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50 & 100 YEARS AGO

50 YEARS AGO

"Man and his machines" — After expressing the fear that technical colleges are not educational institutions but teaching shops, [Mr Harry Rée] emphasized that "in building a world where machines do the work which used to be done by men, it is not good enough to build men who can only work like machines"...

He concluded by envisaging the great contribution educational institutions could make by a counter attack on the creeping disease of passive pleasures which is eating away the soul of modern man. "If we could make the effort...we should look upon automatic factories and computing machines as our benefactors enabling us and our children to taste to the full the real joys of life."

From *Nature* 1 October 1955.

100 YEARS AGO

"The omission of titles of addresses on scientific subjects" — What this busy world wants is help to get at what we are interested in with the least possible waste of time.

This hot haste may seem unbecoming to men of science, or perhaps it may appear that we Americans are in too big a hurry — that we are too much impressed with the motto "time is dollars." But there are many other nimble things we are trying to keep up with, and one of those is the progress of science in Europe, along the lines in which we are especially interested.

If a member of so young and giddy a nation might venture to make a suggestion to older and wiser people, it would be in favour of requesting or requiring the presidents of the various scientific organisations and sections of the British Association to provide headings for their addresses so that those of us who have not the time to read all of these good things may be able at a glance to pick out what we want especially to see.

From *Nature* 28 September 1905.

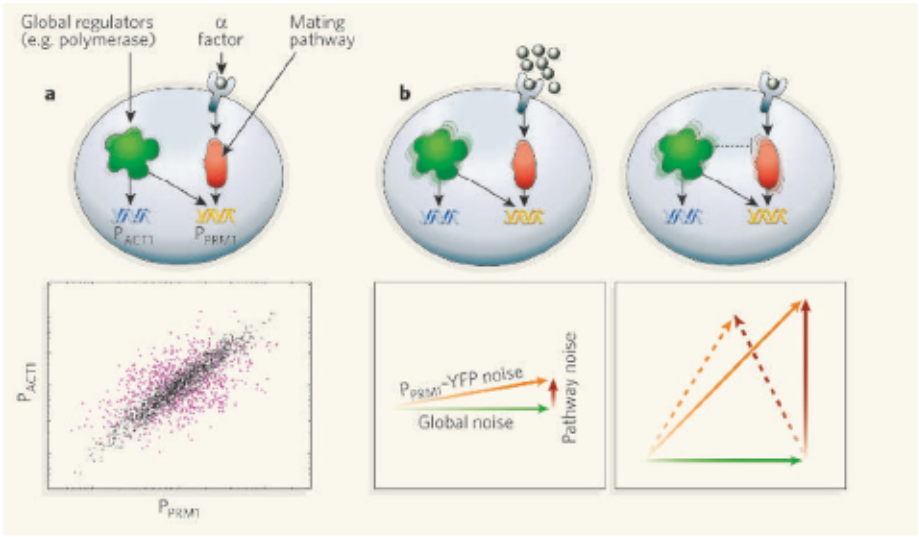

Figure 1 | Noise decomposition in the model of cell behaviour devised by Colman-Lerner and colleagues[1]. **a**, Upper panel, global regulators (green) affect expression of all genes, including that encoding cyan fluorescent protein regulated by the P_{ACT1} promoter and the gene encoding yellow fluorescent protein (YFP) under the control of P_{PRM1}. The mating pathway (red) affects only P_{PRM1}. Lower panel, expected results in two extreme cases: total P_{PRM1} noise may be dominated by global factors (black points) or by pathway noise (magenta points). **b**, Noise depends on pheromone levels. At high concentrations, noise is dominated by global fluctuations, resulting in strong correlation between the two reporter genes (left). In the vector diagram, coloured arrows represent noise amplitudes and their degrees of correlation with other noise sources. At low pheromone concentration (right), there is reduced correlation between the two reporter genes. Within the model, this is interpreted as an increase in pathway-specific noise. If the two noise sources were independent, the magnitude of P_{PRM1} variation would increase (orthogonal solid arrows, bottom panel). However, the authors observe that the magnitude of the P_{PRM1} variation is independent of pheromone concentration, implying a negative interaction between the two noise sources (acute angle between green and dashed red arrows).

pathway is saturated under these conditions[1]). In this case, fluctuations in P_{PRM1} are dominated by the global factors referred to earlier.

But what happens at low pheromone levels? Under these conditions, the authors observed reduced correlation between the two promoters (Fig. 1b, right). If pathway-specific noise were independent of global noise, one would expect the variance in P_{PRM1} activity to be the sum of global and pathway-specific variances (orthogonal green and red arrows in Fig. 1b). This would result in an increased total noise in the P_{PRM1} promoter compared with its value at high pheromone concentration. Interestingly, such an increase is not observed[1]. The missing noise indicates the existence of a negative interaction between global factors and the mating pathway (green and non-orthogonal dashed red arrow in Fig. 1b). The authors interpret this negative interaction as a buffering of pathway noise by the effects of global noise on genes in the mating pathway.

The existence of such an interaction is not surprising: being global, such factors should affect other genes along with components of the mating pathway. However, many regulatory steps may connect the global factor to pathway components — the sign and magnitude of this arrow is not clear. It will be interesting to find out whether the inferred buffering interaction has adaptive significance. This could be explored by examining the response of other mating-pathway targets and the effect of variation on the physiological behaviour of mating. How widespread the buffering is could be examined by similarly analysing other pathways.

In general, correct interpretation of noise experiments can be subtle[6]. For example, the buffering interpretation described above depends on the implicit assumption of the model that global noise affects the P_{PRM1} promoter equally at both pheromone levels (that is, the green arrows in Fig. 1b are equal). In the future, it may be possible to develop higher-resolution analysis of noise correlations, allowing phenomenological models to be replaced by molecular ones. In physics and engineering, analysis of fluctuations often provides unique insights into the dynamics of a system. Normally, such an analysis is limited by the amount of variation present in the system to begin with. Luckily, with living cells, there is no lack of noise to work with. ■

Avigdor Eldar and Michael Elowitz are in the Division of Biology and Department of Applied Physics, California Institute of Technology, Pasadena, California 91125, USA.
e-mail: melowitz@caltech.edu

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