LETTER

REPLY TO EINARSSON:

The computational power of parallel network exploration with many bioagents

Dan V. Nicolau Jr.[a,b], Mercy Lard[c], Till Korten[d,e], Falco C. M. J. M. van Delft[f], Malin Persson[g], Elina Bengtsson[g], Alf Månsson[g], Stefan Diez[d,e], Heiner Linke[c,1], and Dan V. Nicolau[h,i,1]

We very much appreciate Einarsson's interest in our work (1) and his well-articulated observations regarding the computational complexity of dynamic programming algorithms for the Subset Sum Problem (SSP) (2). We would like to distinguish clearly between the concept we propose and the physical device we used to demonstrate that concept.

Our concept comprises the conversion of a mathematical problem into a network of channels and nodes (1). If the network appropriately mirrors the problem, each unique trajectory through it corresponds to evaluating one solution from the pool of all potential solutions. In the case of combinatorial problems, whether nondeterministic-polynomial-time (NP)–complete or not (e.g., simply the problem of generating all 2^K possible subsets from a set of K objects), this solution space, in general, grows exponentially with the "size" of the instance input. Our proposition is that by using a large (and, if self-replicating, growing) number of bioagents, the network, and thereby the solution space, can be explored in a massively parallel fashion, suggesting that it might be possible by this method to solve combinatorial problems efficiently. In contrast, the electronic computer is limited to exploring one solution at a time.

The main purpose of the device was not to present a "ready-to-use" system solving SSP in record time. To do so would be utopic for any first demonstration of a new computing paradigm. Rather, our specific device is designed to illustrate our concept using the example of a primitively encoded network, in which the bioagents generate, by brute force, all possible subsets of the original set, of which there are an exponential number: 2^K. To contrast this computational power directly with the computational power of an electronic machine (figure S1 of ref. 1), we therefore chose to compare the times it would take each system to solve SSP by brute force, not with an optimized algorithm. This distinction is crucial, because the ability to solve any combinatorial problem efficiently by brute force suggests that our concept has the potential to solve efficiently all such (network-encodable) problems. Einarsson (2) points out that "their device requires an exponential amount of computing agents," which, thus, was exactly our point. In contrast, the dynamic programming algorithm he mentions is specific to SSP. Although the same is true for the specific naive device we demonstrated, our concept is general.

Given the potential computational power summarized above, we argue that this technology merits further investigation into its scalability. Is it possible to encode other NP-complete problems into "compact" networks and, by using controlled self-replication, to bring an exponentially growing army of agents to bear on an exponentially growing solution pool? These questions are mathematically and experimentally difficult problems forming the background to ongoing work, in which we hope to be joined by other groups.

Ultimately, solving combinatorial (including NP-complete) problems will require a new, massively parallel computing method, and it is such a system that our paper demonstrates the proof of concept for.

1 Nicolau DV, Jr, et al. (2016) Parallel computation with molecular-motor-propelled agents in nanofabricated networks. *Proc Natl Acad Sci USA* 113(10):2591–2596.

2 Einarsson J (2016) New biological device not faster than regular computer. *Proc Natl Acad Sci USA* 113:E3187.

[a]Department of Integrative Biology, University of California, Berkeley, CA 94720-3140; [b]Molecular Sense, Ltd., Wallasey, CH44 1AJ, United Kingdom; [c]NanoLund and Solid State Physics, Lund University, S-22100 Lund, Sweden; [d]Center for Molecular Bioengineering (B CUBE), Technische Universität Dresden, 01069 Dresden, Germany; [e]Max Planck Institute of Molecular Cell Biology and Genetics, 01307 Dresden, Germany; [f]Philips Research (MiPlaza) and Philips Innovation Services, 5656 AE Eindhoven, The Netherlands; [g]Department of Chemistry and Biomedical Sciences, Linnaeus University, SE-39182 Kalmar, Sweden; [h]Department of Electrical Engineering & Electronics, University of Liverpool, Liverpool, L69 3GJ, United Kingdom; and [i]Department of Bioengineering, McGill University, Montreal, QC, Canada H3A 0C3