

Energy Landscapes: Frequently Asked Questions

The global **microcanonical** and **canonical** partition functions can be written as a **superposition** of contributions from the catchment basins of all the local minima [1]:

$$\Omega(E) = \sum_i \Omega_i(E) \quad \text{and} \quad Z(T) = \sum_i Z_i(T),$$

where $\Omega_i(E)$ and $Z_i(T)$ are the **microcanonical** density of states and **canonical** partition function for local minimum i , respectively.

The **potential** energy surface is independent of mass, temperature and coordinate systems; $\Omega(E)$ and $Z(T)$ provide connections to the thermodynamic potentials in the **microcanonical** and **canonical** ensembles, namely **entropy** and **free energy**.

The canonical equilibrium **occupation probability** of minimum i is $p_i^{\text{eq}}(T) = Z_i(T)/Z(T)$, and the corresponding free energy is $F_i(T) = -kT \ln Z_i(T)$. The free energy of transition state \dagger is $F^\dagger(T) = -kT \ln Z^\dagger(T)$, where $Z^\dagger(T)$ does not include the mode corresponding to the **negative** Hessian eigenvalue.

In the canonical ensemble the equilibrium **occupation probability** and **free energy** of a group of minima, J are

$$p_J^{\text{eq}}(T) = \sum_{j \in J} p_j^{\text{eq}}(T) \quad \text{and} \quad F_J(T) = -kT \ln \sum_{j \in J} Z_j(T),$$

and the free energy of the **transition states** connecting J and L is then

$$F_{LJ}^\dagger(T) = -kT \ln \sum_{(lj)^\dagger} Z_{lj}^\dagger(T), \quad l \in L, \quad j \in J,$$

$$\text{with} \quad k_{LJ}^\dagger(T) = \sum_{(lj)^\dagger} \frac{p_j^{\text{eq}}(T)}{p_J^{\text{eq}}(T)} k_{lj}^\dagger(T) = \frac{kT}{h} \exp \left[-\frac{\left(F_{LJ}^\dagger(T) - F_J(T) \right)}{kT} \right].$$

The total (free) energy is **extensive**, and scales with system size, along with the energy range spanned by the lowest to highest minima. However, **barrier heights** and **energy differences** between minima directly connected by transition states (saddles of Hessian index one [2]) are **intensive** quantities.

The relative **equilibrium occupation probabilities** and **rate constants** [3] between these minima depend on **ratios** of intensive quantities, namely energy **differences** and kT . Hence the equilibrium concentration of a particular defect and the defect migration rate in a crystal do **not** depend on the size of the crystal [4, 5].

In contrast, an **inappropriate** comparison of the **extensive** internal energy with **intensive** barriers leads to the conclusion that '**activated**' processes cease to exist as the system size increases [6, 7].

Genuine **finite size** effects are certainly of interest, for example, the sharpening of **heat capacity** peaks for **first order**-type transitions [8].

It can be helpful to think of the energy landscape in terms of analogies from a mountain range, following **James Clark Maxwell** in his article for *Philosophical Magazine* 'On Hills and Dales' in 1870 [9]. Transition states then correspond to **watersheds**, and steepest-descent paths to **watercourses**.

However, **low-dimensional** projections can also be **misleading** [10–17]. In particular, the system is **never** 'above' the potential energy surface: the potential energy function is defined for any configuration.

The effect of increasing the temperature is to **shift** the **occupation probabilities** to states with **higher entropy** and **higher potential energy**. The **temperature gradients** of the $p_i^{\text{eq}}(T)$ can be related to **peaks** in the heat capacity [18].

We can distinguish **two** contributions to the entropy. There is an (anharmonic) **vibrational** entropy associated with each local minimum, determined by the phase volume contained within the **basin of attraction**.

The contribution associated with the **multiplicity** and **distribution** of the minima is the **landscape entropy** [19–21], or inherent structure [22] entropy, S_{IS} .

Rotational contributions can also be included, but are usually dominated by the **vibrational** component, which is often treated in a **harmonic** normal mode approximation [1].

The landscape contribution is **convoluted** with the local vibrational densities of states to obtain the full **configurational** entropy, S_c .

We can calculate S_{IS} by sampling the **potential energy density** of local minima [21,23]. (Note that some authors refer to S_{IS} as the configurational entropy.)

We can also consider the local densities of states associated with distinct **pathways** between **product** and **reactant** states, and define a **pathway entropy** from the multiplicity of **alternative routes** mediated by different transition states [24–26].

The number of local minima and transition states increase **exponentially** with system size, [5, 22, 27] and the number of transition states per minimum is expected to increase **linearly** [4]. This increase in connectivity **cannot** be represented properly by surfaces in three dimensions [26].

However, **efficient relaxation** to the **global minimum** can be encoded in the landscape if there is a single **funnel** structure, corresponding to a set of kinetically convergent pathways [28]. This is the **organisation** we expect for naturally occurring **proteins** that have a single function [29, 30], and for ‘**magic number**’ clusters, such as buckminsterfullerene [31, 32].

In contrast, landscapes with distinct low energy structures **separated** by high barriers are considered ‘**frustrated**’ [29, 30]. We could also describe such multifunnel landscapes as ‘rugged’, but some authors associate this term with the existence of many local minima.

The existence of more local minima does **not** necessarily lead to more complex behaviour, since funnelled landscapes also exist for **larger** systems. Hence it may be best to refer to **multifunnel** landscapes as **frustrated**.

The presence of multiple low energy morphologies provides a mechanism to encode **multifunctional** properties [33]. Such multifunnel landscapes have been characterised for certain **biomolecules** [34, 35], which may constitute **evolved** multifunctional systems. Hence we have a **design principle** for achieving targeted properties, such as **switches**, for potential technological applications.

References

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