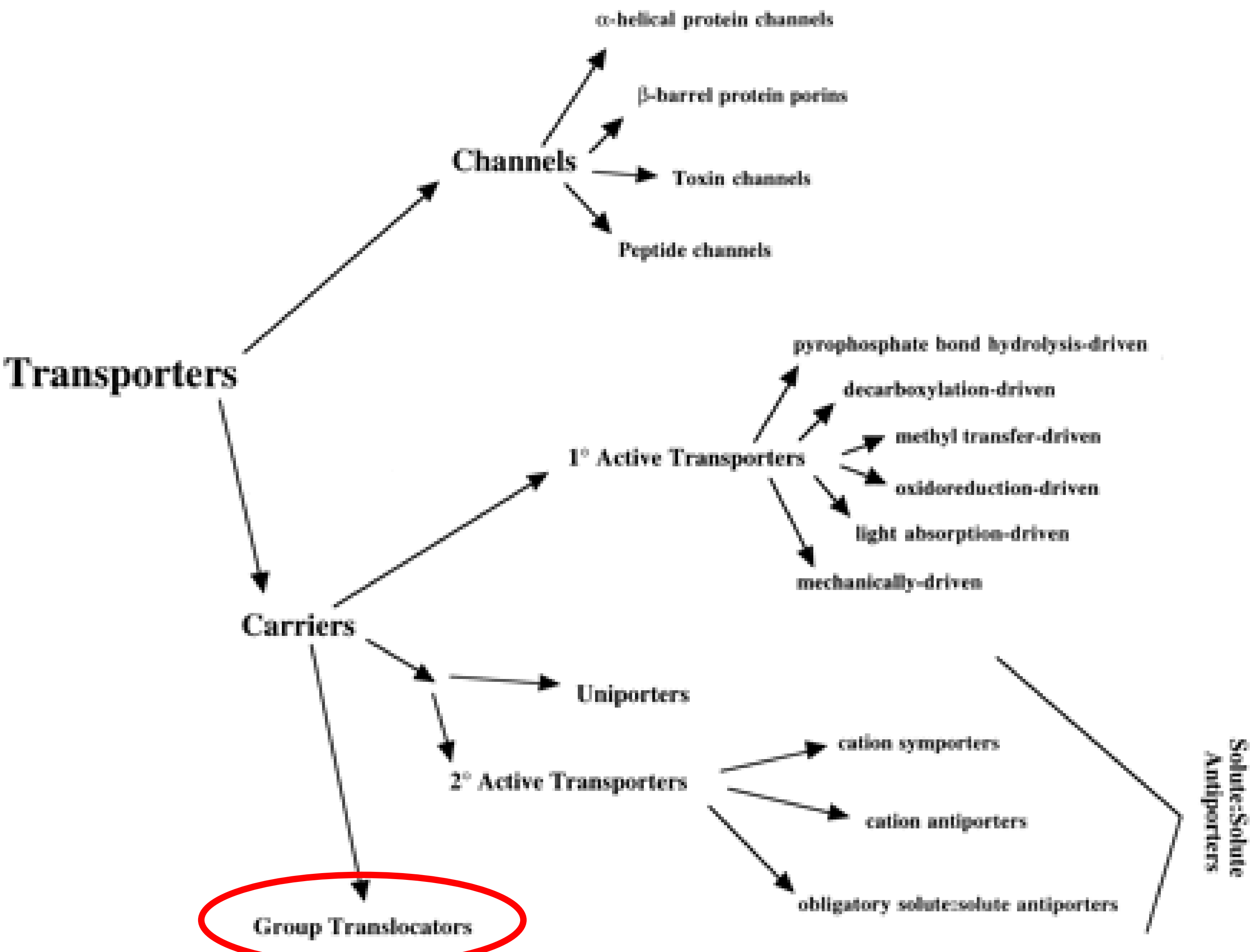
I. Systems for transporting nutrients into the cell:

- A. Function: uptake of small molecules (sugars, amino acids, small peptides, ions, etc.) large molecules must be degraded prior to uptake.

I. Systems for transporting nutrients into the cell:

- B. Types of Transport
  - 1. Passive
  - 2. Facilitated Diffusion
  - 3. Group Translocation
  - 4. Active Transport

Scheme of primary types of transporters found in nature

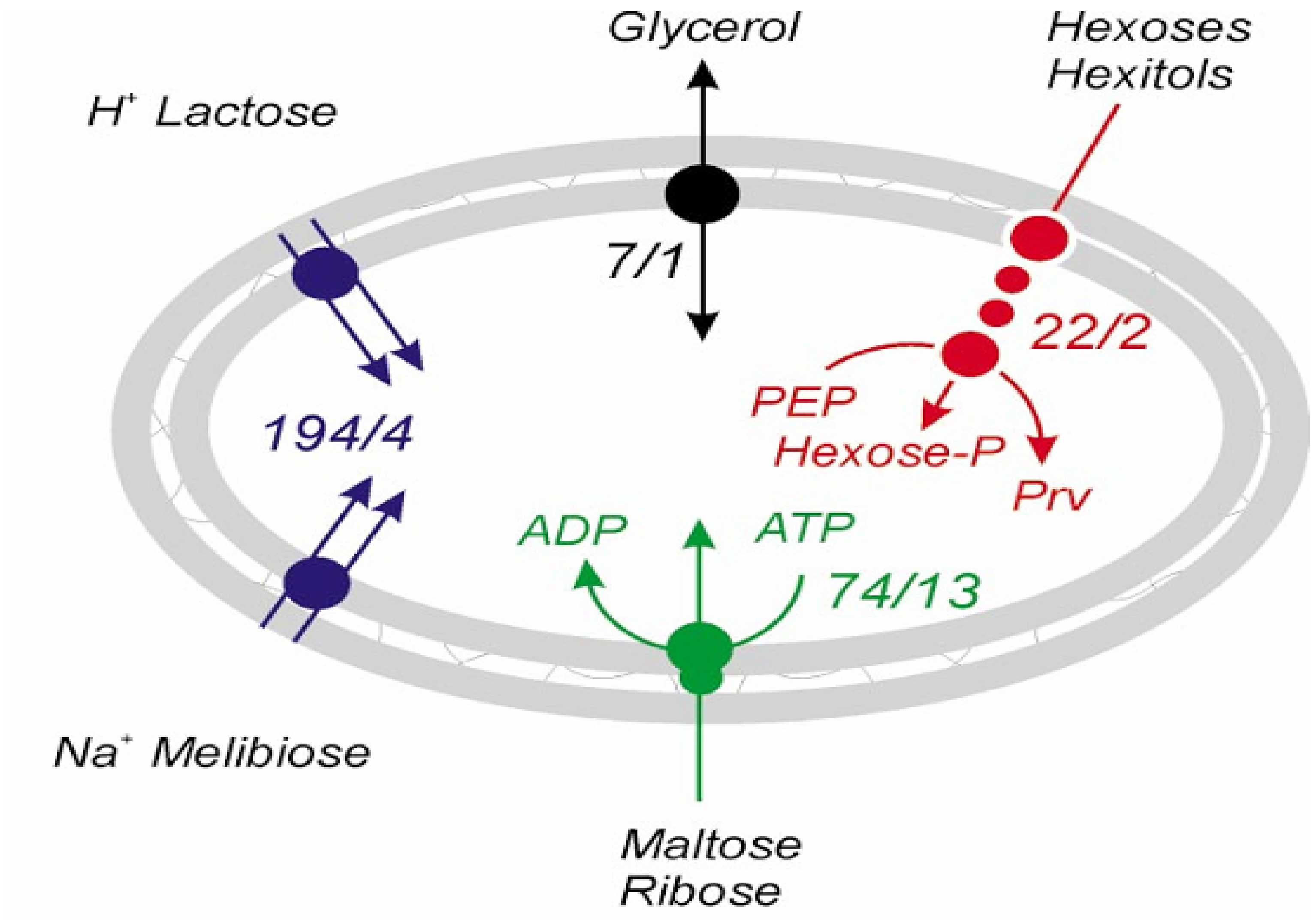


Transporters proteins are initially divided into: i) channels, and ii) carriers.

Channels are subdivided into:
-helical protein channels,
-barrel protein porins (mostly in the outer membranes of gram-negative bacteria and eukaryotic organelles),
-toxin channels, and
-peptide channels.

Carriers are subdivided into:
-primary active carriers,
-secondary active carriers (including uniporters), and
-group translocators that modify their substrates during transport.

The only well-established group-translocating system found in nature is the bacterial phosphoenolpyruvate:sugar PTS, which phosphorylates its sugar substrates during transport.



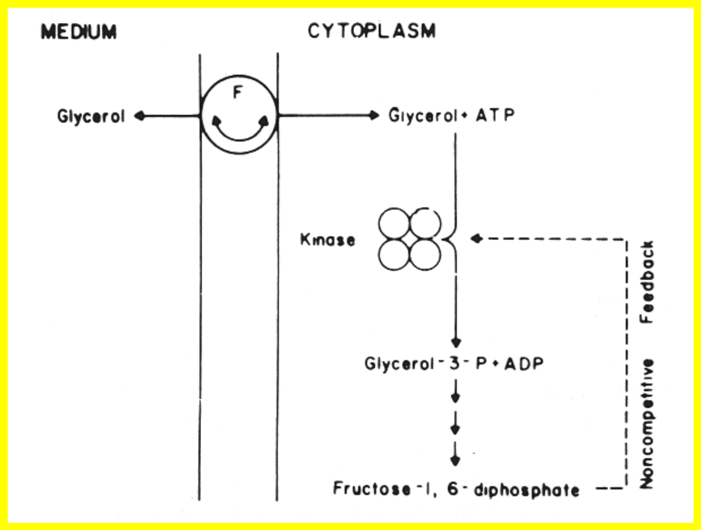
Common transport mechanisms for small solutes in the inner membrane of bacteria. Facilitation (black), secondary ion-symport (blue), primary ATP-dependent transport (green), group translocation (red). The numbers refer to the number of paralogous proteins in E. coli (left) and M. genitalium (right). The genomes of E. coli and M. genitalium contain 4300 and 470 genes of which 25% to 40%, and 10% to 30% respectively, encode putative membrane proteins.

1. Passive transport

- Allows entry of CO_2, O_2, H_2O into cell through outer membrane pores or channels (diffusion).
- Porin proteins in OM of *E. coli* create outer membrane pores allowing entry of molecules with a MW ? 600.
- LamB forms stereospecific channels that funnels maltose and maltodextrins to periplasmic binding proteins involved in their transport (Note: only transport across the OM is passive; transport of maltose across IM is an active process).

2. Facilitated diffusion

example: Glycerol uptake



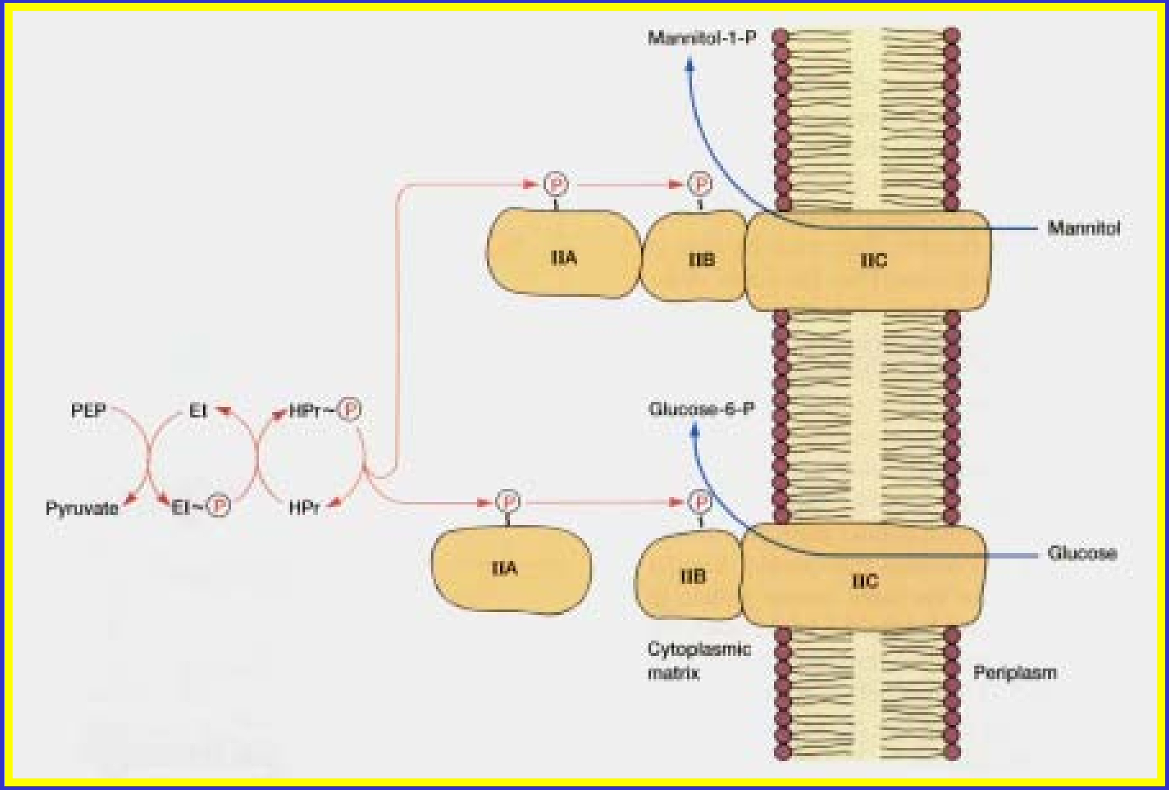
- Membrane bound protein aids diffusion of glycerol across the membrane (down concentration gradient).

- Internalized glycerol is then phosphorylated and cannot diffuse out of the cell.

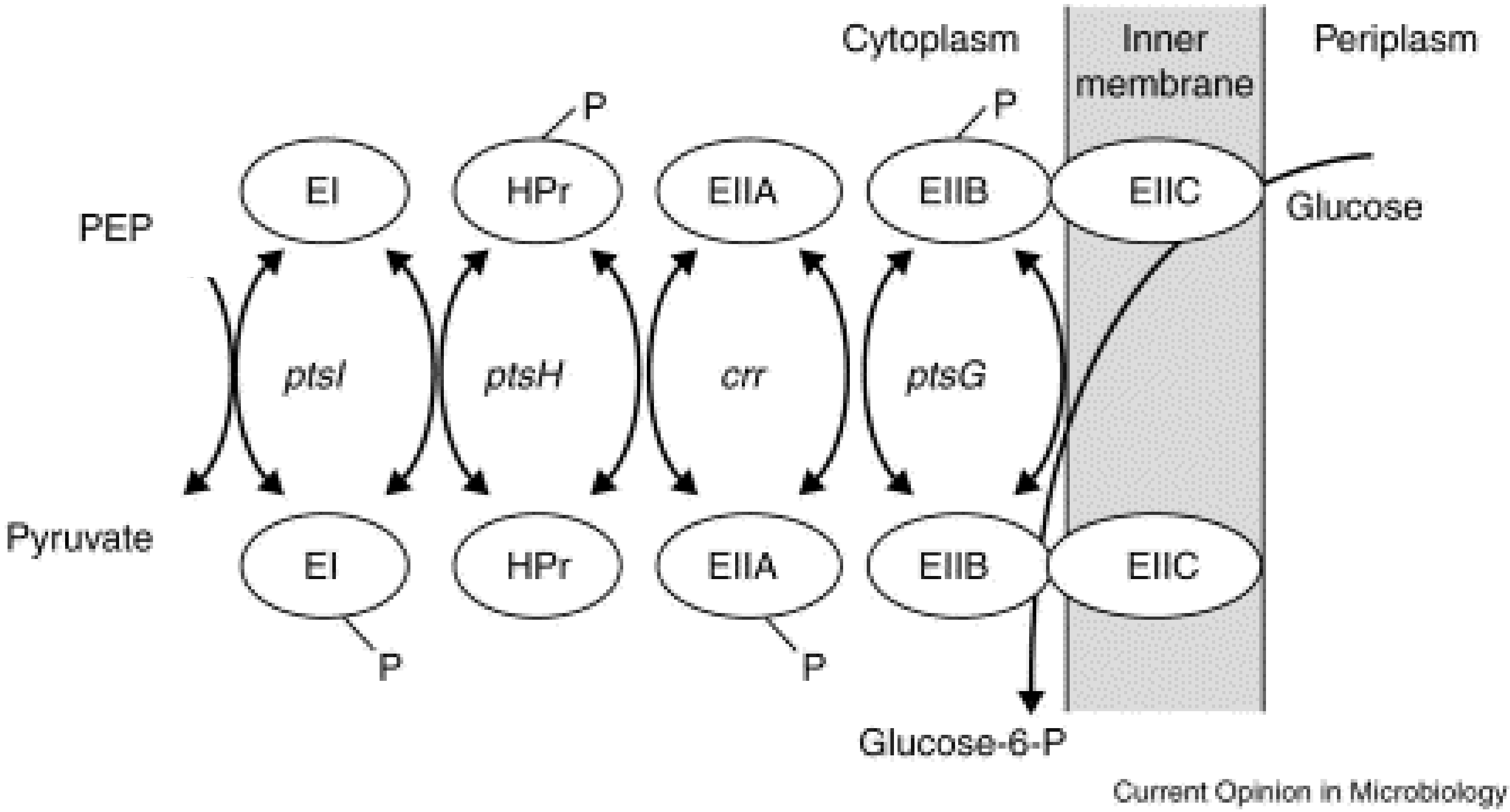
3. Group translocation

- PTS or sugar phosphotransferase system.
- Key soluble proteins phosphorylate specific membrane enzymes which then phosphorylate particular sugars (glucose, mannose) when translocating the across the membrane.
- PTS proteins also inhibit permeases for non-PTS sugars when glucose is transported and stimulate adenyl cyclase when it is not.

Group Translocation: PTS
--Modification of transported product



The PTS phosphorylation cascade.



PEP + Glucose → Pyruvate + Glucose-6-P

The five conserved PTS domains, as exemplified by the glucose PTS in *E. coli*,

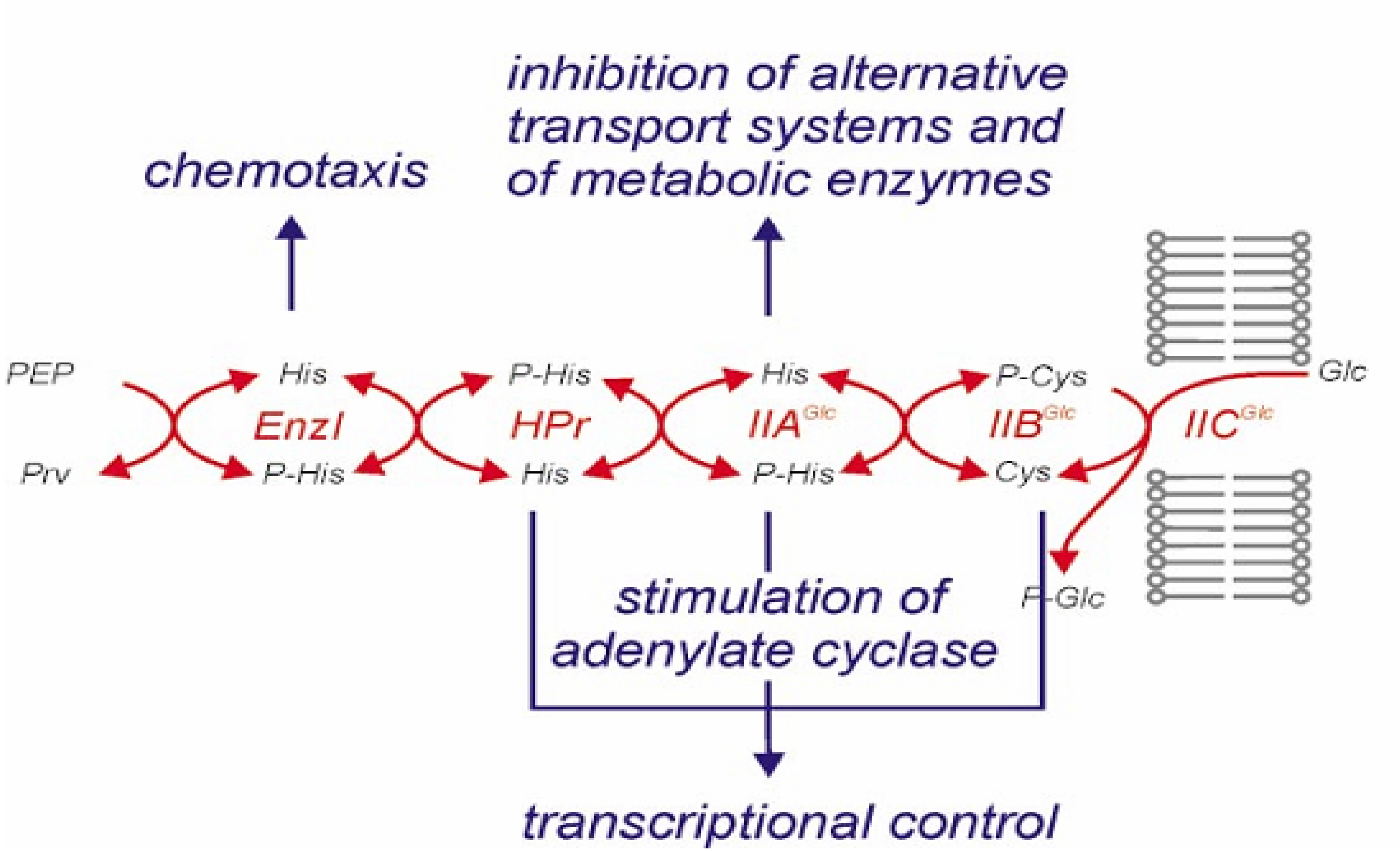
Enzyme I (EI) and HPr are common to most sugars and are encoded by the *ptsI* and *ptsH* genes, respectively.

The Enzyme II components are sugar-specific transporters with three domains, EIIA, EIIB and EIIC. EIIA and EIIB are soluble proteins, whereas EIIC is an integral membrane protein.

For the glucose PTS, the EIIA domain is a single-domain protein encoded by the *crr* gene (part of the *ptsHIcrr* operon).

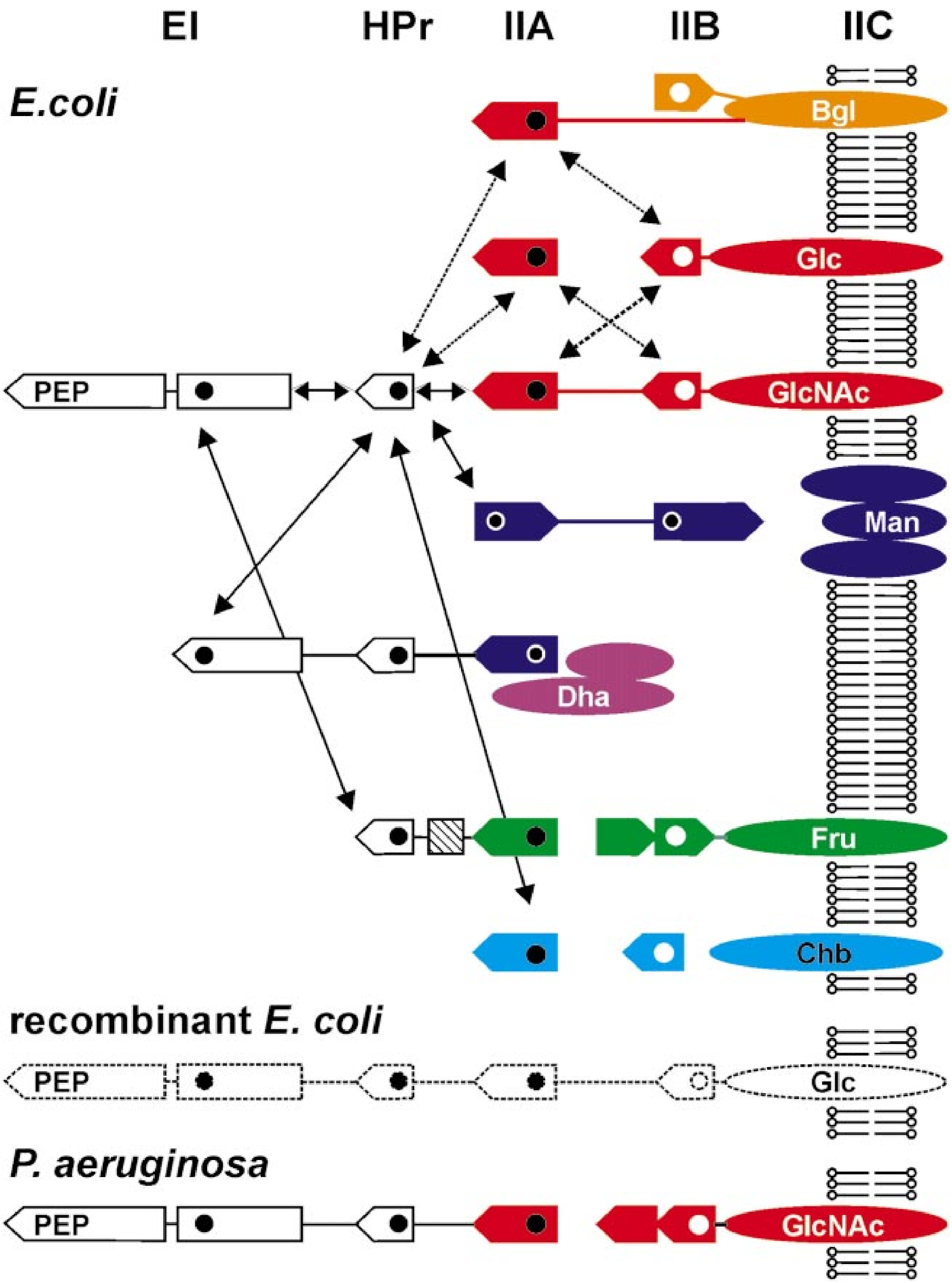
The soluble $EIIB^{Glc}$ domain is part of the EIICB protein, encoded by *ptsG*, and is, thus, located on the cytoplasmic surface of the inner membrane via the integral membrane EIIC domain.

In a process called vectorial phosphorylation, the phosphate, supplied by PEP, passes through the chain of proteins and is eventually transferred to the incoming sugar from the EIIB domain as it passes through the pore created by the EIIC domain.



Phosphotransfer chain of the glucose PTS. Phosphoryl groups are sequentially transferred from PEP to EI (63 kDa), HPr (9 kDa) and hence to the carbohydrate transporter IIAGlc (18 kDa) and IICBGlc (51 kDa). Proteins are phosphorylated at His and Cys.

The red arrows emphasize the reversibility of the phosphotransfer reaction. The blue arrows indicate regulatory interactions but do not imply direct protein-protein contacts between the PTS components and the regulated targets



Modular design of the PTS. Shown are representative examples of the glucose/L-glucoside (red, orange), mannose (blue), fructose/mannitol (green) and lactose/chitobiose (cyan) families from E.coli and P. aerugionsa. Also shown is the heterotrimeric dihydroxyacetone kinase (purple/blue). The functional units EI, HPr, IIA, IIB and IIC are vertically aligned. The FruA subunit of E. coli and IICBGlcNAc of P. aeruginosa have duplicated B domains. Solid and open circles indicate phosphorylated His and Cys, respectively. Arrows indicate phosphotransfer between HPr and the sugar-specific IIA domains, and between homologous IIA and IIB domains of different transporters. The protein symbols are drawn to scale with the pointed end marking the C-terminus.

4. Active transport

- Utilizes integral inner membrane proteins which do not alter the substrate during transport.
- Requires energy to concentrate the substrate against the concentration gradient.
- Sometimes a single permease and transport is coupled to the passage of electrons (proton motive force).
- In others, periplasmic proteins bind to the substrate, and deliver it to the membrane transport system; transport depends on ATP driven conformational changes.

Active Transport 1:

Use of pmf as energy for transport

Protons accumulate in periplasm due to electron transport

Na^+ pushed out, H^+ in (antiport)

Na^+ binds to IM permease--conformational shift?

Na^+ / sugar bind permease

Na^+ / sugar symport