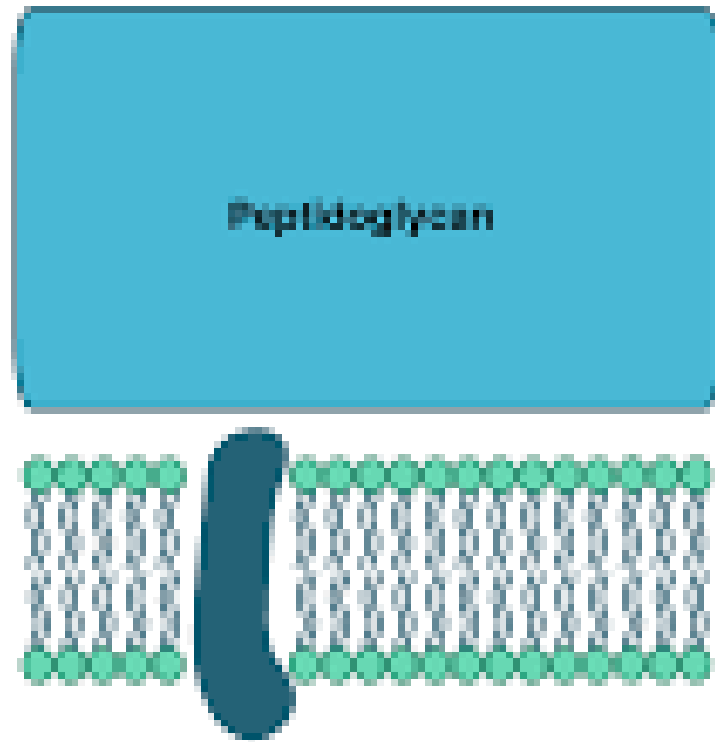


CONTENTS

- Structure of peptidoglycan
- Synthesis of peptidoglycan
- Role of cytoskeleton in cell wall synthesis
- Patterns of cell wall synthesis
- Significance of peptidoglycan cell wall



Gram-positive bacteria

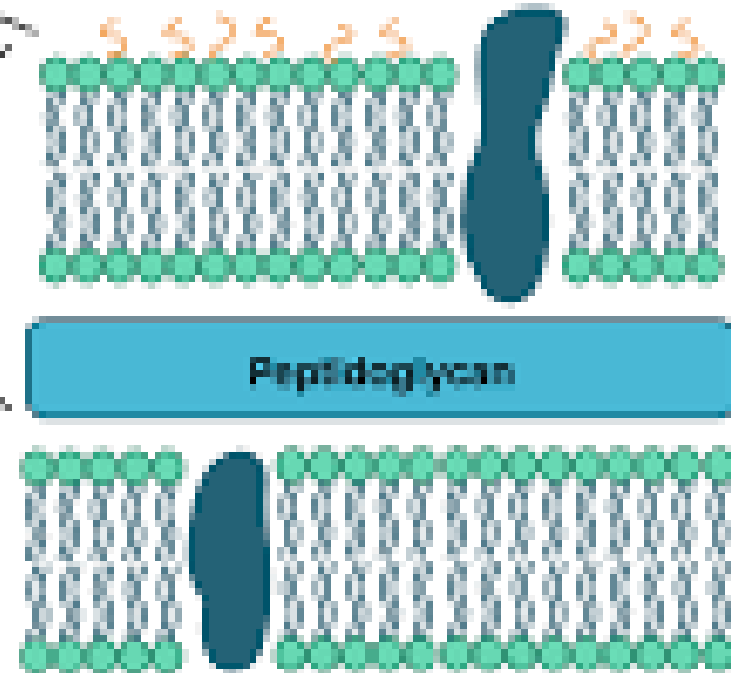


Gram-negative bacteria

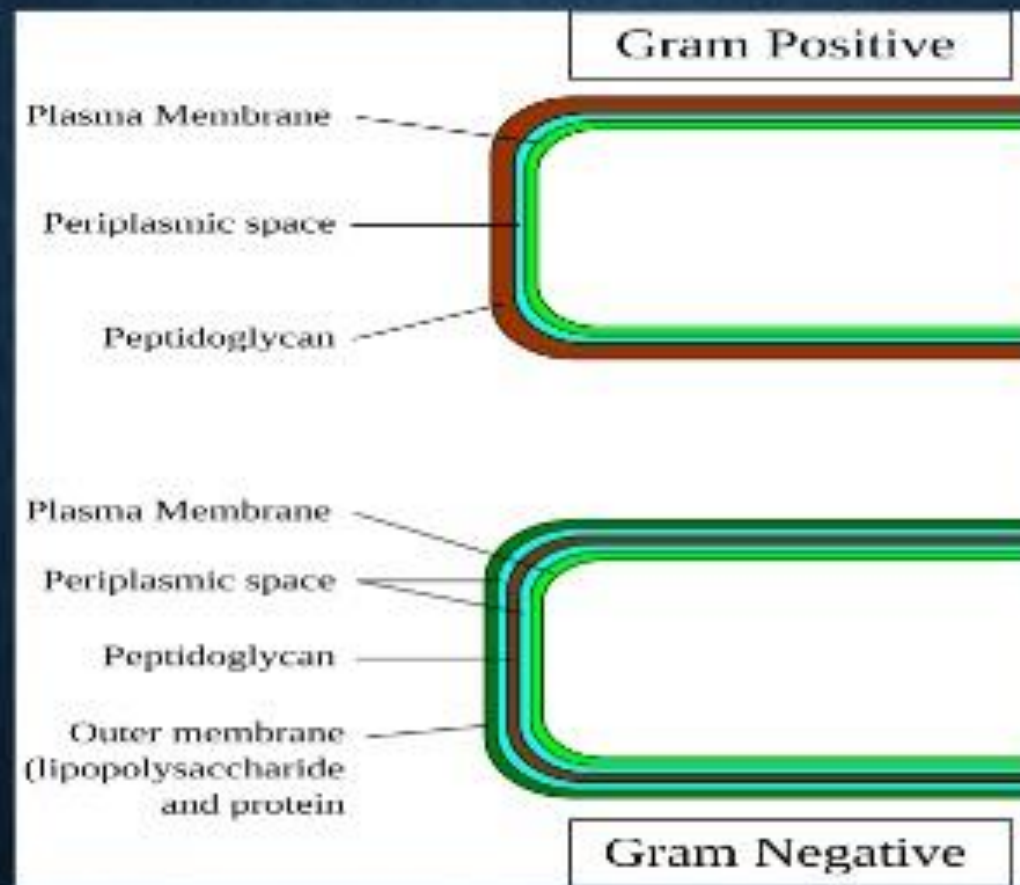
Outer membrane

Cell wall

Plasma membrane



PEPTIDOGLYCAN CELL WALL



ULTRA STRUCTURE OF CELL WALL

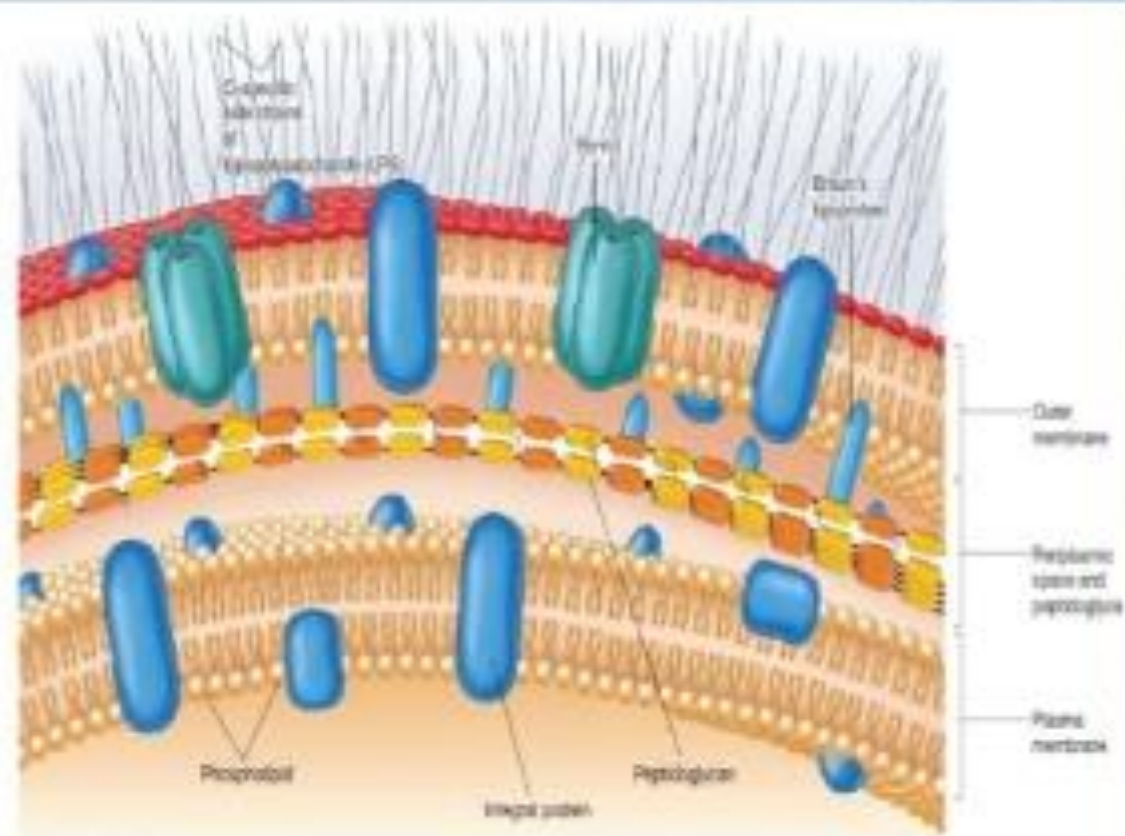


Figure 3.25 The Gram-Negative Envelope.

Gram negative bacterial cell wall

Gram positive bacterial cell wall

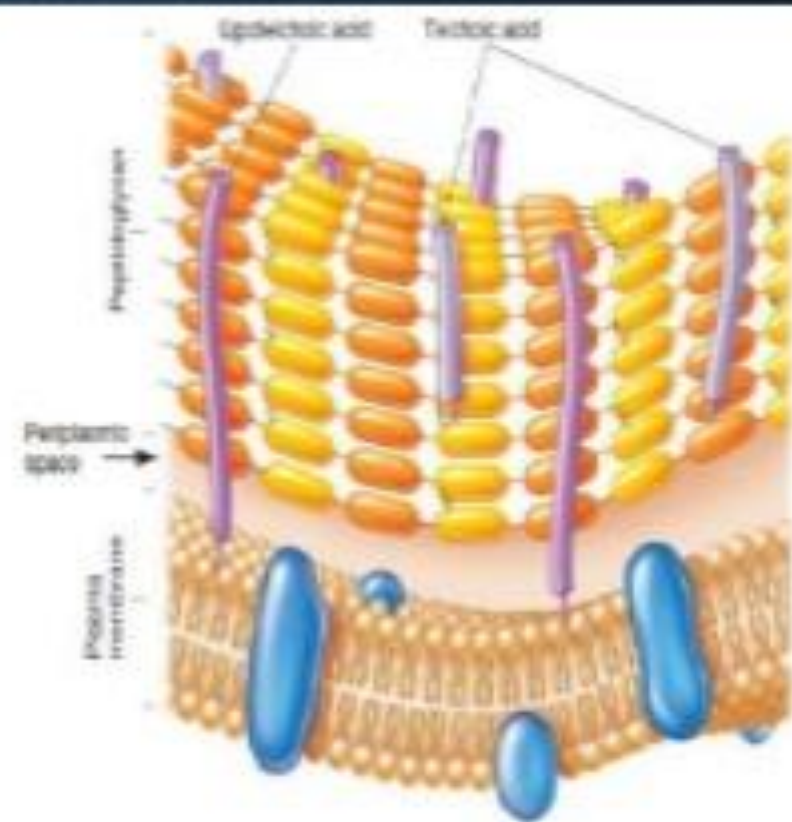


Figure 3.23 The Gram-Positive Envelope.

STRUCTURE OF PEPTIDOGLYCAN

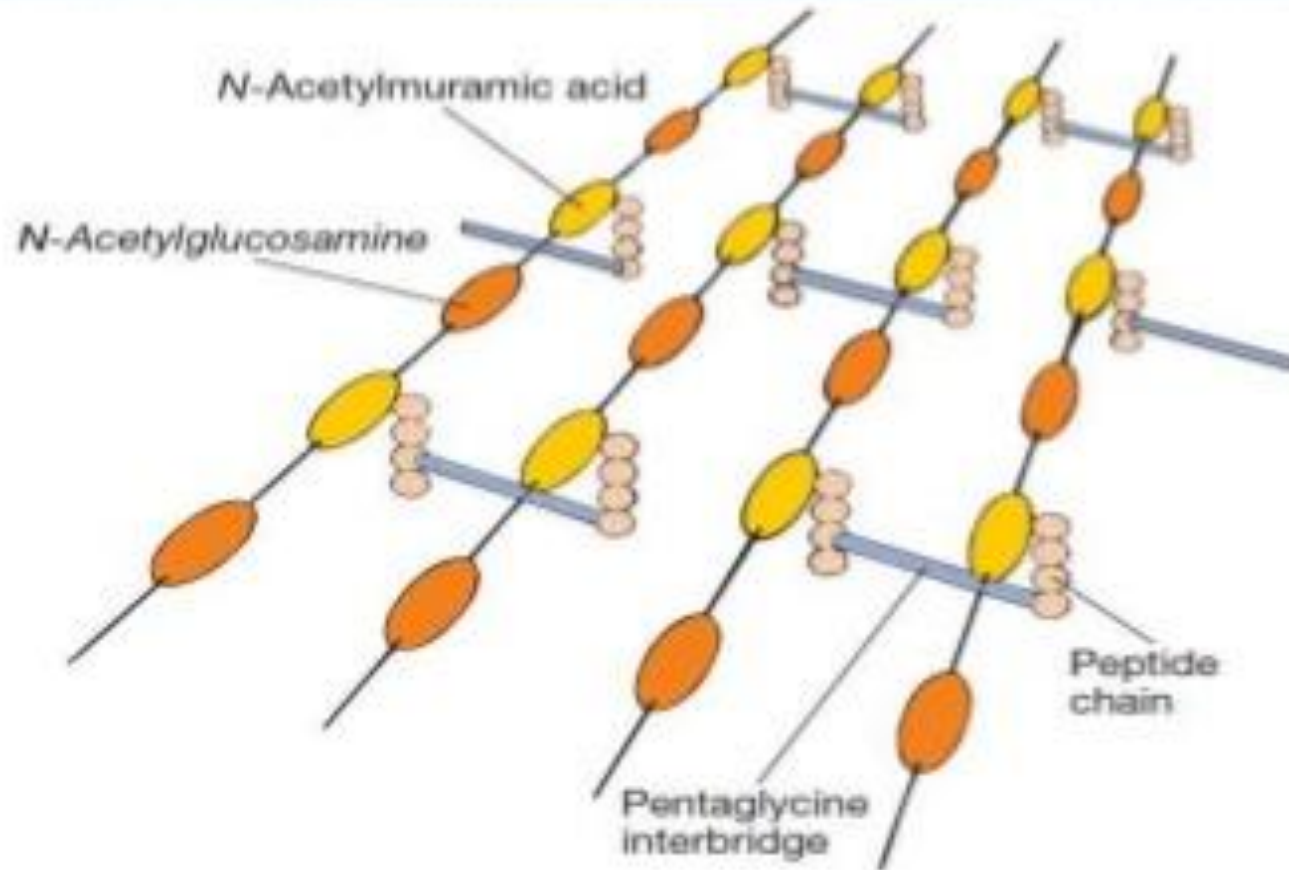


Figure 3.21 Peptidoglycan Structure. A schematic diagram of one model of peptidoglycan. Shown are the polysaccharide chains, tetrapeptide side chains, and peptide interbridges.

SYNTHESIS OF PEPTIDOGLYCAN

SYNTHESIS OF UDP-NAG

Fructose-6-phosphate



glucosamine-1-phosphate



Acetyl-coA

CoA

N-Acetylglucosamine-1-phosphate



UDP-NAG

SYNTHESIS OF UDP-NAM

UDP-NAG



UDP-NAM



Amino acids are added one at a time sequentially.

UDP-NAM Penta peptide

Peptidoglycan cell wall synthesis

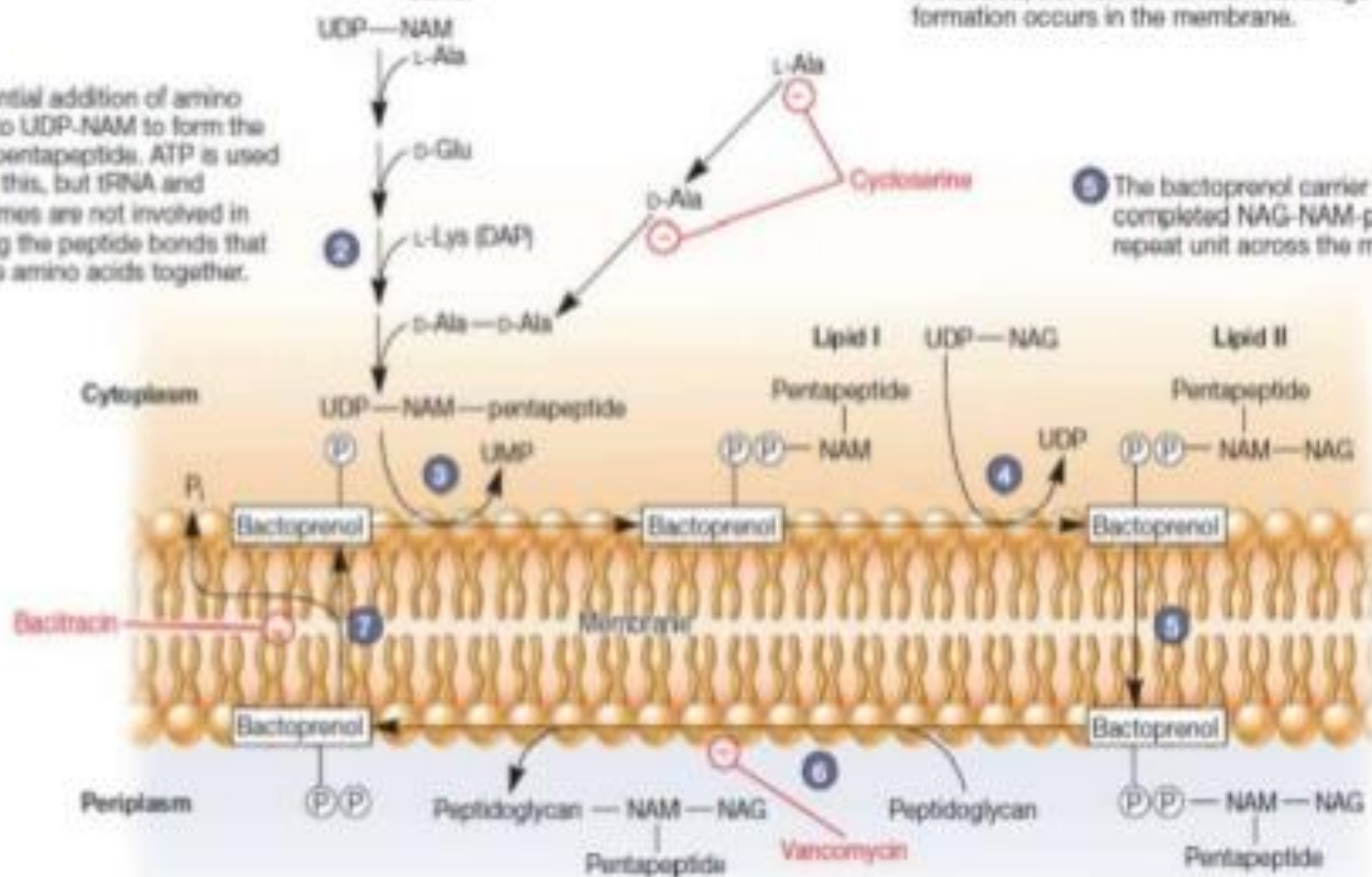
1 UDP derivatives of NAM and NAG are synthesized (not shown).

2 Sequential addition of amino acids to UDP-NAM to form the NAM-pentapeptide. ATP is used to fuel this, but tRNA and ribosomes are not involved in forming the peptide bonds that link the amino acids together.

3 NAM-pentapeptide is transferred to bactoprenol phosphate. They are joined by a pyrophosphate bond.

4 UDP transfers NAG to the bactoprenol-NAM-pentapeptide. If a pentaglycine interbridge is required, it is created using special glycyl-tRNA molecules, but not ribosomes. Interbridge formation occurs in the membrane.

5 The bactoprenol carrier transports the completed NAG-NAM-pentapeptide repeat unit across the membrane.



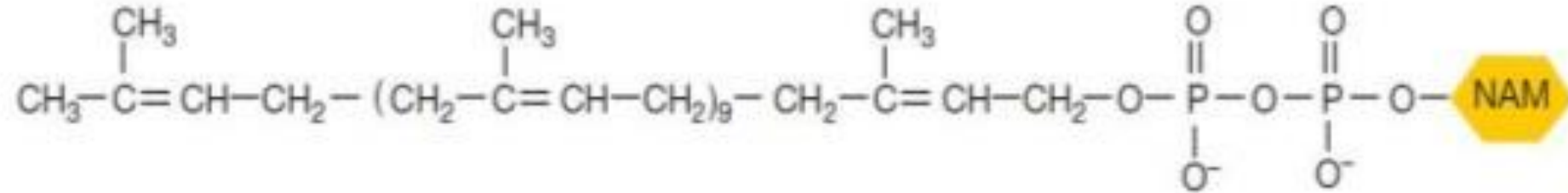
6 Peptide cross-links between peptidoglycan chains are formed by transpeptidation (not shown).

7 The bactoprenol carrier moves back across the membrane. As it does, it loses one phosphate, becoming bactoprenol phosphate. It is now ready to begin a new cycle.

8 The NAG-NAM-pentapeptide is attached to the growing end of a peptidoglycan chain, increasing the chain's length by one repeat unit.

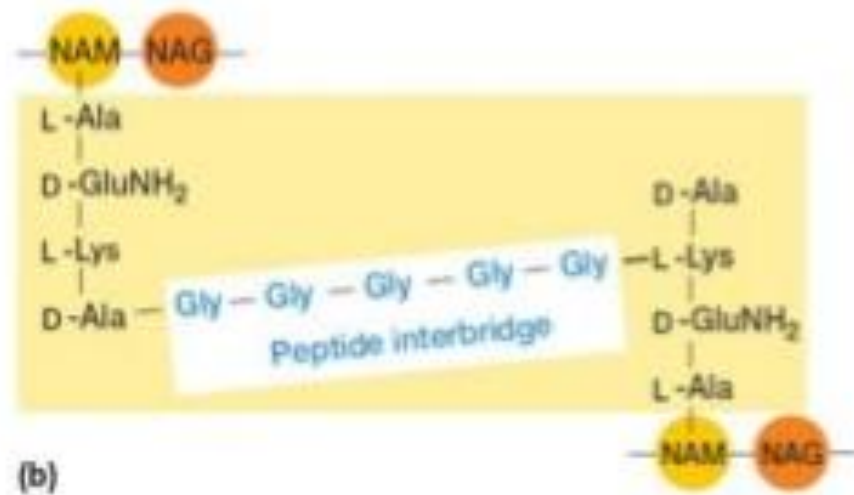
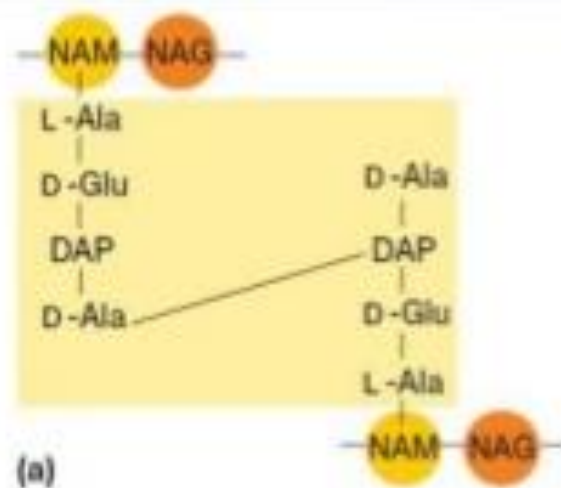
Bactoprenol unit

Pyrophosphate unit



Bactoprenol Pyrophosphate. Bactoprenol pyrophosphate connected to *N*-acetylmuramic acid (NAM).

TRANSPEPTIDATION



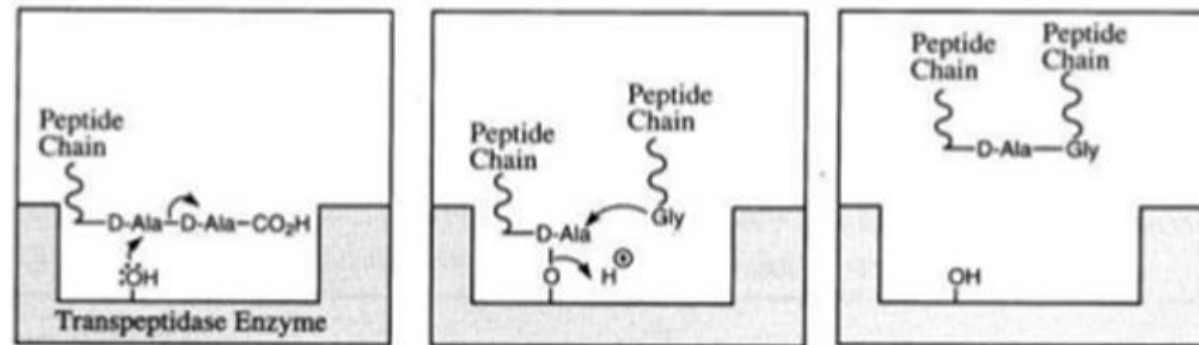
Peptidoglycan Cross-Links. (a) *E. coli*

peptidoglycan with direct cross-linking, typical of many gram negative bacteria.

(b) *Staphylococcus aureus* peptidoglycan. *S. aureus* is a gram-positive bacterium. NAM is N-acetylmuramic acid. NAG is N-acetylglucosamine. Gly is glycine. Although the polysaccharide chains are drawn opposite each other for the sake of clarity, two chains lying side-by-side may be linked together

Transpeptidation mechanism

Normal Mechanism



Mechanism Inhibited by Penicillin

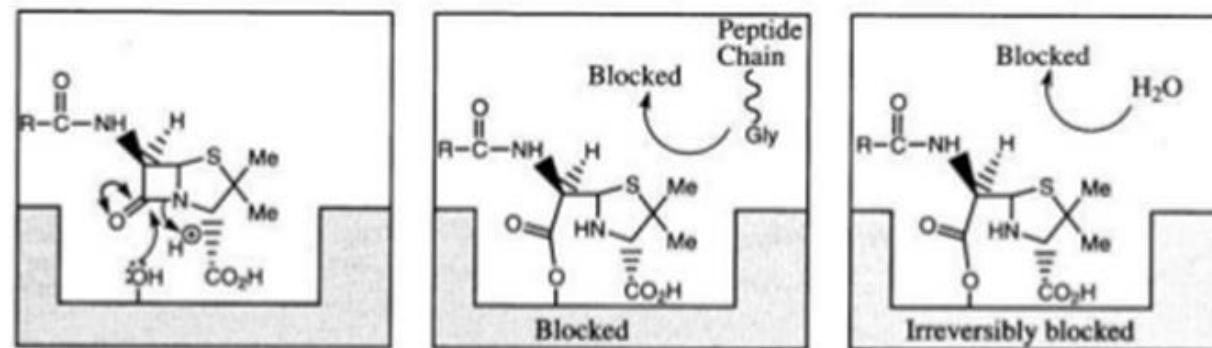
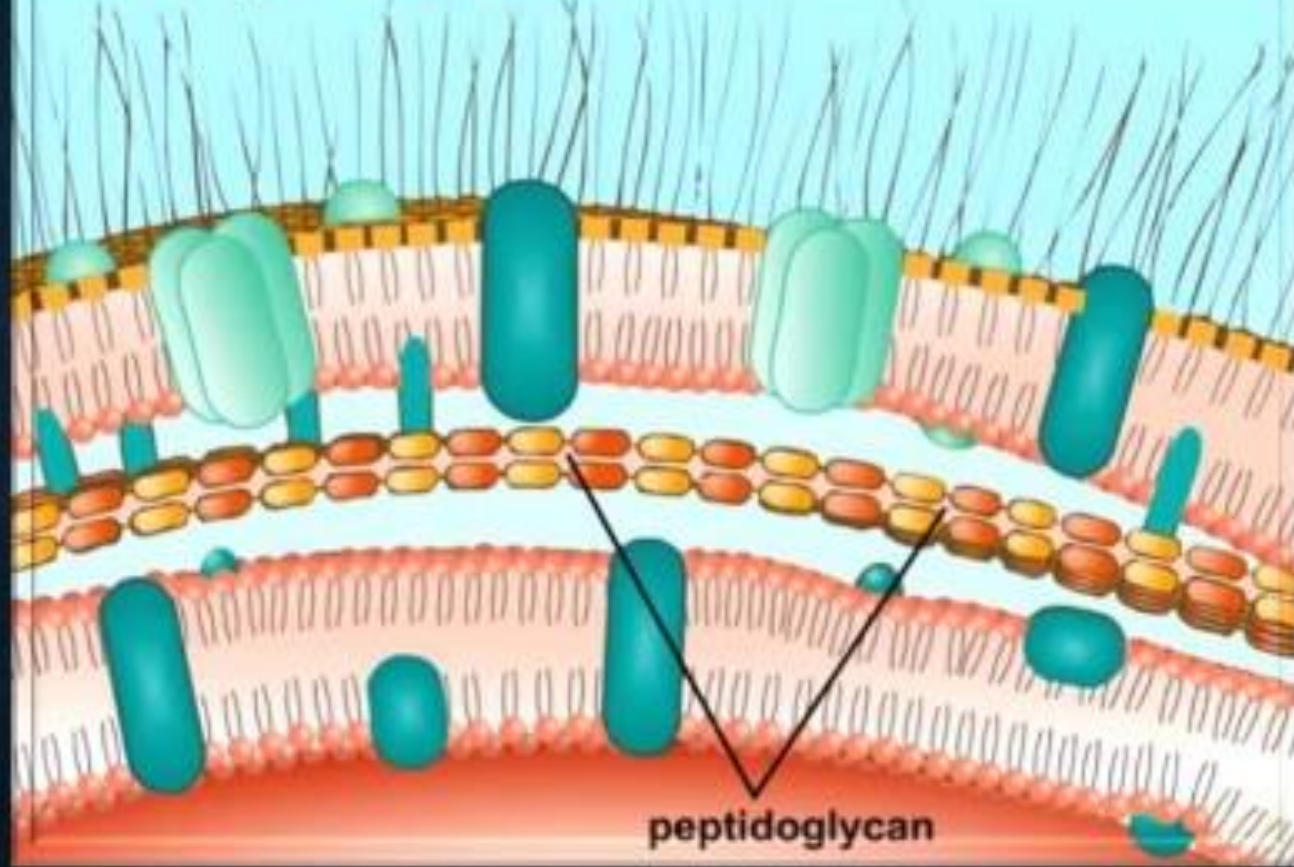


Fig. 14.63 Cross-linking mechanism by transpeptidase enzyme.

Source: Google Images

Gram negative cell wall

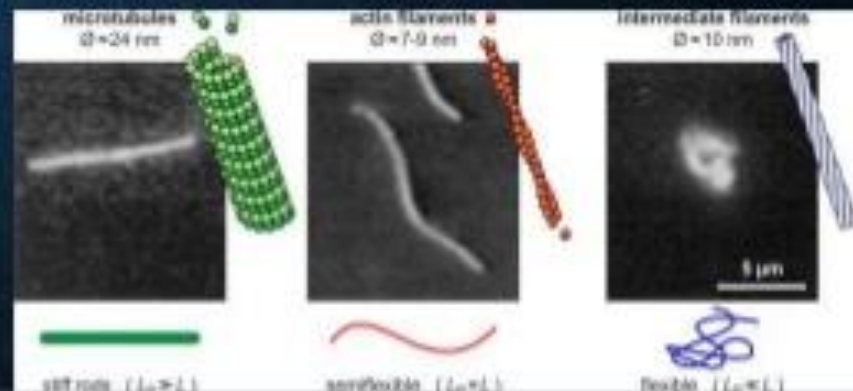


peptidoglycan

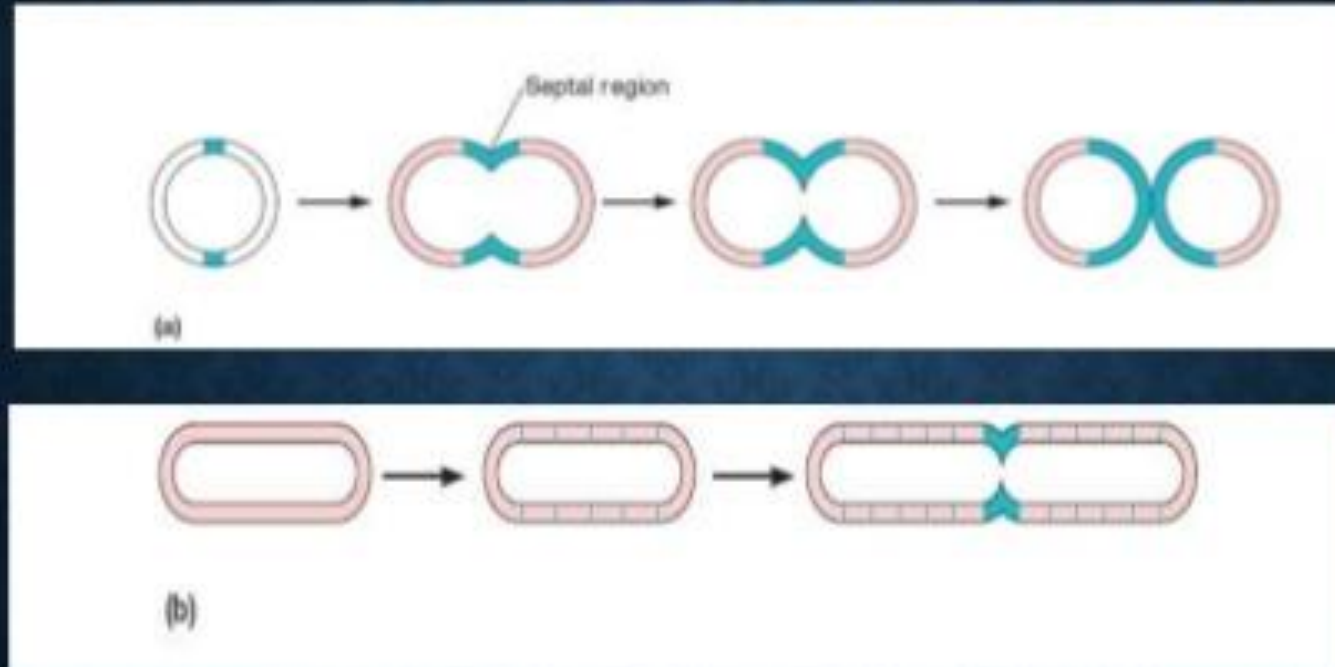
πεπτιδογλυκαν

ROLE OF CYTOSKELETON IN CELL WALL SYNTHESIS

- Cytoskeletal structures formed by MreBCD proteins control cell shape by controlling the cell wall synthesis.
- Any mutations that lead to the defects in bacterial cell shape are directly associated with a defect in cell wall synthesis.
- Multiple mutations in *pbp* genes can convert rod shaped *E.coli* and *B.subtilis* into round or branched cells.(Nelson *et al.*,2000)
- Similarly mutation in TagF (enzyme involved in teichoic acid synthesis) converts *B.subtilis* to round cells. (Henriques *et al.*, 1998)



PATTERNS OF CELL WALL SYNTHESIS

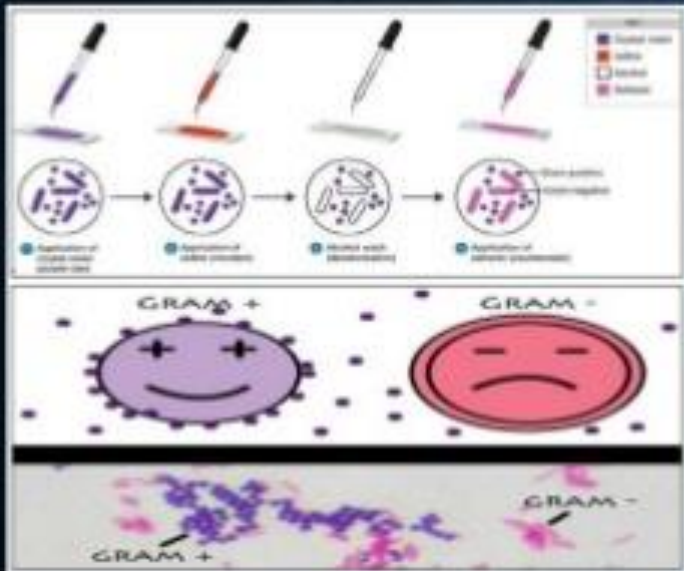


Wall Synthesis Patterns. Patterns of new cell wall synthesis in growing and dividing bacteria.

(a) Streptococci and some other gram-positive cocci.

(b) Synthesis in rod-shaped bacteria (E. coli, Salmonella, Bacillus). The zones of growth are in turquoise. The actual situation is more complex than indicated because cells can begin to divide again before the first division is completed

SIGNIFICANCE OF PEPTIDOGLYCAN



Osmolysis





CONCLUSION

- Peptidoglycan wall is crucial for the bacterial growth, protection and maintenance of the cell shape.
- Cytoskeletons play a crucial role in cell shape determination but the specific effectors of cell wall receptors of cell wall morphogenesis controlled by cytoskeleton is unknown (Scheffers and Pinho, 2005)
- All the factors, responsible for the cell wall synthesis, if studied it would be effective in designing drugs and antibiotics.

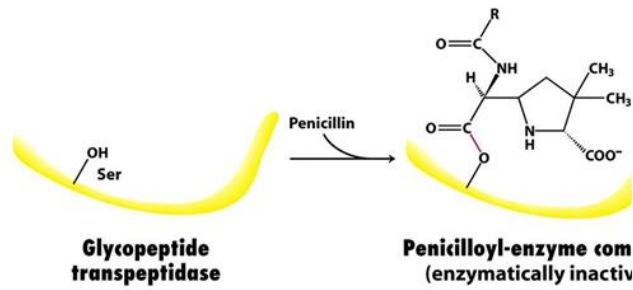
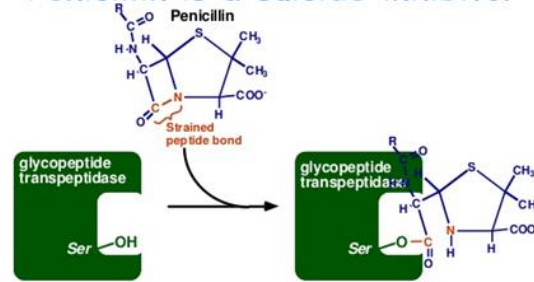


Figure 8-35

-On binding to the transpeptidase, the serine residue at the active site attacks the carbonyl carbon atom of the lactam ring of the penicillin to form the penicilloyl-serine derivative.

-Penicillin acts as a **suicide inhibitor**.

Penicillin is a suicide inhibitor



Glycopeptide transpeptidase catalyzes the formation of cross-links between D-amino acids in the cell walls of bacteria. This enzyme also catalyzes the reverse reaction, the hydrolysis of peptide bonds. During the course of hydrolyzing the strained peptide bond in penicillin, the enzyme activates the inhibitor (penicillin), which then covalently modifies an active site serine in the enzyme. In effect, the enzyme "commits suicide" by hydrolyzing the strained peptide bond in penicillin.

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<p>Similarity in structure of cell wall peptide and penicillin</p>	<p>beta-Lactam</p>	<p>Trace red oxygen and blue nitrogen backbone</p>
<p>D-alanine-alanine</p>		<p>Penicillin</p>

C. Ophardt, c. 2003