## Rethinking Biochemical Sensing - Biomimetic Fluidics based on Stimuli-Responsive Materials

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Since the initial breakthroughs in the 1960's and 70's that led to the development of the glucose biosensor, the oxygen electrode, ion-selective electrodes, and electrochemical/optochemical diagnostic devices, the vision of very reliable, affordable chemical sensors and bio-sensors capable of functioning autonomously for long periods of time (years) remains unrealized. This is despite massive investment in research and the publication of many thousands of papers in the literature. It is over 40 years since the first papers proposing the concept of the artificial pancreas, by combining glucose monitoring with an insulin pump<sup>1</sup>. Yet even now, there is no chemical sensor/biosensor that can function reliably inside the body for more than a few days, and such is the gap in what can be delivered (days), and what is required (years) for implantable devices, it is not surprising that in health diagnostics, the overwhelmingly dominant paradigm for reliable measurements is still single use disposable sensors. Realising disruptive improvements in chem/bio-sensing platforms capable of long-term independent operation requires a step-back and rethinking of strategies, and considering solutions suggested by nature and materials science, rather than incremental improvements in existing approaches<sup>2</sup>.

Through recent developments in 3D fabrication technologies in recent years, we can now build and characterize much more sophisticated 3D platforms than was previously possible. We can create regions of differing polarity and hydrophobicity, mix passive and binding behaviours, and regions of differing flexibility/rigidity, hardness/softness. In addition, we can integrate materials that can switch between these characteristics, enabling the creation of biomimetic microfluidic building blocks that exhibit photoswitchable characteristics such as programmed microvehicle movement (chemotaxis), switchable binding and release, switchable actuation (e.g. valving), and photodetection. These building blocks can be in turn integrated into microfluidic systems with hitherto unsurpassed functionalities that can contribute to bridging the gap between what is required for many applications, and what we can currently deliver<sup>3</sup>. The transition from the current paradigm from engineering inspired 2D fluidics to bioinspired 3D fluids is a major milestone in the evolution of microfluidics. Another lesson we can learn from biofluidics is that the entire system is active. Currently, the only role of the substrate in a microfluidic chip is to define the channels. In biology, the channel walls have a very active role, as has the surrounding tissue. Walls can sense, and respond e.g. open pores and release active agents such as functionalised micro/nanoparticles, vesicles, droplets). Implementation of these disruptive concepts may open the way to biochemical sensing systems with performance characteristics far beyond that of current devices. A key development will be the integration of biomimetic functions like selfdiagnosis of condition and self-repair capabilities to extend their useful lifetime<sup>4</sup>.

## References

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