as high as those following intramuscular injections of 500,000 units suspended in peanut oil and beeswax.

References

1. Atcheson, D. W., and Edmeades, D. T. *Science*, 1945, **102**, 199.
2. Callomon, F. T., Kolmer, J. A., Rule, A. M., and Paul, A. J. *Proc. Soc. exp. Biol. Med.*, in press.
3. Freund, J., and Thomson, K. J. *Science*, 1945, **101**, 468; *Proc. Soc. exp. Biol. Med.*, 1945, **59**, 145.
4. Kirby, W. M. M., *et al.* *J. Amer. med. Ass.*, 1945, **129**, 940.
5. Kolmer, J. A., Bondi, A., Jr., Warner, H. F., and Dietz, C. (To be published.)
6. Nichols, D. R., and Haunz, E. A. *Proc. Staff Meet., Mayo Clin.*, 1945, **20**, 403.
7. Romansky, M. J., and Rittman, G. E. *Science*, 1944, **100**, 196; *Bull. U. S. Army med. Dept.*, 1944, **43**, No. 81.
8. Stebbins, R. B., and Robinson, H. J. *Proc. Soc. exp. Biol. Med.*, 1945, **59**, 255.
9. Zinnamon, B. L., and Seeberg, V. P. *Ven. Dis. Inf.*, 1945, **31**, 26.

Effect of Di-Isopropyl Fluorophosphate (DFP) on the Action Potential of Muscle

René Couteaux,[1] Harry Grundfest, David Nachmansohn, and Mortimer A. Rothenberg

Department of Neurology, College of Physicians and Surgeons, Columbia University, New York City

Di-isopropyl fluorophosphate (DFP) abolishes the nerve action potential, but this effect is reversible for a limited period of time. DFP is a strong inhibitor of cholinesterase. A striking parallelism between the reappearance of the action potential and cholinesterase activity in nerve can be demonstrated during the recovery from DFP poisoning. The inhibition of cholinesterase by DFP can also be reversed *in vitro* during a period of time comparable to that in the experiments on nerves (*1*). These observations are consistent with the concept that cholinesterase activity and, consequently, the release of acetylcholine are essential events in the conduction of the nerve impulse.

It is generally considered that the mechanisms of the axonal and end-plate potentials are basically identical (*4*). The role of acetylcholine in the end-plate potential is supported by the relation between the activity of cholinesterase and the action potential of the electric organ, which may be considered analogous to the end-plate potential (*5*). Further support is found in the persistence of the high cholinesterase concentration at the motor end plate after complete degeneration of the axon (soleplate) (*2, 3*).

No facts are available concerning the chemical mechanism involved in the action potential of muscle, although many physiologists believe that the electrical manifestations of nerve and muscle are fundamentally identical. Muscle fibers and nerves are the only tissues which contain specific cholinesterase (*6*). This makes possible the assumption that acetylcholine plays a role in both tissues. However, the presence of an enzyme alone does not permit an interpretation of its function. We have therefore tested whether DFP abolishes the action potential of muscle as it does that of nerve.

Frogs (*Rana pipiens*) were curarized with crystalline *d*-tubocurarine chloride (Squibb). After curarization, the sartorius muscle was excised and mounted in a specially constructed chamber. The action potentials evoked by single electrical stimuli were recorded by means of a cathode-ray oscillograph. When not stimulated, the muscle was kept immersed in a Ringer solution containing 0.1 mg./cc. of curarine. This solution was then replaced by an identical solution containing DFP. Under the effect of DFP the action potential of the muscle rapidly disappears. With a concentration of 2 mg. of DFP/cc., the action potential is abolished in as little as 8 minutes. With a concentration of 1 mg. of DFP/cc., the abolition takes longer (20–30 minutes). After washing with the curarine Ringer solution (without DFP) the reappearance of the response is observed.

These experiments present the first evidence that acetylcholine may play a role in the muscle action potential. They are consistent with the idea that the natures of axon, end-plate, and muscle action potentials are basically identical.

---

[1] Laboratoire d'Anatomie comparée, University of Paris.

References

1. Bullock, T. H., Grundfest, H., Nachmansohn, D., Rothenberg, M. A., and Sterling, K. *J. Neurophysiol.*, 1946, **9**, 253.
2. Couteaux, R. *Bull. Biol.*, 1942, **76**, 14.
3. Couteaux, R., and Nachmansohn, D. *Proc. Soc. exp. Biol., N. Y.*, 1940, **43**, 177.
4. Eccles, J. C. *Trans. N. Y. Acad. Sci.*, in press.
5. Nachmansohn, D., Coates, C. W., and Rothenberg, M. A. *J. biol. Chem.*, 1946, **163**, 39.
6. Nachmansohn, D., and John, H. M. *J. biol. Chem.*, 1945, **158**, 157.

Derivation, Interpretation, and Application of the Second Law of Thermodynamics

P. G. Nutting

3216 Oliver Street, N.W., Washington, D. C.

The second law of thermodynamics is commonly derived by means of an extended series of differential equations not easy to follow and involving so many assumptions and limitations that the result is not altogether convincing. Its physical interpretation is given in a wide variety of statements. That a number of the fundamental relations of thermodynamics may be simply and directly derived from it appears to have been entirely overlooked. It is here derived as a byproduct of Gibbs's masterful general treatment, but apparently neither Gibbs nor any of his followers ever noted it.

As with the generalized potentials of mechanics, the thermodynamic potential of Gibbs, $U - ST + pv$, is of little interest except in its differential form, $dU - TdS - SdT + pdv + vdp$. This is, of course, zero throughout any body of uniform temperature, pressure, and composition, since the total energy added (dU), the thermal energy ($dQ = TdS$), and the mechanical work ($dW = pdv$) must sum up to zero,

(1) $dU - TdS + pdv = 0$; hence also

(2) $-SdT + vdp = 0$, the Second Law.

This derivation and statement ($SdT = vdp$) of the second law is as simple as could be desired. In this form it is too general to apply to special groups of problems until relations between two or more of its four variables are given. In the form (2), it is essentially an equation of state. Mathematics does not give the relation between vdp and pdv, but physical data indicate that they are proportional to each other and in a few cases equal. They have identical dimensions (energy). The same may be said of SdT and TdS.

In physical terms, the second law states that the thermal and mechanical energy functions (SdT and vdp) remain equal whatever the nature and amount of the external energy (dU) added or removed, for any body in any state, so long as p, T, and composition are uniform throughout.

Some applications of (2) to groups of physical problems will illustrate the methods used and indicate how it may be checked with experimental data. When a body exists in *two phases,* such as a melting solid or a liquid and its vapor, $dT : dp$ is the same for both phases, and (2) becomes $S_2 - S_1 = (v_2 - v_1)\, dp : dT$, the subscripts referring to the two phases. But $T(S_2 - S_1) = L$, the latent heat; therefore

$$(3) \quad L = T(S_2 - S_1) = T(v_2 - v_1)\frac{dp}{dT} = p(v_2 - v_1)\frac{d \log p}{d \log T}.$$

This is the familiar Clausius equation for the variation of vapor pressure with temperature. It applies equally to the change of melting point with pressure. With the limitation that one specific volume is negligibly small compared with the other, $pv_2 = RT$, and (3) becomes the Le Chatelier-van't Hoff equation, $d \log p : d \log T = L : RT$. Other slight modifications give the "reaction isochore" of Nernst and the Arrhenius-Boltzmann equation for atomic heats. The extension to three phases is obvious.

In applying the second law to deformation within a *single phase* it is to be noted that here S and v vary continuously with p and T. Hence, instead of $S_2 - S_1$ and $v_2 - v_1$ we have dS and dv, and therefore (2) takes the form

$$(4) \quad \frac{dT}{dp} = \frac{dv}{dS},$$

which is applicable to changes within a single phase without any other limitation. Within one phase $TdS = dQ = C_p dT$ and $dv = \alpha v dT$. Note that the thermal coefficient of expansion (α) is not limited to constant values as in the inexact integral form, $v = v_0(1 + \alpha(T - T_0))$.

These substitutions of dv and dS in (4) give at once the celebrated Thomson (Kelvin) equation,

$$(5) \quad \frac{dT}{dp} = \frac{T\alpha v}{C_p},$$

for the change in temperature caused by change of pressure, developed by him about 1850 using many pages of differential equations still copied in even modern texts. Equation (5) has been amply verified by experimental data and has been applied by the writer (paper in press) to the Washington monument data on steel tape of Van Orstrand. In (5), v is the volume of unit mass, since specific heat (C_p) is so limited. The heat developed in any volume is $dQ = T\alpha v dp$. Writing $dv = v\beta dp$, $dT : dp = \beta : \alpha$. The entropy of deformation $dS = \alpha v dp$.

A simple, useful relation between heat and work is obtained by multiplying (4) by p/T. Thus,

$$(6) \quad \frac{pdT}{Tdp} = \frac{pdv}{TdS} = \frac{dW}{dQ} = \frac{d \log T}{d \log p},$$

a dimensionless ratio that may be read directly from a log T, log p plot of data. For viscous flow (steady state) $dw = dQ$.

These single-phase relations (4, 5, and 6) hold for either adiabatic or isothermal conditions with corresponding volume coefficients. Isothermal $\beta = k\beta$ adiabatic ($k = C_p : C_v$, the ratio of specific heats), while for the α's this ratio is $1 - k$. The relations between p and v are consistent with $pv^k = \text{constant}$, which has been shown to hold well for metals as well as gases.

The derivation of the second law here given indicates that the first and second laws are but conjugate parts of a single general expression for equilibrium. In the simple form ($SdT = vdp$) given, the second law was shown to lead directly to the well-known Clausius equation for vapor pressure and the Thomson equation for single-phase heat of compression. Similar applications to groups of problems of wide variety are indicated. The second law has been a *bête noir* of theoretical physics, but it should become a friendly work horse, easily managed, useful, and well understood.