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基于微加工技术的集成细胞芯片的实验研究

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摘　要：

细胞电生理检测芯片已成为后基因时代生物科学研究的重要工具,但是目前的细胞胞外电生理测试工具发展迅速, 但存在功能单一化、指标不够稳定的缺点,如信较低,难于重复与对照,且不能实现多参数同时检测,已成为细胞电生理快速分析发展的瓶颈。集成型细胞芯片通过传感器件的网络化和集成化,将细胞的电学信息学信息、动力学信息等生理活动信息转换为可检测的信号,并细化为微观信息量进行实时分析,实现快速微量的细胞功能信息和待测物质性质的检测, 在细胞生物环境监测和药物开发等领域有广泛应用前景。本文设计了一种新型的集成了细胞微电极阵列、电阻抗传感器及光寻址电位传感器三个传感单元的阵列化芯片,首分析了各单元用于细胞电生理测量的界面模型;在此基础上重点分析了各细胞传感器单元的特性曲线测试、表面处理测试,并初步进行细胞电生理参数的分析。结显示,MEA 加入测试液测试后,噪声水平在80μV 左右,且器件适于细胞培养及动作电位测试; IDA 器件上培养的肾细胞在药物作用下会引起细胞阻抗变化率12 %～的变化;LAPS 器件的酸化率灵敏度在50. 65mV/ p H ,在肾细胞酸化率测试中,高浓度52氟尿嘧啶会引起的细胞正常代谢率下降(相对酸化率下降50 %) 。说明药物浓大,作用时间越长,对细胞的活性影响越大,这与IDA 器件的测试结果一致。最后得到了在器件特性、系统优化及细胞测试的一些初步结果,对芯片进行了芯片各单互补性分析,为细胞传感器的多功能化发展开拓了一个新的应用领域。

关键词：细胞传感器， 细胞电生理，微电极阵列、叉指电极 光寻址电位传感器

Research of Integrated Cellular Chip Based on Microfabrication

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Abstract:

Bio-cellular chips have been important tools to detect extracellular physiology in post-gene era, but most of these tools are confronted with the embarrassments of mono function, unstable parameters, low S/N ratio and difficulty of repetition. However, the integrated chip can transform the electrical, chemical and motile signals of cells into detectable ones by the integration and network of different sensor units with on-line analysis. The research on a novel integrated cellular physiologic sensor is reported i this article, which includes Micro-electrodes Array Sensors (MEAS), Interdigitated Array (IDA) for impedimetric analysis, and Light-addressable Potentiometric sensors (LAPS), etc. to record the extracellular metabolism chemical and biological substances, action potential and livable characteristics of living cells. The cell- sensor interfaci model of each unit was first introduced, the characteristic curves were then measured, and the fundamental electro-physiological cellular analysis was finally tested and analyzed. The average noise level of MEA is about 80μV after measuring solution was added, the chip is biocompatible for cell culture and suitable for AP measurement; cultured kidney cells on the surface of IDA chip will cause an cellular impedance change of 12%~16% when exposed to 5-Fluororacil; and the sensitivity of H+-LAPS is 50.65mV/pH. When kidney cells were cultured on LAPS and exposed to high concentration of 5-Fluororacil, the normal metabolism of cells will be affected, which was sim with the IDA results. This research will be interesting and useful for multi-functionalized cellular detecting platform and facilitate a lot to the lab-on-chip research in near future.