審 査 の 結 果 の 要 旨

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This PhD thesis, entitled “Development and applications of a bio-hybrid platform for myocyte investigation using Thin-Film Transistor technology” （in Japanese: 薄膜トランジスタ回路による筋細胞の培養・計測・スクリーニング技術の構築） is written in English, and composed of 6 chapters detailed as follows.

The 1st chapter is the “Introduction” of the thesis. In this chapter, the electrical conduction system of the heart is explained and the state of the art of the devices for in-vitro cardiac cell sensing is exposed. The question to be answered concerns the overcoming of present devices limitations: single modal sensing, poor spatial resolution and sensing area. The thesis proposes to develop integrated Bio-MEMS devices, based on Thin-Film Transistor (TFT) technology, with unprecedented large sensing area, with high resolution and multi-modal sensing possibility, and applied to the analyses of in-vitro cardiac cell culture.

The 2nd chapter concerns the “Theory” related to this research work. In this chapter, the theory related to the structure and the electrical function of cardiac cells is explained. Then, the various optical and electrical techniques mainly for in-vitro analyses are shown. In particular, the techniques implemented on the TFT platforms are detailed: electrophysiology, electrochemistry, impedance spectroscopy, dielectrophoresis. Finally, the theory and functioning of Thin-Film Transistors is also presented.

The 3rd chapter concerns the “Methodology” used during the PhD study to achieve the purpose of the research. In this chapter, the realization, characterization and control of the TFT platform are detailed. Then, the biological materials and experiments (like cells preparation and cell culture conditions) are presented. Finally, the different experimental set-ups for electrophysiology, electrochemistry and dielectrophoresis are explained.

The 4th chapter concerns the “Results” obtained with the various sensing techniques. The main part of this chapter deals with 2D electrophysiology measurements to analyze: 1) the evolution of cardiac cell cultures with time and temperature, 2) the variation of the activity according to the position in the culture, 3) the propagation of the signal activity in the culture. All the measurements were combined and confirmed with optical observation. Then, to demonstrate the possibility to integrate in the future electrochemical sensors on the same platform, electrochemical analyses of tyramine, a vasoactive amine which has effect on heart rate, were demonstrated. Finally, local placement of cells on the surface of the platform by dielectrophoresis demonstrated the possibility to perform also cell patterning.

The 5th chapter concerns the “Discussion” based on the results and the theory previously presented. The main part of the discussion concerns the electrophysiology results. The meaningfulness of the results is demonstrated (signal activity amplitude, frequency, shape) by comparing the results obtained with more standard techniques, optical analyses and theoretical knowledge. In addition, the limits of TFT platforms are also investigated, in particular the difficulty to perform real time 2D mapping of the activity of the cells. Finally proposal to resolve these limitations, and to add further sensing techniques are addressed.

The 6th chapter deals with the “Conclusions” of the whole work. After summarizing all the different parts, it emphasis the superiority of the TFT devices over presently available devices for large scale, high resolution, multi-modal analyses of cells culture. Future research outlook is also proposed. New lab-on-chip devices in which co-culture of several types of cells, tissue or organoids connected through the TFT platform to spiking neuron network (SNN) systems would allow to create bio-hybrid systems where communication between the biological elements could be investigated and modulated in real-time.

In overall, the thesis demonstrates a substantial advancement in the field of engineering concerning sensing devices for biological applications. This research showed for the first time in the world cardiac cell culture analyses using devices with unprecedented large sensing area, high resolution and multi-modal sensing possibilities, fabricated with TFT technology which is used for the first time for bio-sensing. The meaningfulness of using TFT technology for advanced sensing devices has been demonstrated by simultaneously providing multi-modal information on cell culture over a large area.

Therefore, this thesis has been approved as a doctoral dissertation for the degree of Doctor in Engineering.

よって本論文は博士（工学）の学位請求論文として合格と認められる。