# 論文の内容の要旨

## Nano-scale Transport Driven by Motor Proteins along Precisely Assembled Microtubules
### -A System for Direct Molecular Handling to Achieve High Sensitive Detection of Multiple Analytes-
### （微小管の精密組み立てによる生体分子モータ駆動ナノ輸送
### ー高感度多種分析のための直接分子操作システムー）

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The dimensions of the systems have been drastically scaled down in the last decades. The increasing demand of this miniaturization has brought about several challenges such as handling and transport of tiny amounts of materials. Microfluidics, a popular method, is not always appropriate when the amount of molecules to be handled is extremely small. Direct transport, as in intracellular transport, has potential to overcome the handling challenges due to the scaling down technology.

In this work, a heterogeneous integrated system, i.e. bio/MEMS hybrid system, has been proposed to build a nano-scale transport system based on kinesin motion along immobilized microtubules. In such a system, specificity and throughput of the bio-world can be successfully integrated with the handling and manipulation capabilities of MEMS technology to deliver systems capable of working at the nano-scale with high efficiency.

Kinesin is a molecular motor providing unidirectional motion on rail structures called microtubules. Orientation of the rail structures provides a controlled transport system. Although there have been some research on the microtubule assembly, so far, no technique could provide enough freedom to build a complex multidirectional microtubule network. However, to build a real nano system with a high level of transport capabilities, multidirectional assembly in a very small area is essential.

This research proposes an innovative method to build a multidirectional and multilayered assembly of microtubule networks. The technique was named as *Picking and Relocation of Individual Microtubule Process* abbreviated as *PRIM Process*. This method was based on individual manipulation of polarity-marked microtubules using MEMS tweezers. Isolated single microtubules were individually captured and then relocated on a predefined docking zone. As a result, due to the high-degree of freedom provided by direct manipulation of microtubules, multidirectional orientation and stacking was achieved in a very small area. Furthermore, it is demonstrated that micrometer precision could be achieved to relocate the captured microtubules onto predefined areas. Even three-dimensional relocation was performed to combine microtubule networks in different layers on a chip. Kinesin-coated bead motion on top of the assembled microtubules was successfully realized proving that the assembly method did not disturb the kinesin activity.

Building a system to handle target molecules requires a capturing process. Biofunctional beads were used to realize this process. Based on specific interactions between the target molecules and biofunctional coating of the beads, very efficient capturing could be achieved. To avoid any possible hindrance of kinesin motion and good integration with the *PRIM Process*, the transport mechanism was separated from the capturing mechanism. Several different carriers, such as beads, oil droplets, lipid vesicles, needles were adopted and successful transport was shown. To show the

efficiency of the sorting and transport mechanism, a sorting device was built. Two different target molecules (biotin & antibody) were captured separately on two kinds of beads with appropriate coatings (streptavidin & protein A) and transported to different directions determined by the orientation of the microtubules in a microfluidic device.

Bottom-up functionalities, e.g. specificity and throughput of the bio-world were combined with top-down fabrication and handling capabilities of MEMS technology in this research. The resulting hybrid technology, a combination of bottom-up and top-down approaches, has enabled a unique nano-transport system through the assembly of a complex microtubule network. Such a multidirectional, multilayered transport network based on direct manipulation of single microtubules is achieved for the first time. These results show the importance and the potential of hybrid bio/MEMS systems.