Mechanisms of selective transport through nano-channels: Theory vs. experiment

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***Short Abstract* — Proper functioning of living cells involves continuous transport of various molecules into and out of the cell, and between different cell compartments. Such transport requires discrimination between different intra- and extra-cellular molecular signals and requires mechanisms for directional, selective and specific transport. Specifically, transport devices must be able to selectively transport only certain molecular species while effectively filtering others, even very similar ones, many times in the presence of the large amounts of non-specific competitors. Understanding mechanisms of selective transport is a fundamental biological question and has important applications in nano-technology and nano-medicine. I present a theoretical model that captures essential features of these mechanisms. I compare theoretical predictions to experimental data on transport through artificial nano-sorting devices and find good agreement.**

I. Background

Proper functioning of living cells involves continuous transport of various molecules into and out of the cell, and between different cell compartments. Such transport requires discrimination between different intra- and extra-cellular molecular signals and requires mechanisms for directional, selective and specific transport.

Specifically, transport devices must be able to selectively transport only certain molecular species while effectively filtering others, even very similar ones. In many cases, molecular transport is directional and selective without an input of metabolic energy, and without specific gating that involves transition from a 'closed' to 'open' state during transport. Examples of transport of this type include selective permeability of porins and efflux pumps in bacteria transport through the nuclear pore complex in eukaryotes.

Transport devices of this type commonly contain a long channel or a pore through which the cargoes translocate by facilitated diffusion. The selectivity and directionality of transport is usually based not merely on the molecule size but a combination of the size, strength of the interaction with the channel, the speed of the spatial diffusion through the channel, and its geometry [1-5].

Moreover, large body of experimental data on biological channels, and artificial nano-pores shows that the cognate cargoes in many cases interact strongly with the channel - stronger that the ones that are filtered out - and can transiently bind to binding sites inside the channel [1-5] Precise mechanisms and conditions of optimal selectivity of transport through narrow pores are still unknown. Understanding the mechanisms of selectivity of transport through such channels is an important biological question, and also has important applications In addition, it poses a fundamental physical question: how does one make a selective channel that is always open, and does not have a movable 'gate' specifically attuned to its cognate cargoes? Moreover, such channels must be able to select for their cognate cargoes over a vast background of non-specific competition. Although these systems span a wide spectrum of scales and biological functions, it has been suggested that they might share common mechanisms of selectivity and directionality [1-5].

II. Results of the model

We study transport through narrow channels in the framework of a general kinetic model. The model naturally allows one to treat multiple particle occupancy of the channel, and inter-particle interactions for arbitrary non-uniform channels. Where the analytical theory cannot be extended, we use computer simulations.

We find that two main ingredients - i) transient trapping of the cargoes inside the channel and ii) competition for space in the confined volume of the channel provide selective transport and are sufficient to explain the available experimental data [2,5].

Transient trapping increases the probability of individual particles to translocate through the channel, thereby increasing transport efficiency.

We find that, surprisingly, the crowding of the particles inside the channel does not affect the probabilities of individual particles to translocate through the channel. Rather, crowding of the particles inside the channel mainly affects the entrance to the channel, which becomes blocked if either the flux or the trapping time is too high. This provides a mechanism of selectivity based on the balance between the transport efficiency and transport speed [1,2,5].

This selectivity is enhanced further when particles that spend longer in the channel are present in the mixture with the non-specific competitors whose trapping time is low. This is a novel mechanism of selectivity enhancement and provides an explanation of how selective transport can be maintained in the biologically relevant case when large amount of background competition is present [2].

We compare theoretical predictions with experimental data [2,4] and find good agreement [5]. These results provide a framework for design of artificial nano-molecular filters [2,4].

References

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