Chapter 8
Conclusion

Alain Bosseboeuf and Kukjin Chun

A lot of works on micro/nano biosystems has been already performed and they will deeply modify medecine practise and pharmaceutical research by providing low cost and fast biomedical analyses that could be done by non experts. To reach this goal, limitations of bioMEMS must not be underestimated and remaining challenges to overcome the commercialisation bottleneck must be well identified and overcome [1]. Indeed, beside legal and ethic issues, many labs-on-chip and μTAS proposed by research laboratories are still far from a possible introduction into the market. Despite the great opportunities for bioMEMS in healthcare and medical applications, it will take some time to reach its full potential. The same situation occurred in the past for MEMS and similar reasons can be found The challenges facing bioMEMS in the future are:

(i) a not suitable choice of materials and technology that does not warrant reliability or a real low cost of fabrication.

  – For example, PDMS (PolyMethylDiSiloxane) is a widely used polymer in research laboratories because it allows a rapid and easy prototyping but it is water permeable, allows adsorption of hydrophobic molecules, it has short term stability after surface treatment, it undergoes swelling in organic solvents, it requires very specific processes for electrodes integration and it is not suitable for fast processing as required for high volume production, So its uses in real applications is highly questionable. Similar or other

A. Bosseboeuf (✉)
Center for Nanoscience and Nanotechnology, CNRS, University Paris Sud-University Paris-Saclay, 10 Boulevard Thomas Gobert, 91120 Palaiseau, France
e-mail: alain.bosseboeuf@c2n.upsaclay.fr

K. Chun
Department of Electrical and Computer Engineering, Seoul National University, 1 Gwanak-ro, Gwanak-gu, Seoul 08826, South Korea
e-mail: kchun@snu.ac.kr

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issues may exist for other polymers or inorganic material, so their choice must be carefully done. It is also useful to consider other substrate materials than polymers, glass or silicon, like paper [2, 3], or a printed circuit board (PCB) [4].
- Many BioMEMS requires clean rooms and sophisticated equipements for their fabrication. So even if they use cheap materials they will be expensive to fabricate except if they have a low footprint and need to be fabricated in large quantities. This can nevertheless be acceptable if they offer a large added value by integrating a large set of functions and by minimizing the need of external equipements.

(ii) Tests or operation too far from real situations.

- Often, bioMEMs are tested with simple, well controlled or pre-processed samples containing the biological species to be detected. However, in real situations, it migh be necessary to handle and analyze more complex fluids. For example, for human diagnostics, this can be body fluids like blood, saliva, plasma, serum, urine,…So pretreatment or fractionation should be included.
- BioMEMs typically need external equipments for their operation for fluid injection, flow control, detection, power supply, etc. Ideally this should be also miniaturized, notably for portable point-of care systems.
- Miniaturization and low sample volumes often lead to a low signal/noise ratio and thus to the need of expensive, bulky and sophisticated electronic equipments or optical equipments for measurements. Improved techniques for sample concentration and hybridization signal amplification must then be developed. Likewise; integrated sensors, electronics and signal processing should be favoured when possible. CMOS lab-on-chip [5] or interfacing with a smartphone [6] are possible solutions. This was successfully demonstrated in the later case for cholesterol testing, label free bio detection, Elisa assays. and red and white blood cells counting.
- Packaging and resistance to environmental disturbances (temperature, humidity, chocs,…) is hardly considered although it might be a major issue to get robust micro/nano biosystems working in non-air conditioned rooms and stable at room temperature.
- Ease of use and ergonomy must be improved and quantitative and automated measurements must be realized.

Beside looking for solutions to overcome the commercialization barrier of bioMEMS, many investigations remain to be done. It is beyond the scope of this book to provide an exhaustive list of all current challenges in the broad field of micro/nano biosystems but some of them were yet identified in the different chapters. Concerning desease diagnosis by bioMEMS, many studies are focused on cancer, diabetes and aging diseases but many other diseases could also potentially benefit from an earlier and faster detection with micro/nanobiosystems to reduce

their mortality such as malaria, HIV and Tuberculosis but also swine flu, Zika virus or Ebola virus which are a major concern nowadays.

Facing silver age, healthcare is more important than ever in in vitro diagnostics, pharmaceutical research, and drug delivery along with implantable medical devices. All of these applications are promising and require new innovative technologies such as integration with microelectronics and bio-compatible packaging with biodegradability. Neuroprosthetic devices are developed to replace lost sensory functions, e.g., hearing and sight and to control paralyzed and prosthetic limbs. The microelectrode array is one of the fundamental elements for interfacing with the neural tissue. For most neuroscience applications to investigate the neuronal circuits within the central nervous system, the array should have a significant number of stimulation and/or recording sites arranged in 3-D and an implantable signal processing electronics to process signals as well as signal transmitting and receiving while minimizing number of output leads by multiplexing. BioMEMS provides significant opportunities for improving drug delivery by miniaturazing passive and active components to reduce both the volume and power required and make them more portable or implantable with very small quantities at the point-of-care.

One of the emerging fields is the application to precision agriculture. In precision agriculture, monitoring and controlling the physiological conditions of plants is of critical importance for productivity and quality control. Technologies have been limited to indirect measurement of variables such as temperature, humidity, and solar intensity to figure out how the plants react to environment. However, the first chance is being unfolded to introduce bioMEMS for the direct sensing of in vivo plant states. Interrogating the in vivo plant state is not too different from taking the measurement in miniaturized environment and animal organs. Any small-scale technology developed for medical examinations can be readily modified and applied to monitoring internal reactions of plants such as sap flow rate, electrical conductivity, pH, and ionic composition. Such direct information will be useful for irrigation control and resistance against disease and environmental condition change. Precision agriculture is the area that requires high efficiency and minimum impact on environment.

We will conclude this book by giving a non exhaustive list of general guidelines useful for the design of state-of-the art micro-nano biosystems:

- As already mentionned, to improve the performances and added value of bioMEMS, the maximum amount of fluidic, biochemical operations and detections should be integrated on the same chip including pre-treatments steps like lysis, purification, pre-concentration, filtering, etc.…. Whenever possible, hybrid integration of electronics or optics should also be considered.
- Highly selective bio markers or label free detection techniques are essential for cell-based diagnosis and sorting
- Biocompatibility and biofouling must be carefully considered to avoid channel clogging or sample contamination.
- Cell orientation and elongation might depend on fluidic microchannel geometry so this aspect must not be forgotten.

– Whenever possible, automatic fluidic flow like capillary flow, or measurements on stagnant samples, must be chosen respectively to eliminate on-chip or off-chip pumps and valves or the need of a microfluidic circuit.

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