for many applications — in biomedical devices, for example, or as coatings to prevent the icing or fouling of surfaces. Currently, the main weakness of SLIPS is their durability, which is limited by how long the lubricant stays in the pores without evaporating or leaking. Another problem is that there are strict limitations on the chemical properties of the lubricants: they must be immiscible with both water and oil, but they should also penetrate into the pores of the underlying material. The authors' preliminary studies into these issues are encouraging, but additional research is needed before applications will emerge. ■

Michael Nosonovsky *is in the Department of Mechanical Engineering, College of Engineering & Applied Science, University of Wisconsin–Milwaukee, Milwaukee, Wisconsin 53211, USA.*
e-mail: nosonovs@uwm.edu

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SYNTHETIC BIOLOGY

A yeast for all reasons

Scientists have begun to overhaul a yeast's genome to make it more stable, engineerable and evolvable. Remarkably, the part-natural, part-synthetic yeast cells function and reproduce without obvious ill effects. SEE LETTER P.471

PETER J. ENYEART & ANDREW D. ELLINGTON

The baker's yeast *Saccharomyces cerevisiae* is a model organism, and therefore one of the best-understood biological systems on the planet. Nevertheless, the Byzantine complexity of its inner workings still keeps bioengineers up at night, and continues to provide fodder for experimentation. If scientists could 'refactor' model organisms — that is, recode their genomes to be simpler and more amenable to human understanding and tinkering — then science and biotechnology based on those organisms could proceed at an accelerated pace. On page 471 of this issue, Dymond *et al.*[1] present a major advance towards this end: the construction of a functional, partly synthetic version of the *S. cerevisiae* genome.

Rewriting genomes to meet the specifications of humans has been a stated goal of synthetic biology for some time[2]. But the labour and expense involved in actually making such radical changes to genomes, coupled with uncertainties about the chances of improving on what nature spent billions of years perfecting, have meant that only a few serious tilts at genome re-engineering have been made. Previous noteworthy examples include the refactoring of 12,000 base pairs (about 30%) of a virus genome[3] and the removal of 'amber' stop codons — nucleotide sequences that signal the termination of translation — from the bacterium *Escherichia coli*[4], a feat that should allow researchers to rewrite portions of the bacterium's genetic code at will. And, of course, the genome of a *Mycoplasma* bacterium has been synthesized *de novo* by workers at the J. Craig Venter Institute in Rockville, Maryland, and used to infuse a working cell[5].

Dymond *et al.*[1] have now raised the bar by starting work on eukaryotes (organisms such as fungi, plants and animals), which have much larger and more complex genomes than bacteria. More specifically, the authors have replaced sections of two chromosomes of *S. cerevisiae* — 90,000 bases at the end of chromosome IX, and 30,000 bases at the end of chromosome VI — with synthetic DNA. Their eventual goal is presumably to replace the entire genome of 12 million base pairs with a human-designed sequence.

To make their synthetic DNA, Dymond *et al.* entirely removed 20 regions from the naturally occurring yeast chromosomes. Most of these regions were repetitive sequences (which can cause DNA segments to be deleted or even cause chromosomes to mis-segregate), or sequences that were non-functional or redundant. The authors also recoded all genes longer than 500 bases to contain 'watermarks' — sequences that allow the synthetic DNA to be easily differentiated from natural sequences using standard laboratory methods, but that do not change the sequences of proteins encoded by genes. As in the previously reported work[4] in *E. coli*, Dymond and colleagues[1] modified amber stop codons in the DNA of *S. cerevisiae* so that they could be recoded in the future, for example to encode unnatural amino acids for insertion into yeast proteins.

Astoundingly, the authors found that yeast cells containing the modified genome suffered no growth defects and displayed minimal differences in gene expression in comparison with the wild-type strain. The entire sequence of the artificially added DNA was faithfully reproduced by living cells, which is either a testament to the robustness of human engineering or a sign that God's fingerprints are fainter than creationists would have you believe.

In addition to the changes mentioned earlier, Dymond and co-workers introduced sequence elements known as loxPsym sites after every non-essential gene in their synthetic DNA, and at several other positions. In the presence of an enzyme called Cre recombinase, these loxPsym sites stochastically recombined with each other, either deleting or inverting the intervening sequence of DNA. The authors were thus able to generate a vast library of yeast genomes, containing all manner of random architectures, at will. Such libraries could be screened or evolved to find new yeast strains that are better suited to living in a given environment. Moreover, because yeast is used to produce alcohol, proteins and high-value organic compounds, new strains generated in this way might prove to be useful for industry, in the same way that a simplified *E. coli* strain has proved to be an excellent platform for producing large quantities of proteins[6].

The obvious extension of Dymond and colleagues' work is to rebuild the entire yeast genome. However, given that the currently completed synthetic sequences represent only about 1% of the whole genome, rebuilding the remainder is a daunting task. One issue is that, even though the aggregated cost of the materials, apparatus and consumables used in DNA synthesis has been steadily decreasing, the construction of entire genomes remains inordinately expensive[7].

Even more problematic is the cost of labour. A comparison of recent endeavours in genome synthesis and modification (Table 1) reveals

TABLE 1 | LABOUR REQUIRED FOR GENOME SYNTHESIS

Organism (year)	DNA bases synthesized (% of genome)	DNA bases per year of labour*
T7 bacteriophage (2005)[2]	12,000 (30)	1,300
Mycoplasma mycoides (2010)[5]	1,080,000 (100)	15,000
Escherichia coli (2011)[4]	4,600,000 (100) or 28,000 (0.6)†	96,000 or 600†
Saccharomyces cerevisiae (2011)[1]	120,000 (1)	2,700

*Estimated as follows: total bases synthesized/[number of authors × 3], assuming that 3 years is the average time spent by a person on genome-synthesis projects.
†Depending on whether the entire genome or only synthetic oligonucleotides are counted.

that DNA synthesis at the scale of the yeast genome will require either armies of scientists — such as the wonderful group of undergraduate students currently working on similar projects[8] with Dymond and co-workers — or new methodologies. The authors' landmark work[1] confirms that automated DNA synthesis and assembly techniques are becoming necessary, and that the total synthesis of genomes is likely to supersede piecemeal approaches to genome modification. Given a little push here and there from technological advances, the age of designer genomes is nigh. ■

Peter J. Enyeart *is at the Institute for Cell and Molecular Biology, University of Texas at Austin, and* **Andrew D. Ellington** *is in the Department of Chemistry and Biochemistry, University of Texas at Austin, Austin, Texas 78712, USA.*
e-mails: peter.enyeart@mail.utexas.edu; andy.ellington@mail.utexas.edu

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QUANTUM PHYSICS

Single electrons take the bus

Single-electron circuitry is a promising route for quantum information processing. The demonstration of single-electron transfer between two distant quantum dots brings this technology a step closer. SEE LETTERS P.435 & P.439

TAKIS KONTOS

The realization of electronic machines that exploit the laws of quantum mechanics is a dream for many physicists. Among the different architectures proposed so far for meeting this goal, one very promising option is based on quantum dots: nanometre-sized electron boxes, or conducting islands, that can comprise as little as one electron. As with classical electronic devices, the construction of such a quantum machine requires 'wires' to connect up the elements of the machine's internal electronic circuitry. But in the quantum world, making such wires is not a trivial matter.

Two papers in this issue, one by Hermelin *et al.*[1] (page 435) and the other by McNeil *et al.*[2] (page 439), demonstrate wires, or 'buses', that can carry only a single electron and interconnect two distant quantum dots. These findings provide a building block for the implementation of large-scale networks of quantum dots, which will be necessary to scale-up techniques for local quantum manipulation that are currently performed only at the single-quantum-dot level[3].

In quantum dots, confinement can be such that the characteristic charging energy of the dot — the energy it takes to add an extra electron to it — exceeds thermal fluctuations at cryogenic temperatures. In such a situation, known as a Coulomb blockade, electrons passing through the quantum dot have to do so one by one. This fact, combined with the discreteness of the quantum dot's energy spectrum, makes the dots ideal sources of single electrons[4].

The usual way to extract a single electron from a quantum dot is to raise the last occupied energy level of the dot to well above the characteristic energy (the Fermi level) of the electronic reservoir to which the dot is coupled. This can be done with the help of an electrostatic 'gate' electrode. In this manner, the electron 'sitting' on the last occupied energy level is forced energetically to 'fall off' into the electronic reservoir; conversely, an electron can be absorbed from the electronic reservoir by lowering a previously unoccupied energy level below the Fermi level. Because an electron emitted in such a way rapidly mixes with other electrons in the electronic reservoir, knowledge of that electron's initial electronic state will be deficient, and any quantum information stored in the electron will be lost. This explains why extracting an electron from a dot and capturing it in another one is far from trivial.

To isolate a single electron and implement a single-electron bus, Hermelin *et al.*[1] and McNeil *et al.*[2] took an alternative approach that involves moving a quantum dot rather than acting directly on its energy levels. The basic idea is to distort the electrostatic potential that traps the dot's electron, using an acoustic wave that propagates across the surface of the device hosting the dot. The acoustic wave, which is induced by a microwave pulse, allowed the authors to expel a single electron from the dot and, subsequently, to transfer it to a receiving dot through an empty channel, in which the electron 'surfs' on the acoustic wave.

Hermelin *et al.* and McNeil *et al.* demonstrated successful single-electron transfer between the dots by detecting coincident emission and capture at both dots. These were detected with devices that are routinely used for charge detection in quantum dots[3]: sensitive electrometers that are placed closed to the dots. The efficiency of the authors' approach[1,2] was such that it allowed, for example, McNeil *et al.*[2] to reliably transfer single electrons back and forth between the dots over a cumulative distance of about 0.25 millimetres — nearly a macroscopic distance. Hermelin *et al.* went on to show that, after initially loading a dot with two electrons, it is possible to split them apart: one stays in the dot and the other is captured by a receiving dot.

These experiments[1,2] are particularly relevant with a view to using single-electron buses for retrieving and distributing quantum information stored in quantum dots that are embedded in complex networks. It has been shown[3,5] that electronic spin can be manipulated quantum mechanically with ever-increasing fidelity. It is therefore possible to imagine manipulating an information-encoding single spin in one quantum dot, then transporting it to another distant dot in the network. What's more, by using a double quantum dot, one could foresee the creation of an arbitrary two-electron superposition spin state[5] and its transfer between distant quantum dots. This would pave the way for studying quantum entanglement of two electrons in a solid-state environment.

All of these exciting possibilities offered by the set-ups of Hermelin *et al.* and McNeil *et al.* require that single-electron transfers do not degrade quantum information, an aspect that is not addressed in their work. Because new electron-manipulation techniques always come with unexpected dissipation mechanisms, it is not clear whether the electrons can retain their spin state, and so the encoded information, during their travels in the channel. However, recent advances in spin manipulation and control[5,6] call for optimism. We should therefore be confident that the demonstrated single-electron bus will go quantum in the not-so-distant future. ■

Takis Kontos *is at the Laboratoire Pierre Aigrain, École Normale Supérieure, 75231 Paris Cedex 05, France.*
e-mail: kontos@lpa.ens.fr

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