A nonequilibrium equality for free energy differences

C. Jarzynski

Institute for Nuclear Theory, University of Washington

Seattle, WA 98195*

chrisj@t6-serv.lanl.gov

(February 1, 2008)

Abstract

An expression is derived for the classical free energy difference between two configurations of a system, in terms of an ensemble of finite-time measurements of the work performed in parametrically switching from one configuration to the other. Two well-known equilibrium identities emerge as limiting cases of this result.

Typeset using REVTEX

^{*}Present address: Theoretical Astrophysics, T-6, MS B288, Los Alamos National Laboratory, Los Alamos, NM 87545

Consider a finite classical system in contact with a heat reservoir. A central concept in thermodynamics is that of the work performed on such a system, when some external parameters of the system are made to change with time. (These parameters may represent, for instance, the strength of an external field, or the volume of space within which the system is confined, or, more abstractly, some particle-particle interactions which are turned on or off during the course of a molecular dynamics simulation.) When the parameters are changed infinitely slowly along some path γ from an initial point A to a final point B in parameter space, then the total work B performed on the system is equal to the Helmholtz free energy difference AB between the initial and final configurations [1]: B is B in the parameters are switched along B at a finite rate, then B will depend on the microscopic initial conditions of the system and reservoir, and will on average exceed AB:

$$\overline{W} \ge \Delta F.$$
 (1)

Here and in Eq.2 below, the overbar denotes an average over an ensemble of measurements of W, where each measurement is made after first allowing the system and reservoir to equilibrate at temperature T, with the parameters fixed at A. (The path γ from A to B, and the rate at which the parameters are switched along this path, remain unchanged from one measurement to the next.) The difference $\overline{W} - \Delta F$ is just the dissipated work, W_{diss} , associated with the increase of entropy during an irreversible process.

Eq.1 is an inequality. By contrast, the new result derived in this paper is the following equality:

$$\overline{\exp{-\beta W}} = \exp{-\beta \Delta F},\tag{2a}$$

or, equivalently,

$$\Delta F = -\beta^{-1} \ln \overline{\exp -\beta W}, \tag{2b}$$

where $\beta \equiv 1/k_BT$. This result, which allows one to extract equilibrium information (the free energy difference ΔF) from the ensemble of non-equilibrium (finite-time) measurements

described above, is independent of both the path γ from A to B, and the rate at which the parameters are switched along the path.

Before proceeding with the proof of Eq.2, we establish notation, and then relate Eq.2 to two well-known equilibrium identities for ΔF . Since we have fixed our attention on a particular path γ in parameter space, it will be convenient to henceforth view the system as parametrized by a single quantity λ , which increases from 0 to 1 as we travel from A to B along γ . Let $\mathbf{z} \equiv (\mathbf{q}, \mathbf{p})$ denote a point in the phase space of the system, and let $H_{\lambda}(\mathbf{z})$ denote the Hamiltonian for the system, parametrized by the value of λ . Next, let Z_{λ} denote the partition function, let $\langle \cdots \rangle_{\lambda}$ denote a canonical average, and let $F_{\lambda} = -\beta^{-1} \ln Z_{\lambda}$ denote the free energy, all with respect to the Hamiltonian H_{λ} and the temperature T. We are interested in the following scenario, which we will refer to as "the switching process": the system evolves, in contact with a heat reservoir, as the value of λ is switched from 0 to 1, over a total switching time t_s . Without loss of generality, assume a constant switching rate, $\dot{\lambda} = t_s^{-1}$. For a given realization of the switching process, the evolution of the system is described by a (stochastic) trajectory $\mathbf{z}(t)$, and the work performed on the system is the time integral of $\dot{\lambda}$ $\partial H_{\lambda}/\partial \lambda$ along this trajectory:

$$W = \int_0^{t_s} dt \,\dot{\lambda} \, \frac{\partial H_{\lambda}}{\partial \lambda} \Big(\mathbf{z}(t) \Big). \tag{3}$$

Now imagine an *ensemble* of realizations of the switching process (with γ and t_s fixed), with the microscopic initial conditions for the system and reservoir generated from a thermal equilibrium ensemble at temperature T. Then W may be computed separately for each trajectory $\mathbf{z}(t)$ in the ensemble, and the overbars appearing in Eqs.1 and 2 indicate an average over the distribution of values of W thus obtained.

In the limiting cases of infinitely slow and infinitely fast switching of the external parameters, we know explicitly the ensemble distribution of values of W, and thus can readily check the validity of our central result. In the slow limit $(t_s \to \infty)$, the system is in quasi-static equilibrium with the reservoir throughout the switching process, hence $W = \int_0^1 d\lambda \, \langle \partial H_{\lambda} / \partial \lambda \rangle_{\lambda}$ for every trajectory in the ensemble. Eq.2b then reduces to:

$$\Delta F = \int_0^1 d\lambda \left\langle \frac{\partial H_\lambda}{\partial \lambda} \right\rangle_\lambda. \tag{4}$$

In the opposite limit $(t_s \to 0)$, the switching of the Hamiltonian is instantaneous, and so the work performed is simply $W = H_1 - H_0 \equiv \Delta H$, evaluated at the initial conditions [2]. Since we have a canonical distribution of initial conditions, Eq.2b becomes, in this case:

$$\Delta F = -\beta^{-1} \ln \left\langle \exp -\beta \Delta H \right\rangle_0. \tag{5}$$

These two results, Eqs.4 and 5, are well-established identities for the free energy difference ΔF [3,4]. Note that both give ΔF in terms of equilibrium (canonical) averages. By contrast, in the intermediate case of finite t_s , our ensemble of trajectories lags behind the equilibrium distribution in phase space as H_{λ} changes with time. In this sense, Eq.2 is an explicitly non-equilibrium result.

To prove our central result, it is instructive to first consider what happens when there is no heat reservoir during the switching process. The evolution of the system is then described by a deterministic trajectory $\mathbf{z}(t)$ which evolves under $H_{\lambda}(\mathbf{z})$, as λ changes from 0 to 1 over a time t_s . Consider an ensemble of such trajectories, defined by a canonical distribution of initial conditions (at a temperature T). This ensemble is described by a phase space density $f(\mathbf{z},t)$ which satisfies $f(\mathbf{z},0) = Z_0^{-1} \exp{-\beta H_0(\mathbf{z})}$, and which evolves under the Liouville equation, $\partial f/\partial t + \{f, H_{\lambda}\} = 0$, with $\lambda = \lambda(t) = t/t_s$. Here, $\{\cdot, \cdot\}$ denotes the Poisson bracket. Since the evolution is deterministic, a particular trajectory in this ensemble is uniquely specified by single point: there is exactly one trajectory which passes through a given \mathbf{z} at time t. This means we can define a "work accumulated" function $w(\mathbf{z},t)$, as follows. For the trajectory which passes through the point \mathbf{z} at time t, $w(\mathbf{z},t)$ is the work performed on that trajectory (the time integral of $\lambda \partial H_{\lambda}/\partial \lambda$) up to time t. Since the total work W is just the work accumulated up to time t_s (Eq.3), the ensemble average $\overline{\exp{-\beta W}}$ may be expressed as

$$\overline{\exp{-\beta W}} = \int d\mathbf{z} f(\mathbf{z}, t_s) \exp{-\beta w(\mathbf{z}, t_s)}.$$
 (6)

Now, the work done on an isolated Hamiltonian system is equal to the change in its energy. Thus, $w(\mathbf{z},t) = H_{\lambda}(\mathbf{z}) - H_0(\mathbf{z}_0)$, where $\mathbf{z}_0 = \mathbf{z}_0(\mathbf{z},t)$ is the initial condition for the trajectory which passes through \mathbf{z} at time t, and $\lambda = \lambda(t)$. Furthermore, Liouville's theorem tells us that phase space density is conserved along any trajectory, hence $f(\mathbf{z},t) = f(\mathbf{z}_0,0) = Z_0^{-1} \exp{-\beta H_0(\mathbf{z}_0)}$. Combining these results immediately gives

$$f(\mathbf{z}, t) \exp -\beta w(\mathbf{z}, t) = Z_0^{-1} \exp -\beta H_{\lambda}(\mathbf{z}). \tag{7}$$

Eq.6 then becomes

$$\overline{\exp -\beta W} = Z_0^{-1} \int d\mathbf{z} \, \exp -\beta H_1(\mathbf{z}) = Z_1/Z_0. \tag{8}$$

Since $\Delta F = -\beta^{-1} \ln(Z_1/Z_0)$, we have established the validity of Eq.2 for the case in which the system is isolated during the switching process.

Now consider the situation in which the system is coupled to a reservoir. We assume that the system of interest and the reservoir together constitute a larger, isolated Hamiltonian system. Let \mathbf{z}' denote a point in the phase space of the reservoir, let $\mathcal{H}(\mathbf{z}')$ be the Hamiltonian for the reservoir alone, and let $\mathbf{y} = (\mathbf{z}, \mathbf{z}')$ denote a point in the full phase space of system and reservoir. Motion in the full phase space is deterministic, and governed by a Hamiltonian $G_{\lambda}(\mathbf{y}) = H_{\lambda}(\mathbf{z}) + \mathcal{H}(\mathbf{z}') + h_{int}(\mathbf{z}, \mathbf{z}')$, where the interaction term h_{int} couples the system of interest to the reservoir. Let Y_{λ} be the partition function for G_{λ} . We explicitly assume the reservoir to be large enough, and the interaction energy h_{int} small enough [5], that when λ is held fixed the system of interest samples its phase space according to the Boltzmann factor $e^{-\beta H_{\lambda}(\mathbf{z})}$. Now imagine that, at t=0, we populate the full phase space with a canonical distribution of initial conditions, using the Boltzmann factor $e^{-\beta G_0(\mathbf{y})}$. (This corresponds to allowing the coupled system and reservoir to equilibrate at temperature T, before each realization of the switching process.) From this ensemble of initial conditions, an ensemble of trajectories $\mathbf{y}(t)$ evolves deterministically under G_{λ} , as λ switches from 0 to 1. Since the system of interest and reservoir together constitute an isolated Hamiltonian system, the work W performed on the system of interest is equal to the change in the total energy of the system and reservoir: $W = G_1(\mathbf{y}(t_s)) - G_0(\mathbf{y}(0))$. Therefore, applying the analysis of the previous paragraph to the situation considered here, with \mathbf{y} , G_{λ} , and Y_{λ} replacing \mathbf{z} , H_{λ} , and Z_{λ} , respectively, we get

$$\overline{\exp{-\beta W}} = Y_1/Y_0. \tag{9}$$

The right side of Eq.9 depends only on the initial and final Hamiltonians G_0 and G_1 , and on the temperature T, which means that the ensemble average $\overline{\exp{-\beta W}}$ is independent of the switching time t_s (and also of the path from A to B in parameter space). But we already know that $\overline{\exp{-\beta W}} = \exp{-\beta \Delta F}$ in the limit $t_s \to \infty$, since $W = \Delta F$ for every member of the ensemble, in that limiting case. We therefore conclude that

$$\overline{\exp{-\beta W}} = \exp{-\beta \Delta F} \tag{10}$$

for all values of t_s (and all paths γ). This proves our central result, Eq.2.

Eq.9, which tells us that the ensemble average $\overline{\exp{-\beta W}}$ is independent of both γ and t_s , is identically true, given the formulation of the problem. However, in going from Eq.9 to Eq.10, we invoke a result from quasi-equilibrium statistical mechanics, which relies on the assumption of weak coupling (small h_{int}). Eq.2, therefore, is valid for sufficiently weak coupling between the system of interest and the reservoir. This may be seen more directly by writing an explicit expression for the ratio Y_1/Y_0 appearing on the right side of Eq.9: only if h_{int} may be neglected does this ratio immediately reduce to Z_1/Z_0 (= $\exp{-\beta \Delta F}$).

Note that the inequality $\overline{W} \geq \Delta F$ (Eq.1) follows directly from the equality $\overline{\exp{-\beta W}} = \exp{-\beta \Delta F}$ (Eq.2a), by application of the mathematical identity $\overline{\exp{x}} \geq \exp{\overline{x}}$ [6]. This establishes $\overline{W} \geq \Delta F$ directly from a microscopic, Hamiltonian basis, rather than by invoking the increase of entropy. (In the limit $t_s \to 0$, we have $\overline{W} = \langle \Delta H \rangle_0$, and Eq.1 reduces to the Gibbs-Bogoliubov-Feynman bound [6], $\langle \Delta H \rangle_0 \geq \Delta F$.)

It is also worthwhile to point out that the right side of Eq.2b may be expanded as a sum of cumulants (see Eq.[9] of Ref. [4]):

$$\Delta F = \sum_{n=1}^{\infty} (-\beta)^{n-1} \frac{\omega_n}{n!},\tag{11}$$

where ω_n is the *n*'th cumulant of the ensemble distribution of values of W. If this distribution happens to be Gaussian (as may be expected for sufficiently slow switching), then only the first two terms survive, and we have

$$\Delta F = \overline{W} - \beta \sigma^2 / 2,\tag{12}$$

where $\sigma^2 \equiv \overline{W^2} - \overline{W}^2$ is the ensemble variance of W. The dissipated work W_{diss} (= $\overline{W} - \Delta F$) is then related to the fluctuations in W by: $W_{diss} = \beta \sigma^2/2$. This is a fluctuation-dissipation relation, and has been obtained within the context of numerical simulations by Hermans [7]. (A related result for microcanonical ensembles has been derived by Ott [8].)

The central result of this paper, Eq.2, makes a concrete prediction regarding the outcome of an ensemble of measurements, which in principle is subject to experimental verification. Moreover, this result ought to be valid quite generally, provided the coupling to the reservoir is sufficiently weak, and quantal effects may be ignored. In practice, however, the applicability of Eq.2 may be severely limited by the following considerations. If the fluctuations in W from one measurement to the next are much larger than k_BT (i.e. if $\sigma \gg \beta^{-1}$), then the ensemble average of $\exp -\beta W$ may be dominated by values of W many standard deviations below \overline{W} . Since such values of the work represent statistically very rare events, it would require an unreasonably large number of measurements of W to determine $\overline{\exp -\beta W}$ with good accuracy. Therefore, given a specific system of interest, switching path γ , and switching time t_s , the fluctuations in the work W must not be much greater than k_BT , if we are to have any hope of verifying Eq.2 experimentally. This condition pretty much rules out macroscopic systems of interest. In recent years, however, the direct manipulation of nanoscale objects — and the measurement of forces thereon [9] — has become feasible. Such systems may offer the best chance for experimentally testing the new result of this paper.

So far, we have implicitly assumed that our system is coupled to a *physical* heat reservoir. It is interesting, however, to discuss this problem within the context of numerical simulations. On a computer, a heat reservoir must somehow be "mocked up". One way to accomplish this is with a Nosé-Hoover (NH) thermostat [10], or some variant thereof. In its simplest

form, this method replaces the reservoir with a single variable ζ ; motion in the extended phase space (\mathbf{z}, ζ) is governed by the NH equations

$$\left\{\dot{q} = p/m \;\; , \;\; \dot{p} = -\nabla\Phi_{\lambda} - \zeta p\right\}_{n}$$
 (13)

$$\dot{\zeta} = (K/K_0 - 1)/\tau^2. \tag{14}$$

[We have assumed a kinetic + potential Hamiltonian: $H_{\lambda} = p^2/2m + \Phi_{\lambda}(\mathbf{q})$. The index n runs over all D degrees of freedom of the system, $K = p^2/2m$ is the total kinetic energy of the system, $K_0 = \beta^{-1}D/2$ is the thermal average of K, and τ is a parameter which acts as a relaxation time.] For λ fixed, a trajectory $\mathbf{z}(t)$ generated by these equations of motion samples phase space according to the Boltzmann factor $\exp{-\beta H_{\lambda}(\mathbf{z})}$, provided that the evolution is sufficiently chaotic.

It is interesting to ask, does Eq.2 remain valid if the system evolves under the NH equations, rather than under the influence of a physical reservoir? Let us consider an ensemble of initial conditions in the extended phase space, described by the density

$$f(\mathbf{z}, \zeta, 0) = cZ_0^{-1} \exp{-\beta Q_0(\mathbf{z}, \zeta)},\tag{15}$$

where $Q_{\lambda}(\mathbf{z},\zeta) \equiv H_{\lambda}(\mathbf{z}) + D\zeta^2\tau^2/2\beta$, and $c = (D\tau^2/2\pi)^{1/2}$ is a normalization factor. (The distribution $cZ_{\lambda}^{-1} \exp{-\beta Q_{\lambda}}$ is stationary under the NH equations when λ is held fixed, and may be viewed as the "canonical" distribution in the extended phase space.) Allowing these initial conditions to evolve under the NH equations, as λ changes from 0 to 1, we obtain an ensemble of trajectories described by a time-dependent density $f(\mathbf{z},\zeta,t)$. As before, the work performed on each member of the ensemble is defined to be the time integral of $\dot{\lambda} \partial H_{\lambda}/\partial \lambda$. We now introduce a "work accumulated" function $w(\mathbf{z},\zeta,t)$, analogous to $w(\mathbf{z},t)$ introduced earlier. It is straightforward to establish that

$$f(\mathbf{z},\zeta,t) = f(\mathbf{z}_0,\zeta_0,0) \exp\left[D\int_0^t \zeta(t')dt'\right]$$
(16)

$$w(\mathbf{z}, \zeta, t) = Q_{\lambda}(\mathbf{z}, \zeta) - Q_{0}(\mathbf{z}_{0}, \zeta_{0}) + \beta^{-1} D \int_{0}^{t} \zeta(t') dt', \tag{17}$$

where (\mathbf{z}_0, ζ_0) are the initial conditions associated with the trajectory which passes through (\mathbf{z}, ζ) at time t, and the integral $\int_0^t \zeta \, dt'$ is performed along this trajectory. Then, repeating

the steps leading to Eq.8, we again get $\exp{-\beta W} = \exp{-\beta \Delta F}$, where the overbar now denotes an average over our ensemble of NH trajectories. Thus, Eq.2 remains valid (given the canonical distribution of initial conditions specified by Eq.15) when the system is coupled to a Nosé-Hoover thermostat, as per Eqs.13 and 14. This result is identically true: no weak coupling assumption is necessary, nor do we need to assume that the evolution is chaotic.

It may similarly be established that Eq.2 is valid, without additional assumptions, when the thermostat is numerically implemented using the Metropolis Monte Carlo algorithm, rather than Nosé-Hoover dynamics. In that situation, both the system and the Hamiltonian evolve by discrete steps, and the work performed is a sum of changes in H_{λ} , evaluated at successive locations of the system in phase space [11].

Numerical simulations of this sort are often used to compute free energy differences of physical, chemical or biological interest [12]. Typically, a number of simulations of slow switching from one configuration to another are performed, and the resulting average work is used as an upper bound on ΔF , as per Eq.1; reversing direction, a lower bound is established [11]. The central result of the present paper may be useful in this situation: rather than taking the straight average of W, one can instead perform the average of $\exp{-\beta W}$, then take the logarithm and multiply by $-\beta^{-1}$, as per Eq.2b. In principle this converges to the exact value of ΔF (rather than to an upper or lower bound) as the number of simulations tends to infinity. In practice, however, the same note of caution applies here as in the case of coupling to a physical heat bath: if the fluctuations in W from one simulation to the next are much larger than k_BT , then prohibitively many simulations may be necessary to determine $\overline{\exp{-\beta W}}$ with the desired accuracy. Thus, we may expect Eq.2 to be useful in free energy computations, only if σ is not much larger than β^{-1} . Whether or not this condition holds for a given system will depend on factors such as the number of degrees of freedom, the switching time t_s , the switching path γ , and the numerical implementation of the heat bath.

To summarize, the central result of this paper is an equality which gives the free energy

difference ΔF between two configurations A and B of a classical, parameter-dependent system, in terms of an ensemble of finite-time measurements of the work performed on the system as it is switched from A to B. The derivation of this result relies on the assumption of weak coupling between system and reservoir, but otherwise follows directly from the properties of Hamilton's equations. Two well-known equilibrium identities for ΔF , Eqs.4 and 5, emerge as limiting cases of this more general, non-equilibrium result. Practical considerations in all likelihood limit the applicability of Eq.2 to systems of no more than a moderate number of degrees of freedom (e.g., nanoscale systems). Finally, the equality may be useful when numerical simulations of thermostatted systems are used to compute free energy differences.

ACKNOWLEDGMENTS

It is a pleasure to acknowledge that numerous stimulating discussions — including those with G.F.Bertsch, A.Bulgac, M.DenNijs, P.DeVries, G.J.Hogenson, J.Hunter III, D.B.Kaplan, W.P.Reinhardt, T.Schaefer, D.Thouless, and R.Venugopalan — contributed to the derivation and understanding of the results presented in this paper. This work was supported by the Department of Energy under Grant No. DE-FG06-90ER40561.

REFERENCES

- [1] L.D.Landau and E.M.Lifshitz, *Statistical Physics*, 3rd ed., Part 1, section 15 (Pergamon Press, Oxford, 1990). We use the term "configuration" to denote a fixed set of parameter values. The free energy, an equilibrium quantity, is a function of configuration and temperature.
- [2] An exception to this statement occurs if the system in question is confined within an box with perfectly hard walls, and if changing λ corresponds to moving these walls. In this case, Eq.2 remains true for any finite t_s , but does not reduce to Eq.5 in the limit $t_s \to 0$.
- [3] J.G.Kirkwood, J.Chem.Phys. **3**, 300 (1935).
- [4] R.Zwanzig, J.Chem.Phys. **22**, 1420 (1954).
- [5] F.Reif, Fundamentals of Statistical and Thermal Physics (McGraw-Hill, New York, 1965), p. 95.
- [6] D.Chandler, Introduction to Modern Statistical Mechanics (Oxford University, New York, 1987), Sec. 5.5.
- [7] J.Hermans, J.Chem.Phys. **95**, 9029 (1991).
- [8] E.Ott, Phys.Rev.Lett. 42, 1628 (1979), see Eq.[15] and footnote (7) therein.
- [9] See, e.g., N.Agraït, G.Rubio, and S.Vieira, Phys.Rev.Lett. 74, 3995 (1995).
- [10] S.Nosé, J.Chem. Phys. 81, 511 (1984), W.G.Hoover, Phys. Rev. A 31, 1695 (1985).
- [11] J.E.Hunter III, W.P.Reinhardt, and T.F.Davis, J.Chem. Phys 99, 6856 (1993).
- [12] For reviews, see T.P.Straatsma and J.A.McCammon, Annu.Rev.Phys.Chem. 43, 407 (1992); M.Karplus and G.A.Petsko, Nature 347, 631 (1990); D.L.Beveridge and F.M.DiCapua, Annu.Rev.Biophys.Biophys.Chem. 18, 431 (1989); C.L.Brooks III, M.Karplus, and B.M.Pettitt, Adv.Chem.Phys. 71, 1 (1988).