The empowering 'reactions' in life are those that create highly specific and often quite extreme **disequilibria** (e.g. [ATP] is driven and maintained in all cells  $\approx 10^{10}$  out of equilibrium; and since the free energy ATP can supply is the log measure of this numerical factor, *the disequilibrium is the free energy*, and is zero if ATP is at equilibrium with respect to its hydrolysis products – no matter what the concentration of ATP).
- Each such creation requires an engine that, in the way here described, uses the statistical irreversibility of 'forward', fluctuation-driven, disequilibrium-dissipating reaction events in one process to **trap and accumulate 'backward', fluctuation-driven, disequilibrium-creating events** in another. In all understood examples, as is illustrated in the case of nitrogenase, this involves making the completion of each driving reaction event contingent upon, i.e. triggered by and after the fact of, the completion of a driven reaction event.
- Whereas disequilibrium conversion (aka "free energy transducing") processes are the core enabling devices of "bioenergetics" and therefore of life, they do *not* involve, or work by, the "consumption" of energy, or even the transfer of energy from the driving to the driven process. Energy is neither consumed nor transferred. The only essential role of the driving reaction is to supply **irreversibility**; which is why its own state of disequilibrium is the essential causative factor.
- The transitional first step in the **emergence of life from inanimate matter** necessarily entailed the abiotic generation, in a favorable physical context, of certain specific disequilibria, e.g. fixed C, fixed N, and a surrogate for the ATP disequilibrium (most likely of  $[PPi]$  vs.  $[Pi]^2$ ). Arguably, these are feats which the geochemistry of alkaline hydrothermal vents, acting in the Hadean, uniquely enabled.