

Synthetic biology goes live

Dek Woolfson

(University of Bristol, UK)

On 14 November last year, the Biochemical Society, the Royal Society of Chemistry, the think-tank BioCentre and the University of Bristol co-hosted a debate on synthetic biology, which was webcast live. Dek Woolfson co-chaired the event from Bristol. Here are his reflections and conclusions from the evening, including some advice on how we might approach the broader issues of the subject and events like this in the future.

Don't be alarmed. Craig Venter hasn't created life using nothing but a DNA synthesizer. The title of this report refers to a live link up between the Chemistry Centre, Burlington House, London and the Great Hall at the University of Bristol. The aim was to have a broad and public debate on the emergence and implications of synthetic biology and the event was webcasted live. Credit to the hosts and their teams as, by and large and despite some technical glitches, the link, broadcast, associated tweets and the evening as a whole all went well.

Ehsan Masood (Editor, *Research Fortnight*) chaired the evening from London, where the panel members were: Lionel Clark (who has responsibility for strategic research programmes at Shell, and was speaking in his capacity as Chair of the UK Synthetic Biology Roadmap group); Professor Rob Edwards (a molecular plant biologist, and Chief Scientist at the Food and Environment Research Agency); Alexandra Daisy Ginsberg (a designer, artist and writer interested in synthetic biology); and Helena Paul (co-director, EcoNexus, a public-concern group analysing the impact of new technologies on society and the environment). I chaired the Bristol end and acted as another panel member; I'm a chemist/biochemist working on protein engineering and design. So this was quite a diverse bunch.

To set the tone and to give some context, Ehsan introduced the panel and gave us each a few minutes to say what 'synthetic biology' means to us in the broadest sense. This was useful and worked well. One thing that came out of this – for me at least – was that the non-scientists were clearly the more articulate and forthright. They stated their positions clearly, whereas the scientists were a little (too) circumspect. This ran through the subsequent responses to questions and in discussions; it is the first of my main conclusions, and something that I'll return to at the end.

I could give a blow-by-blow account of questions and responses, but I think it better to give some of the themes from the discussions. However, before I start, let's get a couple of things cleared up: what synthetic biology is, and what it isn't.

Synthetic biology is work in progress

To me, synthetic biology is an attempt to make the engineering of biological systems easier; that is, more systematic, predictable and reliable. I think that this view and aim is pretty much shared by all practising synthetic biologists, most scientists who take a view on the field and funders. The synthetic-biology approach can be taken at all levels from the design and engineering of molecules (DNA, proteins, and so on), through rewiring networks and pathways in cells (cascades of transcription factors and metabolic pathways included), and up to the supracellular level, possibly even taking in tissue engineering. This is more controversial, as this broad-church definition casts the net wider than some of the more-traditional synthetic biologists might like. However you define it, the key is being systematic and predictive in all of these endeavours. This is my second conclusion: keep synthetic biology broadly defined, but demand that whatever we do under the synthetic-biology banner, it has to be systematic.

Synthetic biology makes certain assumptions: namely, that biology is modular; and that its modules can, to all intents and purposes, be ripped out of their normal context and then stitched together in new ways and in very different settings. Presumably, most chemists and biologists agree with the former. For me, the second point is still a hypothesis that needs testing. Moreover, experience shows that, although biological modules can be combined, to get working systems requires a little tweaking. For example, fusing two protein domains often requires some empiricism to obtain appropriate linkers that maintain structure and couple function; and making new circuits and gene networks needs some experimentation with different combinations of host strains, vectors, promoters and so on. Thus, and this is my next conclusion, synthetic biology is still a hypothesis at the moment. However, it is one that must be tested; and it will need a significant amount of further underpinning basic science to understand how biological systems are put together and function.

Turning to what synthetic biology isn't: it is not simply the transfer of genes from one organism to

another; although much of traditional synthetic biology builds on this concept, the technology that we know now as recombinant DNA or molecular biology. Neither is it, at the other extreme, the 'creation of life' often associated, rightly or wrongly, with Craig Venter's vision of synthetic biology, even though some outside of science would have us believe that it is *just* this. And finally, nor is it some of the things in between these extremes, such as GM crops and foods. No. It is, as stated above, the endeavour to bring genuine engineering-design principles to the construction of biological systems, and, eventually, to do this to make 'useful stuff', a point that I will return to.

Whereas some of these things were discussed at the meeting, they were only touched upon and not addressed from the start, which would have been my preference. I say this with good reason: without a clear definition and a view on the confines of the synthetic biology, debates can go off track and be less constructive than they might have been. This would be my fourth conclusion and a piece of advice for future debates: define the subject and attempt to stick to it; or at least debate around it generally, but closely.

The debate

After an opening question from Ehsan on GM foods, which I shall return to, questions then came from the floor, both in London and Bristol. As might be expected, contentious issues were raised as follows. On these points, Helena Paul was direct and made her position very clear, whereas some of rest of the panel skirted around the issues, which in my view was not so good.

For example, the precautionary principle was raised along with a call for a moratorium on synthetic-biology research until we know that it's safe. In my view, this is somewhat reactionary and unhelpful. It also opens a can of worms: how do we know what's safe until we've had chance to test it in the controlled confines of a research laboratory? What does 'safe' mean? And, how do we assess risk? For me, the latter is a big issue for public discussions on any technology, as it seems that collectively (as the public) we are poor at assessing risk.

There was consensus on the need for more public engagement and debate, which raised some 'hear hears' from both the live audiences and through Twitter. This can only be a good thing, and we scientists should learn to accept and cater for – indeed embrace – the public's thirst for knowledge and opportunities to meet us in the flesh.

Issues around patenting in synthetic biology were also brought up, albeit fleetingly. Here, and to counter some concerns, points were made that patenting is usually necessary to see any invention through to useful products; and that there is an open-access philosophy in

the synthetic-biology movement – making parts freely available while still allowing patenting of functioning useful systems.

Finally, the emergence of DIY biology (also known as garage biology or biohacking) was highlighted, eliciting a small number of responses that this should be off-limits and regulated. But the counter-point was made: "how can DIY *anything* be regulated?" This led to some discussion of dual and military use of synthetic biology, which was again countered by points that all technology is potentially dual use, even the laser pointers that we use during presentations.

These discussions left me pondering a couple of things: first, we have the same or similar debates over all new potential technologies – witness GM foods and nanotechnology – so why can't we nail it once and for all? That might be wishful thinking. Besides, as one of my colleagues pointed out later, there are aspects of synthetic biology that do border on creating life, or at least tinkering with it considerably; and this makes many people, scientists included, feel uneasy. Countering this, now that we live in a world with recombinant DNA, cloning and GM organisms, we'd better



Daisy Ginsberg delivers her opening remarks (MPP Image Creation)



Left to right: Robert Edwards, Helena Paul, Daisy Ginsberg, Lionel Clark and Dek Woolfson (big screen) debate synthetic biology (MPP Image Creation)

get to grips with it in all respects. This leads to my second thought, which is: if only people could see the potential benefits of synthetic biology. It is our job as scientists to explain the science and these benefits, and this is why the issue of public engagement is so important.

Tangible prospects

So, what use is synthetic biology, and what are its benefits? Well, if we get it right, it could be a transformative technology. Imagine biological modules being available and engineerable like the nuts and bolts used by structural engineers, or the circuit boards and electronic components that electrical engineers use to construct our now-essential handheld gadgets. Some of the promises of synthetic biology are sustainable production of biofuels and cheaper routes to drugs, indeed, a new biotechnological industrial revolution. Herein lies the rub. These aspects are often hyped, and not just by scientists: synthetic biology is one of George Osborne's eight priorities for science¹, and is being heralded by some as one of the new technologies that will take us out of the economic downturn. Maybe so, but that remains to be seen, and I reiterate that much basic science still needs to be done if synthetic biology is to become of economic benefit. Thus, and quite rightly, many scientists are circumspect here, aware that we must balance the hype with reality. More realistic and closer objectives include new biosensors and medical diagnostics, and cheaper cell-based routes to fine chemicals. If you are interested in, or are planning any public engagement in synthetic biology, I'd advise having some of the more tangible prospects up your sleeve to counter both the scaremongering and the hype.

Ehsan brought the debate to a close by asking the panel: "with hindsight, would you uninvent the combustion engine?" I rest my case.

Grounded debate

In closing here, I have one further thought, which crystallized after an email exchange with Rob Edwards: the synthetic-biology debate must move on. To some extent, it has been confused by issues hanging on from the GM debate, the overuse of metaphors for what synthetic biology is, and the aforementioned focus on lofty rather than realistic

benefits and goals. As pointed out by Helena Paul, synthetic biology is distinct. Therefore we should have the confidence to discuss it as such and not in the context of previous debates, by turning to unhelpful metaphors, or focusing on grand schemes. In the light of this, an alternative final question might be: "with hindsight, would you undiscover the double helix, or uninvent recombinant DNA?"

On a personal note, I found the event a worthwhile and (mostly) an enjoyable experience, which I would repeat. Although I hope that I'd read my conclusions beforehand, and take some of my own advice: be clear, and stand your ground; define what synthetic biology is and debate around that; point out that synthetic biology is very much work in progress and needs more basic research; find some clear and tangible examples with real-life applications and benefits; and avoid the hype.

Finally, this is a two-way process, and I would call on any social scientists, lobbyists and members of interest groups who are following the synthetic biology debate – perhaps with some concern or even alarm – to make time and take in some of the underlying science. Only in this way can the debate be informed, truly two-way and ultimately useful. ■

I thank George Banting, Rob Edwards, Maggie Leggett, James Lush and Chris Wood for their critical reading of an earlier version of this commentary.

Reference

1. <http://royalsociety.org/news/2012/osborne-at-royal-society>

One clinician scientist's experience of the Royal Society pairing scheme

"I commend this scheme to the house"

David Kavanagh

(Newcastle University, UK)

As scientists, we would like to think that our Government bases policies on sound scientific evidence. Yet scientific representation in the House of Commons is minimal, with most MPs coming from business, finance, law and media backgrounds. This unfamiliarity with the scientific process will lead to apprehensiveness and sometimes some scepticism, resulting in poor policy choices. As scientists, we must

explain our science to government if we are to improve the decision-making process. Our scientific training, however, teaches us how to interact with our scientific peers, not how to engage in the political process. It was because of this that I was so keen to become involved in the Royal Society pairing scheme.

Having been accepted, my 'Week in Parliament' began with a seminar by the Hansard Society explaining

the mechanisms of parliament. Subsequent lectures by the Parliamentary Office of Science and Technology and the Commons and Lords Science and Technology Select Committees focused specifically on the role of science in government.

Interactive sessions followed, taking the role of Government Chief Scientific Adviser and deciding how we would react and advise government in the advent of various crises. These allowed us discuss what our scientific advice might be and what the political ramifications of them would be.

It was then off to meet my host for the week, Chi Onwurah, MP for Newcastle Central and then Shadow Minister for Innovation, Science and Digital Infrastructure (Onwurah was succeeded by Shabana Mahmood in January 2013). With her science portfolio, being paired with Chi provided the perfect opportunity to discover how science policy is formulated. In a hectic few days, Chi hosted a breast cancer charity at the House of Commons, met with an arthritis charity, and had roundtables on innovation at the Google Campus and on science funding at Portcullis House. In spare moments, she would deal with constituents' requests before dashing to the chamber to vote. With such demands on an MP's time, it became clear that brevity, clarity and simplicity were the key to effective engagement.

"Many MPs openly admitted their lack of scientific expertise and were keen to foster closer relationships with the scientific community"

I was also able to attend the Commons Science and Technology Select Committee looking into the merger of the British Antarctic Survey and the National Oceanography Centre, with the committee raising concerns about the process. Chi explained that the Select Committee are happy to receive unsolicited advice on matters in our field of expertise and that we should not wait to be asked.

An evening reception at the Royal Society provided the opportunity to chat with other MPs and Peers about their view of science in government. Many openly admitted their lack of scientific expertise and were keen to foster closer relationships with the scientific community.

In Chi's reciprocal visit to my laboratory, we demonstrated a range of genetic and biochemical experiments which mirrored the Newcastle Renal Complement Group's 15-year journey of discovery, ultimately resulting in a treatment for a severe kidney disease which leads to kidney failure (atypical haemolytic uraemic syndrome). This demonstrated the timeframe required to translate basic scientific research into benefits for patients and the difficulties in funding



Holly Anderson explains how she investigates defects in the complement system in patients with atypical haemolytic uraemic syndrome. Left to right: Holly Anderson, Chi Onwurah MP and David Kavanagh

scientific research for such a period. This highlighted the inherent differences between the short political cycle in Westminster and scientific research.

Chi also has a longstanding interest in scientific careers for women. We therefore organized a roundtable with some of the junior female scientists at the Institute of Genetic Medicine to discuss the hurdles women in science face. Chi expressed concern at the short-term nature of postdoctoral research positions and the instability this creates for researchers. Although acknowledging the likely fiscal constraints following the next election, she discussed the amount of money China and Brazil are investing in science. Indeed, as if to highlight this, one of my students, Geisilaine, is from Brazil and is currently funded by her government to gain experience in world-leading research institutions. Chi then discussed the need for a long-term funding plan for science as part of her 'five-point plan for science'

The Royal Society pairing scheme provides a starting point for a dialogue with government. I found government willing to reach out to the world-leading science this country produces. The knowledge I gained, and continue to gain from ongoing discussions with Chi, will provide invaluable throughout my career. I commend this scheme to the House. ■

Applications for the 2013 Royal Society pairing scheme will be open for approximately 6 weeks from mid-April. Details are available on the Royal Society's website: <http://royalsociety.org/training/pairing-scheme/>