tegration period. This family would have varied continuously from a saturating function to a power function with a notch. Our interpretation is therefore subject to test because it emphasizes a novel factor, the amount of time used by an observer to evaluate a stimulus. If an observer offered rapid brightness judgments, then that observer should produce a more saturating psychophysical function. On the other hand, if an observer were more deliberate, one would expect a power function with a notch. One can even hypothesize an observer who emphasized the later portions of the sensory signal; then one would expect a positively accelerating psychophysical function. These predictions could be tested by (i) varying the instructions to the observer; (ii) measuring the reaction times of brightness judgments, partitioning those judgments into fast and slow groups, and erecting separate psychophysical functions from the partitioned judgments; and (iii) imposing response deadlines of different durations.

We conclude that there may not be any single psychophysical function, and the quest for one may have been in vain. Instead both Stevens' and Fechner's methods may represent equally valid ways of assessing the particular psychophysical functions associated with particular tasks; there may well be many task-specific psychophysical functions. Seen in this way, the psychophysical function is a conjoint property of both the sensory signal itself and the task-dependent analysis of this signal. If this interpretation is correct, we should seek harmony in this field by honoring both Fechner's and Stevens' methods and by using both methods to gain further insight into perception (*19*).

GERALD S. WASSERMAN
GARY FELSTEN
GENE S. EASLAND
Department of Psychological Sciences, Purdue University, West Lafayette, Indiana 47906

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11. Hood and his collaborators also found that very intense increments were somewhat more detectable than would be predicted by a Naka-Rushton saturating rectangular hyperbola. This deviation may occur because a very intense increment produces a complex response; although the stimulus is a pure increment, the response consists of an increment followed by a decrement, which is larger the closer to saturation. Examples of such complex receptor responses are in G. Felsten and G. S. Wasserman [*J. Comp. Physiol. Psychol.* **92**, 778 (1978)].
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A Source of Nonshivering Thermogenesis in Fur Seal Skeletal Muscle

Abstract. *The mitochondria from the subscapular muscle of naturally cold-stressed 10- to 15-year-old northern fur seals (*Callorhinus ursinus*) were loosely coupled upon isolation, whereas the mitochondria from the same muscle of warm-acclimated pups of the same age were tightly coupled. Thus, loose-coupled muscle mitochondria might provide an important vehicle for nonshivering thermogenesis in this species.*

The presence of nonshivering thermogenesis (NST) in skeletal muscles was reported by Jansky and Hart (*1*) as far back as 1963, but the cellular mechanisms inherent in this intriguing mode of heat production have hitherto not been found (*2, 3*). This might well be because most studies have been conducted with laboratory rats. In this report we present strong evidence for a loose coupling of mitochondrial respiration as an important source of nonshivering thermogenesis in northern fur seal (*Callorhinus ursinus*) pups.

Northern fur seal pups (cover picture) are subjected to frequent or constant cold stress as soon as they are born on the Pribilof Islands in the Bering Sea (*4*), where strong winds often play in concert with rain and temperatures of 6° to 8°C. We used a total of 18 animals. Some were obtained directly from the rookery at St. Paul Island, where a field laboratory was made operational in 1977; others were brought to the University of Alaska at Fairbanks in 1978. The animals were kept for a maximum of 5 days under constant cold stress, unless otherwise stated.

Cytochrome c oxidase activity is a useful index of the aerobic oxidative capacity of a tissue (*2*). Since NST is primarily aerobic in nature, muscle groups engaged in its maintenance might be expected to have a high capacity for oxidative metabolism. A survey of specific cytochrome c oxidase activity (*5, 6*) of different muscle groups in the newborn fur seal revealed considerable variation (17 to 25 microgram-atoms of oxygen per minute per gram of muscle), the highest activity being found in the substantial subscapular muscle. Enzyme activities were generally higher in 10-day-olds than in the newborns, indicating some development in oxidative capacity. We therefore used for this study the subscapular muscle (with a specific enzyme activity of about 35 μg-atom oxygen $min^{-1}g^{-1}$) of pups aged 10 to 15 days (*7, 8*).

Immediately after the pups were killed, the subscapular muscles were excised and placed in ice-cold 0.15*M* KCl. The muscles were dissected free of connective tissue and visible fat and were finely minced with scissors. Homogenization of the tissue was performed according to Bullock *et al.* (*9*) by means of Nagarse digestion (*10*). Digestion at a concentration of 1 g of tissue per 5 ml of medium (*11*) containing 20 μg of Nagarse per milliliter was conducted at 0°C by the mixture being stirred magnetically for 30 minutes. Mitochondria were then obtained by differential centrifugation (*12*) with application of a field of 9200*g*

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(average) × minute. The mitochondrial fraction consistently contained approximately 70 percent of the total mitochondrial protein present in the supernatant after sedimentation of nuclei. Integrity was tested by supplying the mitochondria with reduced nicotinamide adenine dinucleotide, which was not oxidized. A total of 163 separate experiments were done.

The oxidative properties of the mitochondria were judged from rates of oxygen uptake with a variety of lipid as well as nonlipid substrates (Table 1). Except for *sn*-glycerol 3-phosphate (where *sn* indicates stereospecific numbering), all of the substrates chosen were oxidized at appreciable rates.

The energy-conserving properties of the mitochondria were examined by measurements of phosphate to oxygen (P/O) ratios (*13*), phosphate acceptor control (*14*), and, wherever this phenomenon was evident, by adenosine diphosphate to oxygen (ADP/O) ratios (*14*). When the glucose-hexokinase trap method (*13*) was used with succinate as substrate, the P/O ratio was 1.2 in a medium lacking bovine serum albumin and 1.4 when albumin was present. Nevertheless, the rate of oxygen uptake in vitro was affected neither by ADP nor by added oligomycin (Fig. 1A), in spite of the fact that oligomycin abolished adenosine triphosphate (ATP) production, as shown by use of the glucose-hexokinase trap method. These mitochondria isolated from naturally cold-stressed animals thus fulfill the requirements for loose coupling, as defined by Ernster and Luft (*15*).

In the presence of 0.5 percent bovine serum albumin the oxygen uptake pattern of the same mitochondria transformed to one that was under distinctive phosphate acceptor control (Fig. 1B), exhibiting ADP/O ratios (*14*) close to the theoretical value of 2.0. Bovine serum albumin is known to restore acceptor control to loosely coupled mitochondria derived from thermogenic adipose tissue (*14, 17*), but guanosine 5′-triphosphate, a factor which usually further enhances respiratory control in brown adipose tissue mitochondria (*14, 18, 19*), had no effect on the muscle mitochondria employed here.

Loosely coupled mitochondria have been found previously in skeletal muscle (*15, 20*) but have been interpreted as artifacts and never associated with nonshivering thermogenesis. Thus, in order to relate the state of mitochondrial respiratory control in vitro to clearly defined conditions in vivo, we designed the following experiment. A 10-day-old pup was kept in dry air at 20°C, which is far above its lower critical temperature (*4*), for 8 days. After this time the respiratory properties of its subscapular muscle mitochondria were investigated as above. The data in Fig. 1, C and D, indicate that the mitochondria of the warm-acclimated pup were under very firm respiratory control even without albumin in the medium and were accompanied by ADP/O ratios approaching the theoretical value. In fact, fortification of the medium with albumin improved the respiratory control to only a small extent. In our opinion, these results should

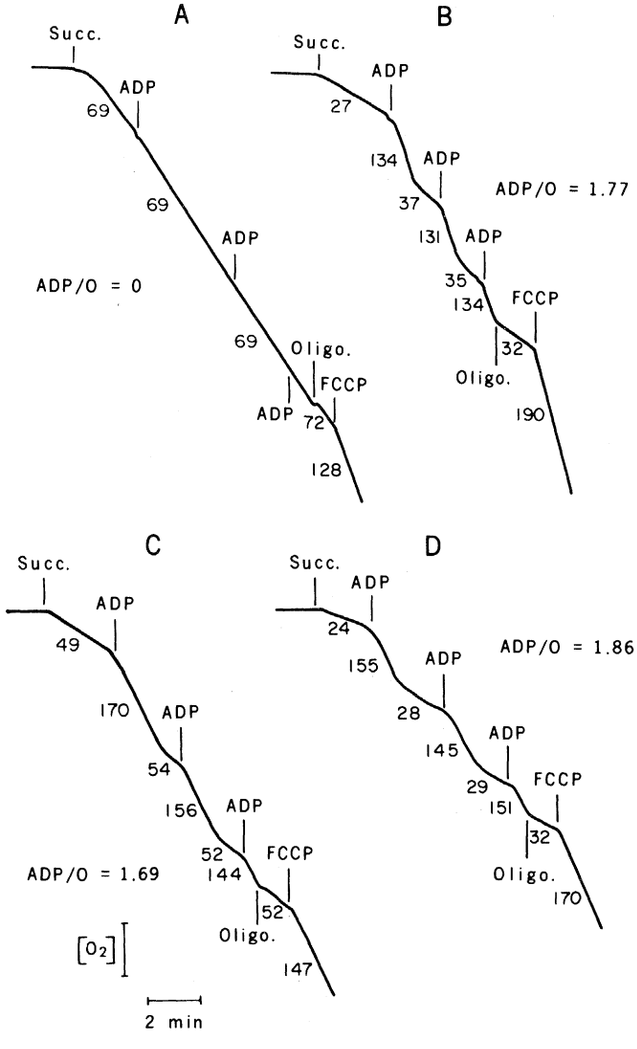

Table 1. Rates of oxygen consumption of subscapular muscle mitochondria isolated from naturally cold-stressed northern fur seal pups. For the first five experiments we used a medium containing 200 m*M* sucrose, 14 m*M* mannitol, 10 m*M* KH_2PO_4, 2.7 m*M* EDTA, 1 m*M* $MgCl_2$, and 27 m*M* K-Hepes buffer, *p*H 7.4. For experiments 6 through 8 the medium contained 50 m*M* KCl, 2 m*M* EDTA, 1 m*M* $MgCl_2$, 5 m*M* KH_2PO_4, 20 m*M* K-Hepes buffer, *p*H 7.4. Rates are expressed as nanogram-atoms of oxygen per minute per milligram of mitochondrial protein.

Experiment	Substrate	Rate
1	10 m*M* succinate*	128
2	10 m*M* *sn*-glycerol 3-phosphate*	11
3	10 m*M* α-ketoglutarate plus 10 m*M* malate†	47
4	10 m*M* pyruvate plus 10 m*M* malate†	40
5	10 m*M* glutamate plus 10 m*M* malate†	41
6	5 μ*M* L-palmitoyl carnitine plus 1 m*M* malate	50
7	3.3 μ*M* L-oleyl carnitine plus 1 m*M* malate	34
8	7.5 μ*M* L-caproyl carnitine plus 1 m*M* malate	58

*0.1 μ*M FCCP and 3 μM* rotenone were added. †0.1 μ*M* FCCP was added.

Fig. 1. Typical oxygen uptake patterns of mitochondria isolated from the subscapular muscle of 10 to 15-day-old northern fur seals (*Callorhinus ursinus*). Traces A and B refer to mitochondria isolated from animals cold-stressed by rain and cold (at 6°C); traces C and D to mitochondria from animals warm-acclimated in dry air at 20°C. For traces A and C, the reaction mixtures contained the following components in a total volume of 1.5 ml: 200 m*M* sucrose, 14 m*M* mannitol, 10 m*M* KH_2PO_4, 2.7 m*M* EDTA, 1 m*M* $MgCl_2$, 3 μ*M* rotenone, 27 m*M* K-Hepes buffer, *p*H 7.4, and mitochondrial suspension (0.2 to 0.5 mg of mitochondrial protein per milliliter). For traces B and D, the medium was fortified with 0.5 percent fatty-acid-free bovine serum albumin. At the points indicated, 10 m*M* succinate (*Succ.*), 100 μ*M* ADP (200 μ*M* ADP was used prior to oligomycin administration), 3 μg of oligomycin (*Oligo.*), and FCCP (0.1 μ*M* for traces A and C; 5 μ*M* for B and D) were added at a temperature of 25°C. The numbers immediately beneath each trace represent the specific respiratory rates given as nanogram-atoms of oxygen consumed per minute per milligram of protein. The ADP/O ratios were calculated according to Chance and Williams (*16*). The vertical bar, lower left corner, indicates 48 ng-atom per milliliter.

eliminate the artifact option suggested by Hülsmann *et al.* (*20*), and rather strongly indicate that loosely coupled mitochondria can be an important source of nonshivering thermogenesis in skeletal muscle.

HANS J. GRAV*
Institute of Medical Biology, Section of Physiology, University of Tromsø, Tromsø, Norway
ARNOLDUS S. BLIX
Institute of Arctic Biology, University of Alaska, Fairbanks 99701

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5. The abbreviations used in this report are ATP, adenosine triphosphate; Hepes, 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid; EDTA, ethylenediaminetetraacetic acid; EGTA, ethylene glycol bis(β-aminoethyl ether)-*N,N'*-tetraacetic acid; and FCCP, carbonyl cyanide *p*-trifluoromethoxyphenylhydrazone.
6. Cytochrome c oxidase activity was measured with a Clark electrode (Yellow Springs Instruments) after treatment of minced tissue in a modified Chappell-Perry medium (1 m*M* ATP, 50 m*M* potassium-containing Hepes buffer, *p*H 7.4, 0.1*M* KCl, 5 m*M* $MgCl_2$, 1m*M* EDTA, 5 m*M* EGTA (*5*) with low concentrations of Lubrol added according to A. Aulie and H. J. Grav (*Comp. Biochem. Physiol.*, in press).
7. The aerobic nature of the metabolism in this muscle was further reflected in a peculiar fiber composition: Standard adenosinetriphosphatase staining (*p*H 9.4) of tissue slices from 10-day-old pups exposed only one type of fibers. Prior incubation of the slices at *p*H 4.1, however, revealed that two subtypes were present. Both fiber types were rich in triglyceride but completely devoid of glycogen (*8*). Electron microscopic examination likewise suggested an apparent increase in the number of both mitochondria and triglyceride droplets in the course of the 10-day neonatal period.
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12. The homogenate was placed in a cooled Sorvall SS-1 or RC-2B centrifuge equipped with an SS-34 rotor running with half-filled 50-ml tubes. The pellet obtained at a field of 1500*g* (average) × minute was discarded and the supernatant was filtered through gauze. The mitochondrial fraction was then obtained at a field of $9200g_{av}$ min. This fraction was washed twice, with the same centrifugal field being used. The final pellet was resuspended in homogenization medium (*11*) and stored at 0°C at a concentration of 30 to 50 mg of mitochondrial protein per milliliter. Protein was determined by a biuret procedure.
13. The P/O ratios were determined by the glucose-hexokinase trap method as follows. Adenosine triphosphate (2 m*M*) was added to the incubation medium and the reaction started by adding 25 units of hexokinase and 5 m*M* KH_2PO_4 with $NaH_2\,^{32}PO_4$ as a tracer. Phosphate uptake was determined by the isotope distribution method [O. Lindberg and L. Ernster, in *Methods of Biochemical Analysis*, D. Glick, Ed. (Interscience, New York, 1956), vol. 10, p. 1], as modified by Grav *et al.* (*14*). The inorganic phosphate (P_i) taken up was related to the equivalent oxygen consumption as measured from polarographic traces.
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* Present address: Institute for Nutrition Research, University of Oslo, Blindern, Oslo 3, Norway.

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Differential Mortality by Sex in Fetal and Neonatal Deaths

Abstract. *Vital statistics data for the United States from 1922 to 1936 and from 1950 to 1972 were used to analyze fetal and early neonatal mortality. This analysis corroborates the previously established pattern of the sex ratio of fetal deaths—highest from months 3 to 5, lower from months 6 to 7 or 8, and increasing at term. It also indicates a postponement of late fetal deaths into the early infant period. Whereas earlier research reports have described the pattern of the sex ratio of fetal deaths, this report repeats this analysis for a recent national data base. This line of analysis is extended by using the patterns observed in the data to produce an empirical estimate of the primary sex ratio. For 1950 to 1972, this ratio (male to female) is conservatively estimated to be 120:100.*

A sex ratio at conception (primary sex ratio) in excess of the sex ratio at birth (secondary sex ratio) is a necessary condition for differential mortality by sex in utero. Although discussions of the primary sex ratio focus on the existence and extent of sex differential mortality in utero (*1, 2*), there is no clear-cut consensus on the primary sex ratio. In fact, estimates of the primary sex ratio (males:females) range from 110:100 to 170:100. The variability in these estimates derives in part from the different data under consideration (*3*) and in part from the subjective judgments that result from each reseacher's examination of the data on hand. Despite the discrepancies among these studies, one overriding similarity emerges in the pattern of the sex ratio of fetal deaths by month of gestation; the sex ratio of fetal deaths is reported to be highest between months 3 and 5, lower between months 6 and 7 or 8, and increases at term (*4*).

Cavalli-Sforza and Bodmer (*2*) have contended that vital statistics provide the best data source for analyzing sex-differential mortality in utero, as vital statistics encompass enough cases to assure the significance of the relatively small differences in sex ratio. Thus, I used annual data for the sex ratio of fetal deaths by month of gestation for the United States from 1922 to 1936 and from 1950 to 1972 (*5*) in conjunction with data on early infant mortality (*6*).

The sex ratios were calculated as the ratio of males to females; after a preliminary graphic analysis of the general trend, least-squares and polynomial regression techniques were used to fit second-degree equations to the fetal death data. This analysis was performed on the arithmetic means of the sex ratio of fetal deaths by months (*7*) (Fig. 1).

Analysis of fetal death data for 1922 to 1936 reveals a nonlinear pattern that reflects the patterns reported in earlier studies (*3*). This pattern can be described by the second-order equation (*8*).

$$SR = 7.5637 - 1.7470M + 0.1155M^2 + e$$
$$\qquad\qquad (0.3370) \quad (0.0256)$$

$$R^2 = .8965$$

where SR = sex ratio of fetal deaths, M = month of gestation, and e = the least-squares residual; the values in parentheses are the standard errors.

The 1950 to 1972 fetal death data are limited to data from months 5 to 10; these data can be described by the second-order equation (*9*).

$$SR = 2.1958 - 0.2295M + 0.0119M^2 + e$$
$$\qquad\qquad (0.1176) \quad (0.0076)$$

$$R^2 = .9116$$

The nonlinear pattern of the 1950 to 1972 data differs from the pattern of the earlier data. The difference may be attributed to several factors. (i) The pattern observed from months 5 to 7 in the 1922 to 1936 data is present at a lower level in the 1950 to 1972 data. (ii) Available data from spontaneous and induced abortions in the first trimester of gestation support the notion that sex ratios of early fetal loss are higher than subsequent fetal death sex ratios (*10*). (iii) The largest difference occurs among fetal

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