of separate terms. Thus in one run, the sum of the terms for harmonics 31–210 was 325.4; while for 211–390 it was 319.6. The first 30 harmonics were eliminated because of the finite length of the series; harmonics over the 390th were not computed, to avoid the Nyquist aliasing frequency.

A similar calculation, but omitting the drift factor, results in a clear demonstration of the $1/f^2$ law for this case.

While this analysis indicates that $1/f$ noise should be generated wherever the motion of a current carrier across a potential barrier will result in a change in potential, the absolute amplitude of the potential fluctuations has not been considered. The amplitude should increase with increased probability of random crossings of the barrier, but decrease with increasing drift current. The net effect will be that $1/f$ noise will only be observable if it is significantly greater than other sources of fluctuation, such as Johnson noise.

It is thus demonstrated that the random potential variation to be expected from ions traversing the potential barriers of a membrane will have a $1/f$ power spectrum. The existence of such a noise spectrum cannot, therefore, be used to substantiate any particular theory of membrane activity.

The application of the calculations to semiconductors is published elsewhere (4).

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Distortion in Coulter Counters and the Applicability of the Collins-Richmond Principle

Dear Sir:

It has been recognized only recently that cell volume distributions obtained with Coulter counter-analyzer systems are distorted by the radial dependence of electric current and voltage near the mouth of the counting aperture (Grover, Naaman, Ben-Sasson, and Doljanski. 1969; Thom, Hampe, and Sauerbrey, 1969). The degree of distortion is nearly constant for cells or particles of different sizes and therefore has little effect upon the determination of average volumes by comparison to known standards. However, this distortion results in a modification of the shapes of distributions for cells and particles that invalidates detailed calculations from them. In particular, these distributions cannot be used, without correction, to determine the kinetics of growth of cells during the generation cycle by the method

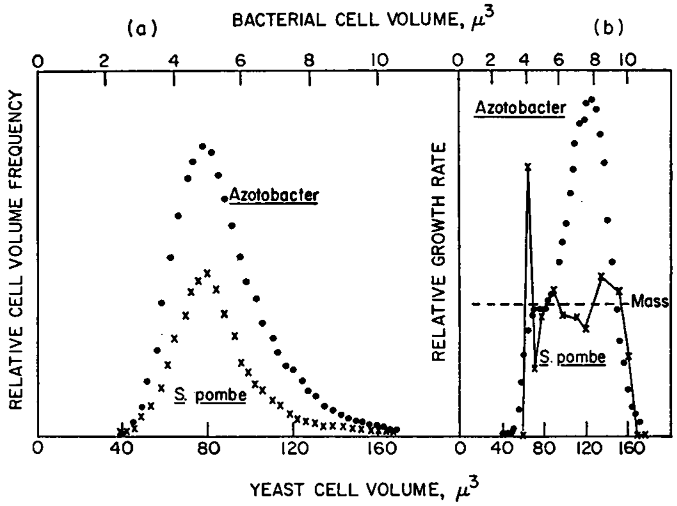

FIGURE 1 Relative cell volume distributions (*a*) and growth rates (*b*) of *Azotobacter agilis* (●) and *S. pombe* (×). (*a*) The cell volume distribution for *S. pombe* was obtained, as described in the text, for a culture growing at 24°C; that for *Azotobacter* is from Fig. 2 of Harvey et al., (1967). (*b*) The growth rate for *S. pombe* was calculated from the data of Mitchison (1957), his Fig. 4, for single cells growing at 25°C under almost identical conditions; that for *Azotobacter* is redrawn from Fig. 4 of Harvey et al. (1967). The rate of increase of yeast cell dry mass was constant during most of the growth cycle, and is shown, for comparison, by the horizontal dashed line.

of Collins and Richmond (1962), as supported by the evidence below. Other difficulties for this approach were discussed earlier (Koch, 1966; Kubitschek, 1969).

To determine the effect of distortion on the analysis of growth rates during the cell cycle, growth rates calculated from volume distributions were compared with values measured directly for single cells of the fission yeast *Schizosaccharomyces pombe* strain NCYC 132, kindly supplied by Professor J. M. Mitchison. He determined the growth rate pattern of individual cells of this strain at 25°C (Mitchison, 1957), and with his colleagues (Mitchison, Kinghorn, and Hawkins, 1963), at 23°C. Cell dry mass, measured by interference microscopy, increased at a constant rate for all or almost all of the generation cycle. Cell volume growth rates increased abruptly to a plateau of relatively constant values after an initial overshoot and oscillation, as illustrated in Fig. 1. The volume growth rates at 23°C for this strain gave the same pattern (not shown), demonstrating both the reproducibility of the optical measurements and the stability of the strain over a period of several years.

To obtain corresponding cell volume distributions, I matched the growth conditions of those earlier experiments by using the same nutrients (wort broth; Oxoid) and by growing the cultures at 24°C. Stationary distributions of cell volumes were obtained for cultures maintained in steady-state growth with a doubling time of 165 min for periods of at least 4 hr. All of these distributions had the same shape; one is shown in Fig. 1 *a*. This distribution for *S. pombe* was compared to that determined by Harvey, Marr, and Painter (1967) for a culture of *Azotobacter agilis*, also shown in Fig. 1 *a*. The two are indistinguishable by X^2 analysis: $P = 0.9$ ($N = 27, X^2 = 16.1$).

Because the cell volume distributions for the two organisms have very similar shapes, their growth rate patterns must also be very similar when calculated by the same method and assumptions. The calculated values of growth rate for *Azotobacter* (Harvey et al., 1967), shown as a function of cell volume in Fig. 1 *b*, increase to a maximum late in the cycle and then fall to zero, so a similar form would be expected for the growth rates of *S. pombe* during its generation cycle. But as pointed out earlier, actual growth rate patterns obtained from microscopic observations of single cells differ in shape, qualitatively as well as quantitatively, (Fig. 1 *b*). Rates of increase of volume rise abruptly at the beginning of the cell cycle, oscillate decreasingly about a relatively constant plateau value during the middle of the cycle, and decrease to zero very abruptly at its end.

These very marked differences between calculated and experimental growth rate patterns support the conclusion that counter distributions are distorted by the variability arising from the radial dependence at the mouth of the sensing aperture. If the data could be corrected for this loss of resolution, volume spectra would be narrower, have flatter tops, and drop more abruptly at their ends. The calculated growth rates for *S. pombe* would then agree more closely with those observed for single cells. A more direct approach would involve the reduction of variability in aperture response by limiting cell trajectories to the central zone of the aperture (Thom et al., 1969). This approach should permit the most reliable measurements of cell volume distributions.

Even with these improvements the calculation of average cell growth rates by the Collins-Richmond method may lead to deceptive growth patterns because the average growth rate may not be representative of the growth rate of any single cell. This would be expected, for example, if cells grew only during the middle period of the cell cycle. Even if all cells grew at the same rate during this period, the variability in cell volume at birth and division would lead to an average growth rate pattern that is bell shaped, failing to reflect the true growth rate pattern for any individual cell.

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