BIOCHIPS: TECHNOLOGIES AND APPLICATIONS

Alberto Pasquarelli

University of Ulm, Dep. of Electron devices and Circuits, Albert Einstein Allee 45, 89069 Ulm, Germany.
E-mail: alberto.pasquarelli@uni-ulm.de

Many knowledge achievements in the life sciences during the last decades have been characterized by a continuous improvement in the resolution power of the investigation techniques, allowing the researchers a top-down approach, from whole organisms, far beyond the cellular size down to the single molecule or even the single atom. This ability to characterize biological structures and observe dynamic processes and interactions in real-time at the nanometric level, offers an extremely powerful tool for the comprehension of the elementary phenomena occurring in the single cell. At this point it became possible to reverse the route strategy, passing to a bottom-up method, to understand the behaviour of cellular ensembles of increasing complexity.
Genomics, proteomics, channelomics etc., are the recently born disciplines coping with DNA-sequencing, gene expression, immunology, regulation of cell activity, intracellular communication etc..
Biochips are in most cases the technological core around which the instrumentation is built. Yet the word Biochip represents a quite wide concept and stays for many different families of devices, which share the common features of being small, integrated and functionalized interfaces between the biology and the instrument. Classification of biochips can be done on the basis of and their target use, their functionalization and the involved technologies.
The most important categories are:

1) DNA-chips for the, spanning from simple glass slides with a few dozens of spots and feature size in the millimetre range, to highly sophisticated devices with extremely high density, which can analyze a whole human genome. Passive functionalization and off-chip synthesis are typical of the simplest designs, while on chip synthesis and/or active read-out are available for high-end products.
2) Protein microarrays, allow the simultaneous analysis of hundreds of molecules extracted from small samples of tissue or body fluids by means of specific antibodies linked to the chip surface. The most important applications are found in the detection of tumours and autoimmune diseases.
3) Patch-clamp devices, replace in automated systems the manual operation of cells pipetting. They are gaining wide acceptance in the pharmacologic research to investigate the effects of drugs on the cellular physiology, particularly on ion channel functions. Different designs are available for single cells experiments, up to large cell populations.
4) MEA. The Micro Electrode Arrays allow the researcher to record the bioelectric activity of grown multicellular structures, like neuronal networks, or tissue slices. Most widely used are passive chips consisting of simple electrode arrays, but there is a significant trend toward the development of active devices with integrated read-out amplifiers, stimulators, chemical sensors and the needed A/D and D/A Converters to allow a pure digital interface with the host instrumentation.
5) Implants. This family of devices can be considered a fall-out of the previous technologies for therapeutic applications and is gaining increasing importance due to the benefits of functional recovery and the correlated social relevance. Cochlear and retinal prosthesis are here the most significant examples.

Among the applications of biochips, the most relevant is the screening of new drugs. This procedure is required and regulated by law, to determine with a high degree of reliability which are the benefits and the risks of pharmaceutical compounds. A typical screening process consists of investigation steps on the following targets: 1) single cells, 2) multicellular cultures, 3) tissue samples, 4) test animals, 5) human volunteers. The biochips can effectively help to achieve a high data throughput in the first three steps thus allowing shorter investigation times and lower cost.

A special aspect in the technology of biochips is represented by the biocompatibility of the employed materials. On the one hand the biologic environment is very complex from a chemical point of view due to the presence of several different ions, enzymes, nutrients, mediators, metabolites, dissolved gases etc., which may react with the biochip and progressively degrade its performances. On the other hand the biochip can deliver substances which may influence the cell functions. Therefore the passivation is an important technological issue especially for long-term in-vivo applications like implants. Several solutions have been proposed and the most promising ones, to date, are based on polymeric materials.