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Membrane channels with large aqueous pores are traditionally regarded as “molecular sieves” that discriminate between different molecules based on their size (1,2). This simplified view, however, contradicts emerging experimental evidence that permeation through these structures involves intimate molecular interactions (3–5). Metabolite-specific channels exhibit affinity to their metabolites; permeating molecules do not just slip through the pore, but feel strong attraction to the pore-lining residues. The now classical example is bacterial porin LamB (6), where the existence of an extended binding zone for oligosaccharides is firmly established. More recent examples include ATP interactions with VDAC (3) and penicillin antibiotic interactions with the general bacterial porin OmpF (4,6–8).

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