obviously necessary to extend the 'simulation work' if it is to keep pace with experimental developments.

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ROTHWELL AND STOCK[1] demonstrated that partially tube-fed rats gained significantly more weight than their free-feeding controls even though both groups ate very nearly the same amount. We suggest the possibility that the weight differences result from changed levels of activity. This approach obviates the paradoxical problems suggested by Rothwell and Stock.

A single energy reservoir model is used, as the rats are mature adult males unlikely to change their fat-free weight on over-feeding. We can describe the rate of change of fat[2] quantities by the following differential equation

$$\alpha \, df/dt = \varepsilon P - \text{BMR} - \delta(l+f) \quad (1)$$

where $\alpha$ is the energy equivalent of fat, $f$, $t$ is time, $\varepsilon$ is the efficiency of food utilisation, $P$ is the average daily food energy intake, BMR is the basal metabolic rate, $l$ is the fat-free weight assumed to be constant or slowly varying, and $\delta$ is a constant independent of the total weight and indicates the average activity level of the rats. We have made no direct distinction between feeding and non-feeding activity of the rats. MacMillan *et al.*[3] have demonstrated densimetrically that in man the BMR is independent of the amount of fat present; we assume this to be valid in the case of rats also. Because the BMR is independent of $f$ we can solve equation (1) directly obtaining

$$w = [(\varepsilon P - \text{BMR})/\delta][1 - \exp(-\delta t/\alpha)] + w_0 \exp(-\delta t/\alpha) \quad (2)$$

where we have replaced $(l+f)$ by the total body weight $w$ and $(l+f_0)$ by the initial total body weight $w_0$.

We used Kleiber's 3/4-power law[4] to deduce the BMR. The BMR of a 'standard' 65-kg man is 6.27 MJ per day (1,500 kcal d$^{-1}$)[5]; thus, the average rat will

have a BMR of 128 kJ per day. Within the rat groupings we scale the BMR by a 2/3-power law as Kleiber's rule only relates to average interspecies quantities.

To use equation (2) we take $\alpha$ to be 39.2 MJ per kg (9,370 kcal per kg)[5]. The value of $\varepsilon$ is unknown but should reflect losses due to the thermic effect and the passing of small energy amounts in the faeces. Antonetti[6] used a value of 0.9 in man. We take $\varepsilon$ to be unity, because this must be the limiting case, and apply it to both tube-fed and free-feeding rats. Table 1 shows the data of Rothwell and Stock[1] and includes the results of our calculations. There is enough information to solve equation (2) for the activity coefficient, $\delta$ (Table 1).

In each case $\delta$ was less for the tube-fed rats than for the control groups, suggesting that the observed weight gain difference can be explained by the decreased activity of the test animals. The possibility that the tube-fed rats might increase their non-feeding activity is not reflected in the decreased values of $\delta$. The average value of the activity coefficient of the controls was $(423 \pm 73)$ kJ per kg per day; the daily activity energy expenditure was $153 \pm 26$ kJ.

We calculate that the average control rat expended about 54% of the total energy on all forms of activity. Rothwell and Stock[1] consider activity energy to be negligible; Miller and Mumford[7] deduce that about 3% of the total energy is expended on activity by severely exercised rats by applying a fixed energy expenditure factor of 0.5 kcal per kg per km to rat, man and elephant. Morrison[8] has measured spontaneous activity calorimetrically and reports it to be 25% of the total energy expenditure. Our results agree slightly better with those of Morrison[8] by assuming $\varepsilon$ to be 0.9 (ref. 6). Repeating the numerical calculation in this case we find $\delta$ to be $333 \pm 56$ kJ per kg per day, giving a 48% value for activity.

We can deduce the level of activity for rats completely tube-fed. We have plotted in Fig. 1 the ratio of the activity coefficient of the tube-fed rats to that of the control group as a function of the fraction of tube-fed energy. We have included the limiting point for no tube-feeding. The linear fit extrapolated to the limit of complete tube-feeding gives a value of 0.25. We conclude that 75% of caged rat
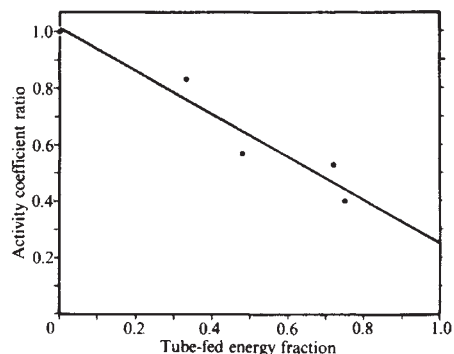


**Fig. 1** The ratio of the activity coefficient of the tube-fed rats to that of the appropriate control group plotted as a function of the fraction of tube-fed energy. The point on the ordinate is the limiting value of the ratio for no tube-feeding. The other points are experimental. The linear least-squares fit is displayed and interpolates to a value of 0.25 for complete tube-feeding.

activity is food related. This value cannot be compared with Morrison's results[8] because our definition of food-related activity is broader

Equation (2) essentially describes the exponential increase of fat and allows an interesting speculation. The equilibrium value is approached to within $1/e$ of its final value in a time given by $\alpha/\delta$ which is $93 \pm 16$ days. If a parameter proportional to the fat store size is sensed as an 'error signal' for a regenerative control process, and if the sensing time is similar to the rise time of the fat store, we can conclude that experimental studies dealing with problems of control must be carried out for times of the order of or longer than 93 days.

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**Table 1** Data and calculated quantities

| Expt | No. of animals | Av. initial weight, $w_0$ (g) | Av. final weight, $w$ (g) | Energy intake, $P$ (kJ d$^{-1}$) | Duration of expt (d) | Fraction of tube-fed energy (%) | BMR, calculated (kJ d$^{-1}$) | Activity coefficient, $\delta$, calculated (kJ kg$^{-1}$ d$^{-1}$) |
|---|---|---|---|---|---|---|---|---|
| 1 Control | 6 | 436 | 480 | 378 | 30 | | 145 | 383 |
| Tube-fed | 5 | 440 | 511 | 388 | 30 | 33.4 | 146 | 314 |
| 2 Control | 12 | 321 | 388 | 405 | 21 | | 118 | 454 |
| Tube-fed | 8 | 320 | 420 | 400 | 21 | 48.1 | 118 | 258 |
| 3 Control | 6 | 300 | 358 | 385 | 23 | | 113 | 525 |
| Tube-fed | 6 | 290 | 385 | 366 | 23 | 71.8 | 110 | 278 |
| 4 Control | 12 | 402 | 442 | 367 | 21 | | 137 | 367 |
| Tube-fed | 9 | 400 | 489 | 367 | 21 | 74.7 | 136 | 147 |