

took advantage of a method for forming ordered organic cyclohexene monolayers on semiconductors¹¹; this method leaves the silicon surface coated with an ordered array of non-reactive C–H groups. The authors hypothesized that any interaction with the deposited pentacene molecules would be weak, and that this would lead to improved growth (Fig. 1b). Their hunch was right. Deposition of pentacene onto these organic-modified surfaces dramatically improves the crystallinity, leading to perfect thin-film crystals approaching 0.1 mm in size — much larger than the size of a single transistor. Similar results were obtained on oxidized silicon surfaces, provided that all of the chemically reactive ‘dangling bonds’ were eliminated. In essence, the new results show that the key to fabricating organic single crystals in thin-film form is to modify the substrate to reduce the bond strength to the organic molecules.

The technological significance of the new results is this: because microelectronic devices are only micrometres (or less) across, it should now be possible to make integrated circuits in which each transistor is made from a single crystal of pentacene, with corresponding improvements in electrical performance. But the results also have broader implications. The trend towards ‘molecular’ electronics is being played out on many length scales, from the micrometre scale of classical microelectronics using organic molecules, down to the use of single molecules³. There is tremendous potential for enhancing chemists’ abilities to design and fabricate ‘designer molecules’ with very specific types of electrical functionality. For instance, specific chemical groups might control the conductivity through a molecule, while other groups might be readily switched between oxidized and reduced states to make a kind of molecular switch^{1–3}.

The practical limitations in this enterprise may not lie in the materials themselves. Rather, they may be in understanding and controlling the properties at the interfaces between organic molecules and the inorganic materials (silicon, metals and so on) that connect them to the macroscopic world¹², and in learning how to coax molecules into assembling themselves into more complex structures. The new work⁸ extends the classical theories of nucleation and growth to more complex organic materials, thereby providing a conceptual link between the two. Given a similar understanding of the electronic properties of the materials and their interfaces, the dreams of cheap, flexible (and perhaps even biodegradable) microelectronics based on organic molecules may soon become a reality. ■

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1. Aviram, A. & Ratner, M. *Chem. Phys. Lett.* **29**, 277–283 (1974).
2. Collier, C. P. *et al. Science* **287**, 391–394 (1999).
3. Joachim, C., Gimzewski, J. K. & Aviram, A. *Nature* **408**, 541–548 (2000).
4. Chiang, C. K. *et al. Phys. Rev. Lett.* **39**, 1098–1101 (1977).
5. <http://www.nobel.se/chemistry/laureates/2000>
6. Crone, B. *et al. Nature* **40**, 521–523 (2000).
7. Schön, J. H., Berg, S., Kloc, Ch. & Batlogg, B. *Science* **287**, 1022–1023 (2000).
8. Meyer zu Heringdorf, F.-J., Reuter, M. C. & Tromp, R. M. *Nature* **412**, 517–520 (2001).
9. Dimitrakopoulos, C., Brown, C. & Pomp, A. *J. Appl. Phys.* **80**, 2501–2508 (1996).
10. Kasaya, M., Tabata, H. & Kawai, T. *Surf. Sci.* **400**, 367–374 (1988).
11. Hamers, R. J. *et al. Acc. Chem. Res.* **33**, 617–624 (2000).
12. Pantelides, S. T., DiVentra, M. & Lang, N. D. *Physica B* **296**, 72–77 (2001).

Demography

Uncertain population forecasts

Nico Keilman

Traditional population forecasts made by statistical agencies do not quantify uncertainty. But demographers and statisticians have developed methods to calculate probabilistic forecasts.

The demographic future of any human population is uncertain, but some of the many possible trajectories are more probable than others. So attempts to forecast demographic aspects of a population, such as its size by a given year, should include two elements: a range of possible outcomes, and a probability attached to that range. Together, these elements constitute ‘prediction interval’ for the population variable concerned. There is a clear trade-off between greater certainty (higher odds) and better precision (narrower intervals). For instance, on page 543 of this issue, Lutz, Sanderson and Scherbov¹ estimate that the odds are 4 to 1 (an 80% chance) that the world’s population, now at 6.1 billion, will be between 5.6 billion and 12.1 billion in the year 2100. Odds of 19 to 1 (a 95% chance) result in a wider interval: 4.3 billion to 14.4 billion.

Demographers have become increasingly concerned about the accuracy of their forecasts, in part because the rapid fall in fertility in Western countries in the 1970s came as a surprise. Forecasts made in those years predicted birth rates that were up to 80% too high and too many young children. The rapid reduction in mortality after the Second World War was also not foreseen; life-expectancy forecasts were too low by 1–2 years; and the predicted number of elderly, particularly the oldest people, was far too low^{2,3}.

Those who use forecasts should be informed about the accuracy of historical predictions. But even more important is the expected accuracy of the current forecast. Statistical agencies traditionally deal with the uncertainty of forecasting population variables by producing two or more predictions of fertility or mortality (or both), and then calculating a range of predictions. For instance, Statistics Norway expects the number of children aged 6–12 in Norway in 2010 to be between 401,000 and 436,000, depending on whether fertility is low or

high — that is, on whether women have an average of 1.5 or 2.1 children, respectively, in 2010. The agency attaches no probability to this interval. Yet those who are planning provisions for education need to know whether the likelihood of this scenario is roughly 30%, 60% or even 90%.

So, during the 1990s, demographers and statisticians developed methods for making probabilistic population forecasts, the aim of which is to calculate prediction intervals for every variable of interest. Examples include population forecasts for the United States, Austria, Germany, Finland and the Netherlands; these forecasts comprised prediction intervals for variables such as age structure, average number of children per woman and immigration flow^{4–8}. Lutz *et al.*¹ present probabilistic population forecasts for the whole world, and for the 13 large regions that they divide the world into (see Table 1 on page 544). Their most important message is that there is an estimated 85% chance that the world’s population will stop growing before 2100.

Yet probability statements of this kind — which give the expected accuracy of a population forecast — must be interpreted with care, because they vary depending on the statistical method used and its assumptions. For instance, Lutz *et al.*¹ estimate that there is a 95% chance that the world population will reach 6.6 billion to 11.4 billion in 2050 (see Fig. 2 on page 544). But the US National Research Council (NRC) uses a different method and has calculated that there is a 95% chance that the 2050 world population will be between 7.9 billion and 10.9 billion⁹.

There are three main methods of probabilistic forecasting: time-series extrapolation; expert judgement; and extrapolation of historical forecast errors. Time-series methods rely on statistical models that are fitted to historical data. These methods, however, seldom give an accurate description of the past. If many of the historical facts remain

unexplained, time-series methods result in excessively wide prediction intervals when used for long-term forecasting.

Judgemental methods can be used to correct or constrain such broad prediction intervals. Expert judgement is also used when expected values and corresponding prediction intervals are hard to obtain by formal methods. In demographic forecasting, the expert-judgement method has been pioneered by Lutz and colleagues^{5,6,10}. A group of experts is asked to indicate the probability that a key parameter (such as the average number of children per woman, or life expectancy) in some future year falls within a certain prespecified range. A weakness of this approach is that experts, often being unduly confident, tend to give over-optimistically narrow prediction intervals¹¹. When the forecasts are later compared with actual data, the intervals turn out to fit the observed trends much less frequently than the probabilities suggested.

Finally, empirical errors observed for past forecasts may be extrapolated to predict the expected errors for the current forecast. For the NRC report⁹, this method was included in the statistical model to calculate the uncertainty of United Nations population forecasts for every country. A problem here is that forecasts prepared in the 1960s or earlier were poorly documented, so data on historical errors do not stretch back as far as one would like.

Elements of the three methods are often used in combination. For instance, time-series methods involve some degree of subjectivity, perhaps in choosing the extrapolation model or the length of the historical data series. These decisions may strongly influence the prediction intervals. And the intervals, whether obtained by time-series methods or expert opinion, are frequently checked against historical error patterns^{4,7}. Lutz *et al.*¹ combined expert judgement with time-series models.

Irrespective of the method used, probabilistic forecasts of the youngest and oldest age groups show the most uncertainty, because fertility and mortality are hard to predict. Short-term forecasts of the demography of developing countries are also subject to great uncertainty, because of the poor quality of their demographic data. Finally, prediction intervals are always narrower when variables are aggregated (for example, when the populations of all countries are added together) rather than looked at individually, because the errors tend to cancel each other out. These kinds of uncertainty assessments are crucial, and statistical agencies would do a great service to users of forecasts if they would adopt probabilistic methods rather than more traditional methods that do not take uncertainty into account. Yet those making use of population forecasts should also keep in mind that

probabilistic statements themselves are uncertain to some extent. ■

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1. Lutz, W., Sanderson, W. & Scherbov, S. *Nature* **412**, 543–546 (2001).
2. Horiuchi, S. *Nature* **405**, 744–745 (2000).
3. Keilman, N. *J. Official Stat.* **13**, 245–277 (1997).
4. Lee, R. & Tuljapurkar, S. *J. Am. Stat. Assoc.* **89**, 1175–1189 (1994).

5. Lutz, W. & Scherbov, S. *Eur. J. Pop.* **14**, 1–17 (1998).
6. Lutz, W. & Scherbov, S. *Z. Bevölkerungswissenschaft* **23**, 83–109 (1998).
7. Alho, J. *A Stochastic Forecast of the Population of Finland Reviews 1998/4* (Statistics Finland, Helsinki, 1998).
8. De Beer, J. & Alders, M. Working Paper no. 45 <http://www.unecp.org/stats/documents/1999.05.projections.html>
9. National Research Council *Beyond Six Billion: Forecasting the World's Population* (Nat. Acad. Press, Washington DC, 2000).
10. Hanika, A., Lutz, W. & Scherbov, S. *Statist. Nachrichten* **12**, 984–988 (1997).
11. Armstrong, J. *From Crystal Ball to Computer* 2nd edn (Wiley, New York, 1985).

Nanotechnology

Boning up on biology

T. Andrew Taton

Attempts to tailor nanometre-scale objects to mimic and interact with natural materials raise the question of how to predict the biological response to these tiny creations.

The science of manipulating matter on the nanometre scale — nanofabrication — has provided researchers with a remarkably diverse set of tools for probing the behaviour of biological structures. At a recent meeting* on the “Biological Applications of Nanotechnology”, scientists at the

*American Chemical Society ProSpectives Conference, Berkeley, California, USA, 3–6 June 2001.

forefront of this research showed how these tools are already being used to sequence genomes, diagnose disease and watch single biomolecules perform their natural functions in real time. But there were also a few hints of a fresh theme emerging from all this work: the design of artificial nanostructures that can interact with and replace natural, biological materials. Studies that aim at

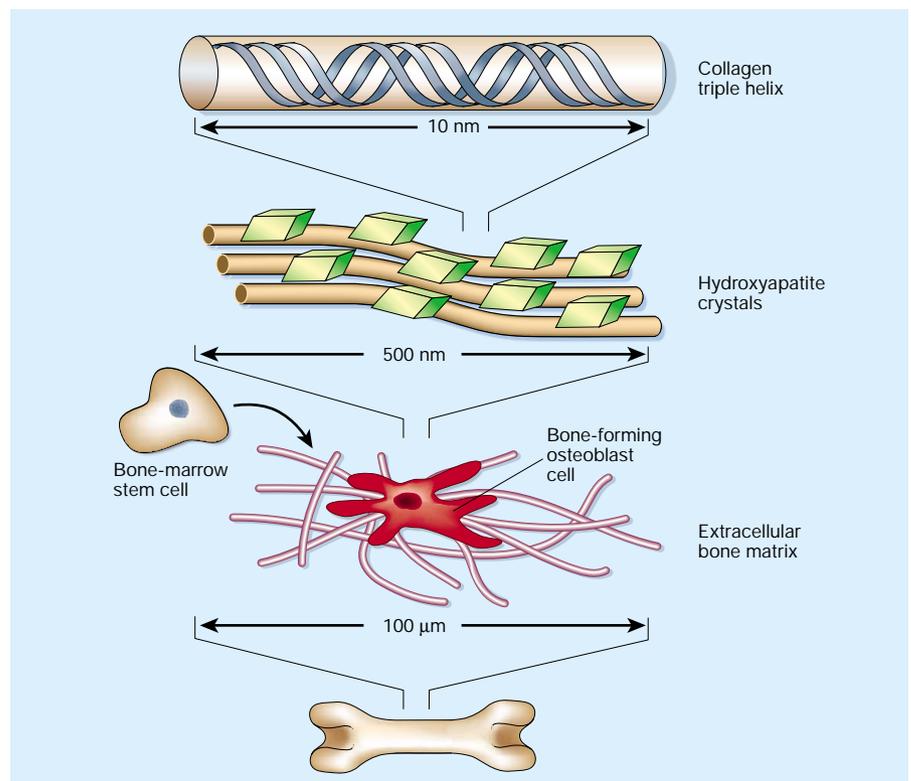


Figure 1 The many scales of organization in natural bone. Collagen triple helices spontaneously form nanoscale bundles of protein, which act as a template for the crystallization of hydroxyapatite nanocrystals. The collagen matrix is also recognized by undifferentiated bone-marrow stem cells, which become bone-forming osteoblasts after signals from bone-specific proteins in the matrix. To duplicate the extraordinary durability and strength of natural bone, researchers must design synthetic materials that match these structural levels of organization from the nanoscale upwards. (Note that this figure shows the dimensional, not sequential, principles of bone construction.)