50 & 100 YEARS AGO

50 YEARS AGO

Modern technology is confronting us with an exceedingly perplexing biological problem… It is the problem of how men and communities can adapt themselves to an environment which is changing with unprecedented speed [and] confronts teachers of all kinds at every level of education. One aspect of it — the higher education of technologists — is…specially important because technologists are now becoming the pacemakers for social change… The technologist is up to his neck in human problems whether he likes it or not. Take a simple example: the civil engineer who builds a road into a new territory in tropical Africa. He may assert that it is not his business to take into account the effect his road will have on primitive villages up-country… but he cannot afford to be utterly ignorant of the implications of his work.

From *Nature* 28 September 1957.

100 YEARS AGO

"Food inspection and adulteration" — [A] more drastic and far-reaching enactment is just now coming into force in the United States, and the working of one of its provisions in particular will be watched with much interest in this country. Its effect is to ensure that articles of food and drugs shall be labelled so as to show the purchaser, within limits, exactly what the articles are. The description must not be "false or misleading in any particular," whether as to composition, quality, origin, or what not. Thus an article must be stated on the label to be "prepared with glucose," "coloured with sulphate of copper," "dyed with aniline dye," or to be "composed of fragments and scraps from a mushroom cannery," and so on, as the case may be. Moreover, in the case of certain drugs — morphia, cocaine, chloral, chloroform, and others — the proportions must always be stated on the label.

From *Nature* 26 September 1907.

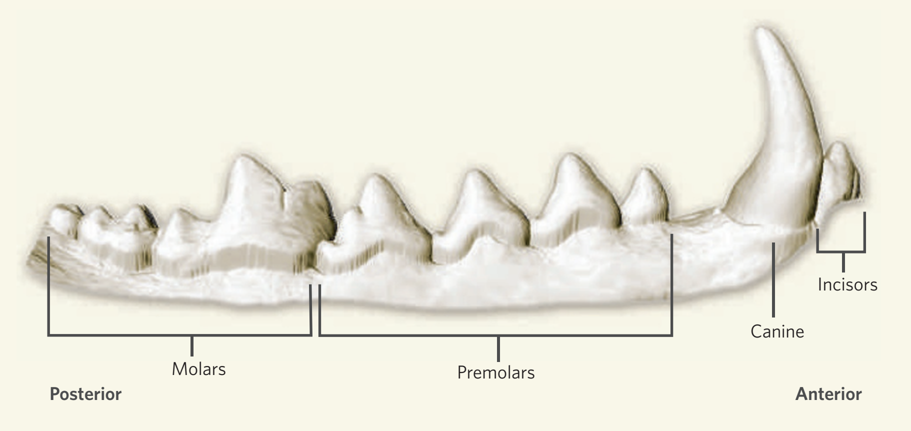

Figure 1 | Dentition of a placental mammal. This example — the lower teeth of a grey fox — shows the three-molar dental phenotype typical of placentals.

relative sizes of the molar teeth, so explaining how these seemingly arbitrary palaeontological observations are related to one another (K. D. Kavanagh, A. R. Evans & J. Jernvall *Nature* **449,** 427–432; 2007).

Embryonic molar teeth start as buds that spring from the dental lamina, a ribbon of epithelial tissue that runs parallel to the future tooth row. Buds initiate anterior-to-posterior, with the dental lamina growing in the same direction. Kavanagh *et al.* show experimentally that signalling molecules produced by developing mouse molars inhibit the development of subsequent buds. The balance between these inhibitors and activator molecules from the surrounding tissue determines when and if an additional molar will form. The higher the ratio of activator to inhibitor (a/i), the more rapidly molar buds will be added to the tooth row. And the more rapidly buds are added, the more there are and the bigger they get, meaning that a/i is a predictor of the relative sizes of the molar teeth (Fig. 2).

Using tooth buds growing in cell culture, Kavanagh and colleagues demonstrate these points by cutting the dental lamina behind the developing first molar. This interrupts the flow of inhibitors and allows the second molar to initiate earlier and grow to a larger size than normal. The inhibitor and activator molecules involved are probably the same as those active in the development of an individual tooth crown, such as Ectodin, Follistatin, Bmp3, Bmp4 and Activin βA.

If this developmental system is shared by all mammals, different dental phenotypes could be generated simply by varying the a/i ratio. Kavanagh *et al.* argue that the system has influenced the evolution of functional diversity in mammalian dentition. To test that possibility, they compile data on the proportional area of the molars of 29 species of murine rodents — close relatives of the mice in which the authors discovered the regulatory system.

The predictive mathematical model they derive from the developmental experiments explains nearly 75% of the diversity in molar proportions in these rodents. No species falls far from the predicted proportions. The axis of dietary specialization parallels the axis of a/i, with herbivorous species at the activator heavy end of the developmental spectrum (where posterior molars are bigger than anterior ones) and animal-eating species at the inhibitor heavy end (where anterior molars are bigger). The authors convincingly argue that selection for diet may often act on the proportional expression of activators and inhibitors to produce a well-adapted dental phenotype.

The predictive power of their model is impressive, but will it hold for all mammals? From my further analyses, the answer is a qualified 'yes'. The results are shown in Figure 3, which depicts the 'morphological space' (morphospace) for different combinations of relative molar size. Nearly 70% of the variation from 35 additional species, representing 13 mammalian orders, is explained by Kavanagh and colleagues' model.

These new data probe the boundaries of their model by including species with phenotypes they did not test: marsupials (which typically have four molars); the bat-eared fox (an unusual

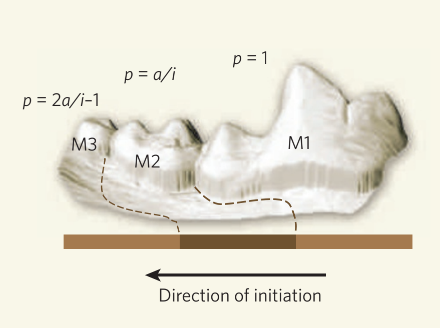

Figure 2 | Predictions of Kavanagh and colleagues' developmental model. The molar teeth — M1, M2 and M3 — develop from the front to the back. The size of the teeth are proportional (p) to the ratio of activator to inhibitor (a/i) molecules. Low a/i results in larger posterior molars, and high a/i results in larger anterior molars (like the ones shown here). Regardless of a/i, M2 will have an absolute size that is one-third of the combined size of all the molars (in species with three molars).