RAMA UNIVERSITY

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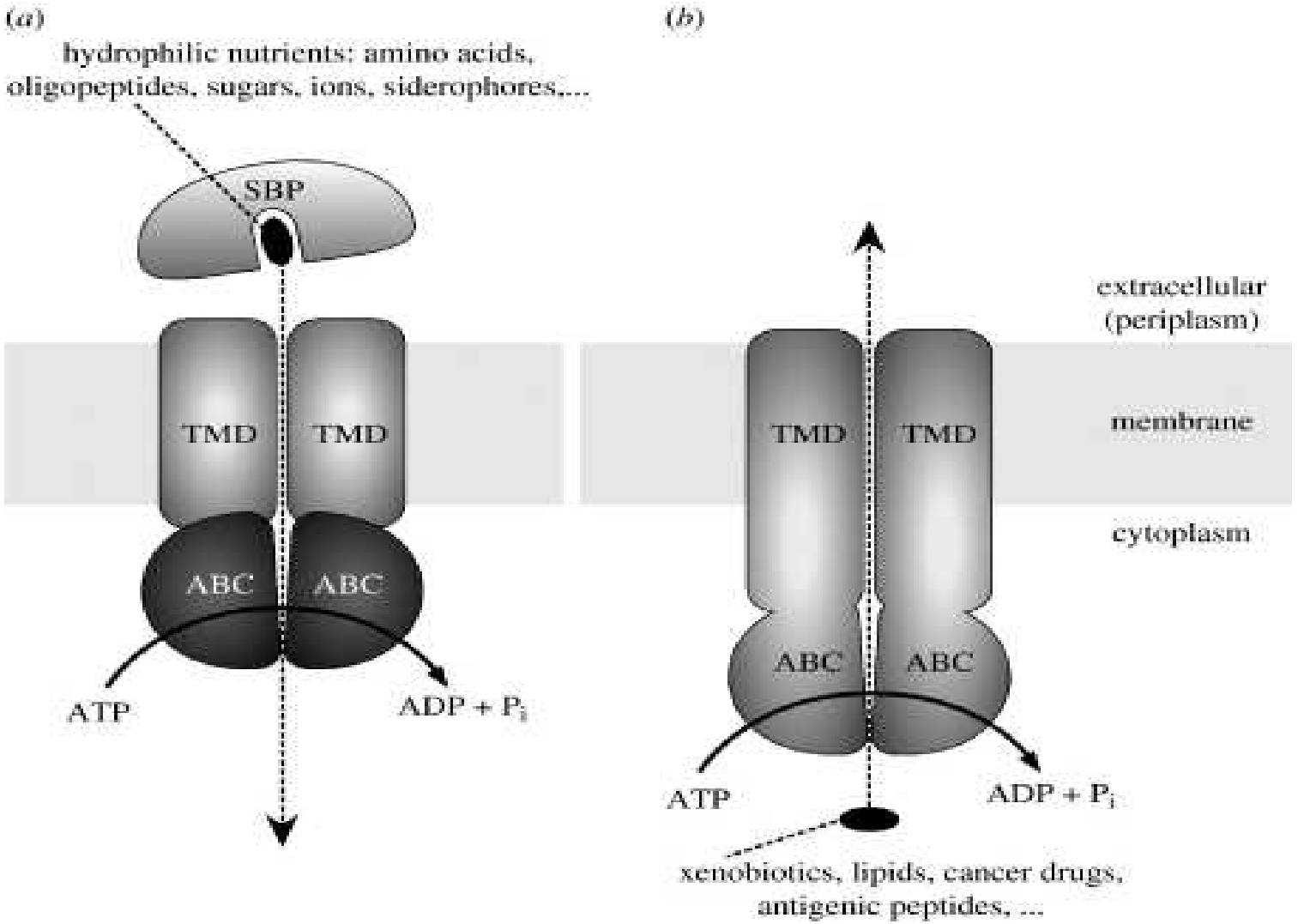
FACULTY OF ENGINEERING &TECHNOLOGY
DEPARTMENT OF BIOTECHNOLOGY

ABC transporter

Membrane protein complexes that use ATP energy to move substances across membranes without modifying the compound being transported. They require an extracytoplasmic substrate-binding protein for proper function. Proteins that actively transport ions are the *ATP-binding cassette* (*ABC*) *transporters*, so called because all of the members of this superfamily share a homologous ATP-binding domain. They convert the energy gained from ATP hydrolysis into trans-bilayer movement of substrates either into the cytoplasm (import) or out of the cytoplasm (export). In both cases, ATP hydrolysis is catalysed by a pair of cytoplasmic ABCs (also termed nucleotide-binding domains, NBDs), whereas the translocation of the substrate is facilitated by a pair of trans-membrane domains (TMDs). More than a hundred family members have been identified in both prokaryotic and eukaryotic cells and all use energy derived from ATP hydrolysis to transport molecules in one direction. In bacteria, most ABC transporters bring a wide range of nutrients, including ions, sugars, and amino acids into the cell, while in eukaryotic cells they transport toxic substances out of the cell. The basic domain architecture and schematic mechanism are shown in figure 1.

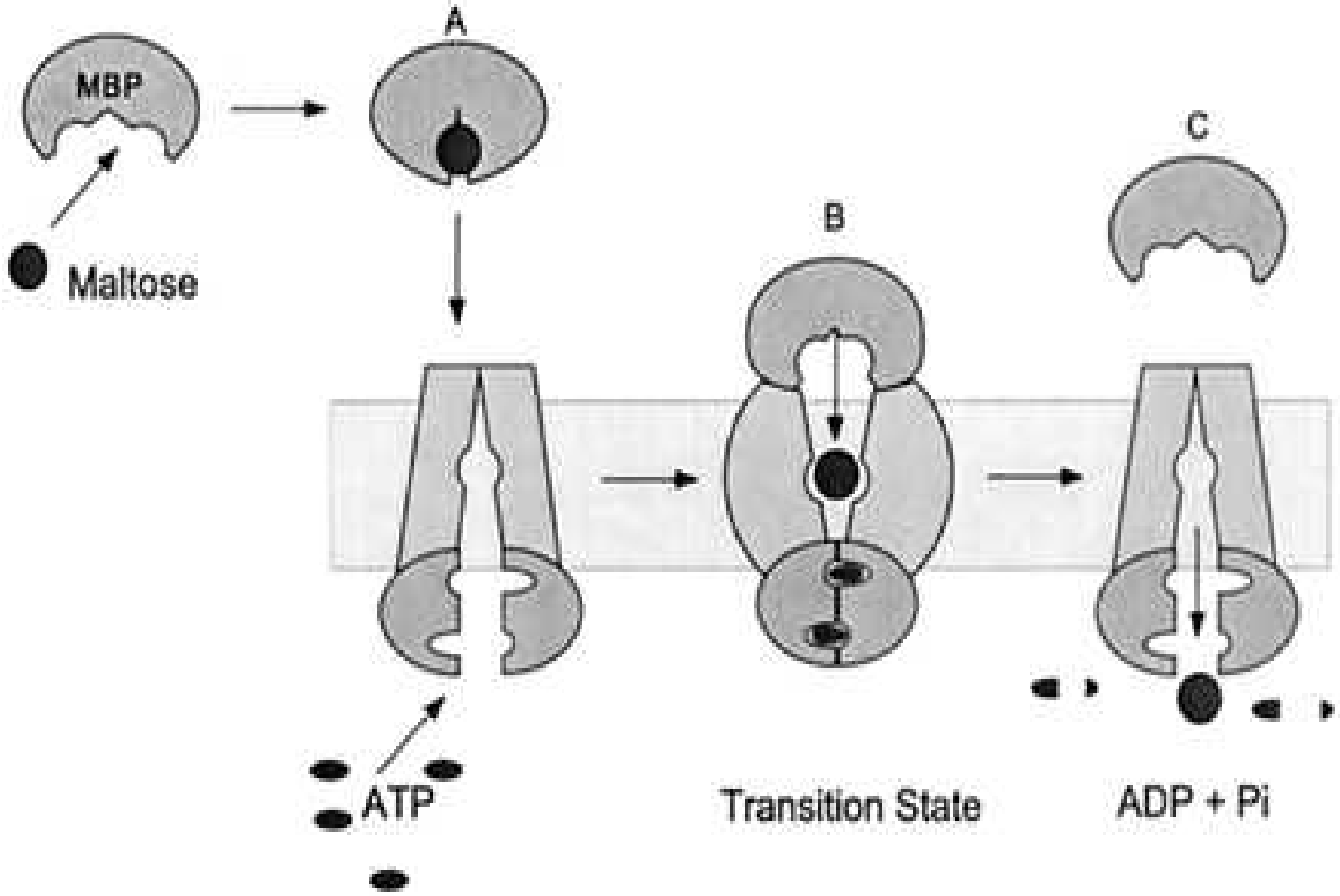

(a)
hydrophilic nutrients: amino acids, oligopeptides, sugars, ions, siderophores,...
SBP
TMD
TMD
ABC
ABC
ATP
ADP + Pi
(b)
extracellular (periplasm)
membrane
cytoplasm
TMD
TMD
ABC
ABC
ATP
ADP + Pi
xenobiotics, lipids, cancer drugs, antigenic peptides, ...

Example of transport through ABC transporter

ATP binding and hydrolysis drive a cycle of conformational changes that allows a substrate to bind on one side of the membrane and to escape on the other side. The most complete set of structures is available for the bacterial vitamin B_{12} transporter BtuCD. ATP binding promotes association of the BtuD subunits, changing their orientations and opening a cavity in the transmembrane BtuC subunits facing the periplasm. A BtuF protein carrying vitamin B_{12} binds and unloads the substrate into the open cavity. ATP hydrolysis and release of ADP and P_i cause dissociation of the cytoplasmic domains resulting in a conformational change that transiently opens a pathway for vitamin B_{12} to exit into the cytoplasm. Two ATPs are hydrolyzed for each vitamin transported.

Maltose transport using ABC transporter

In the periplasmic binding protein-dependent transport systems, the soluble binding protein is the first component to interact with the substrate to be transported, acting as a high-affinity receptor for the substrate in the periplasm. Interaction of the ligand-bound binding protein with the transporter stimulates the ATPase activity of the transporter and initiates transport


MBP
Maltose
A
B
C
ATP
Transition State
ADP + Pi

Model for maltose transport

(A) MBP binds maltose, undergoing a change from an open conformation to a closed conformation, generating a high-affinity sugar-binding site.

In the closed conformation, MBP binds $MalFGK_2$ to initiate transport and hydrolysis.

(B) In the transition state for ATP hydrolysis, MBP becomes tightly bound to $MalFGK_2$, and internal sugar-binding sites are exposed to each other. This opening of MBP in the transition state reduces the affinity of MBP for maltose, facilitating the transfer of sugar to $MalFGK_2$.

(C) Maltose is transported, and MBP is released after reexposure of the membrane-binding site to the cytoplasm. MBP activates the ATPase activity of MalK by bringing the two MalK subunits into close proximity, completing the nucleotide-binding site(s) at the MalK-MalK interface with residues donated from the opposing subunit.