

ФАРМАЦЕВТИЧЕСКАЯ ХИМИЯ

ЛЕКЦИЯ 5

Основные понятия
фармацевтической химии.

Фармакокинетика.

Фармакодинамика.

Молекулярные мишени.

Фармакокинетика (от др.-греч. *φάρμακον* — лекарство и *κίνησις* — движение) — раздел фармакологии, изучающий кинетические закономерности химических и биологических процессов, происходящих с лекарственным средством в организме.

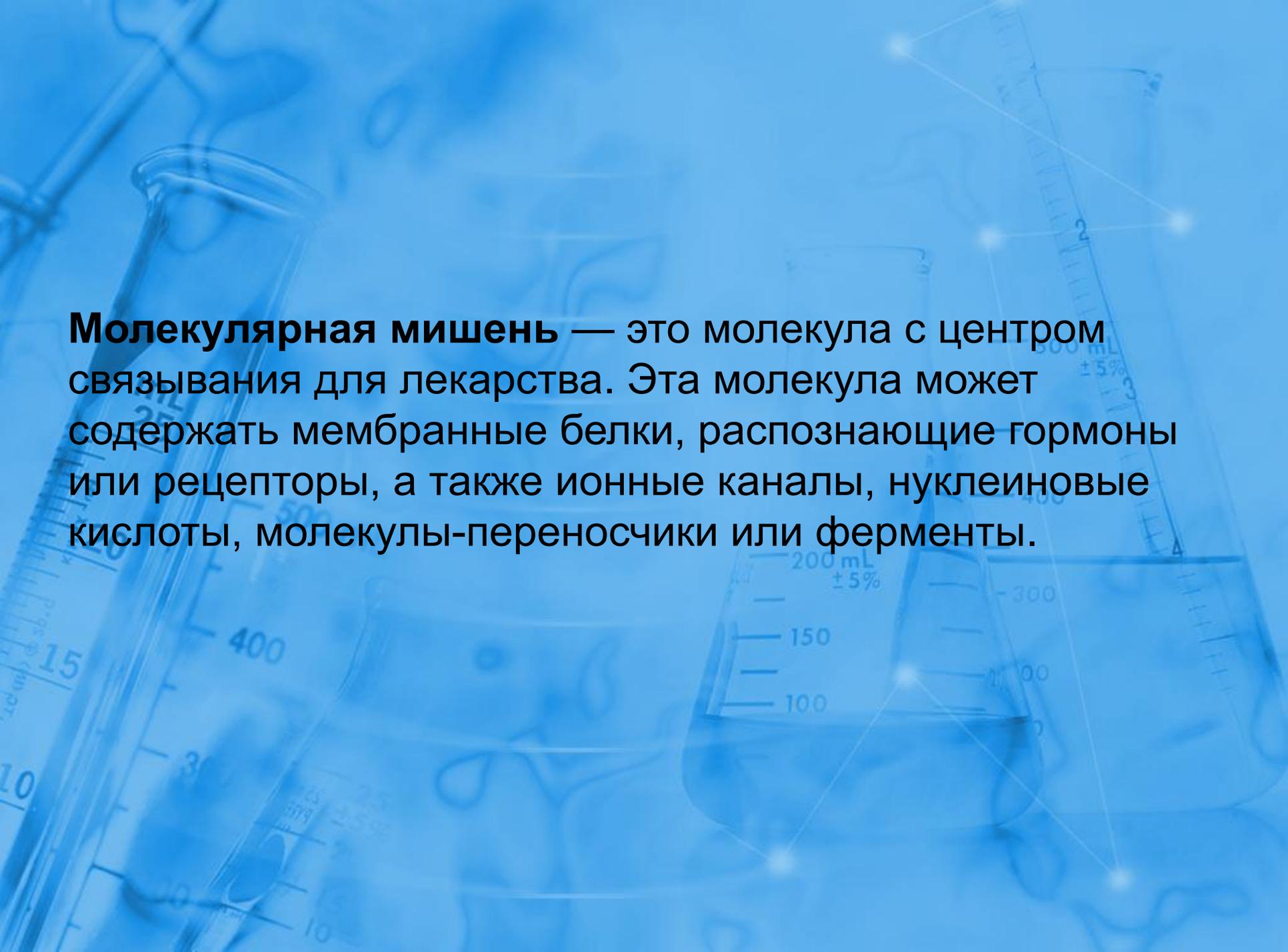
Иначе говоря, фармакокинетика — это судьба отдельно взятой молекулы лекарственного вещества (биохимическая трансформация молекул лекарства в организме).

Основные фармакокинетические процессы: всасывание, экскреция (выведение), распределение и метаболизм.

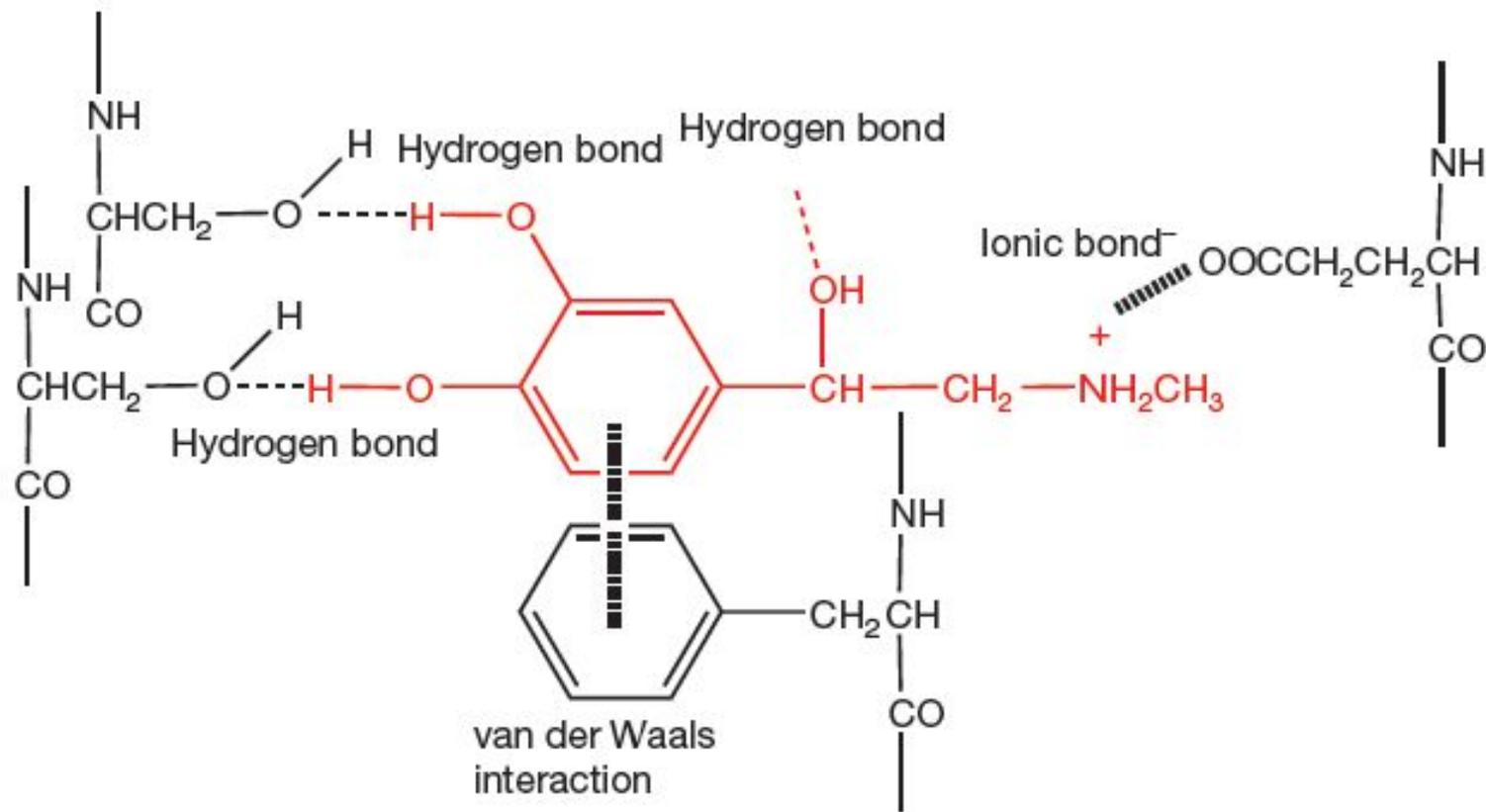
Фармакодинамика — раздел фармакологии, изучающий локализацию, механизм действия и фармакологические эффекты лекарственных средств, силу и длительность их действия. Фармакодинамика — это судьба организма после действия этого лекарственного вещества (механизм действия и эффекты)

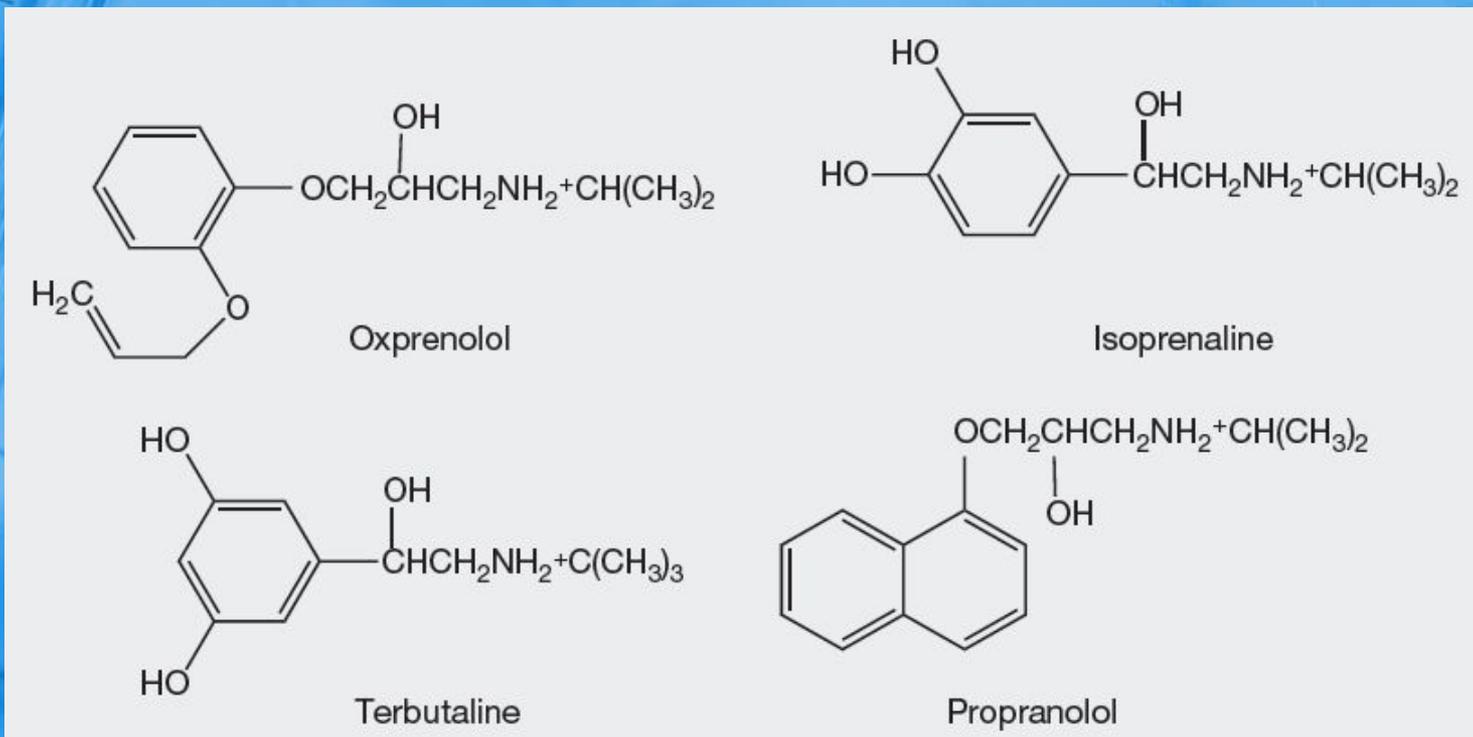
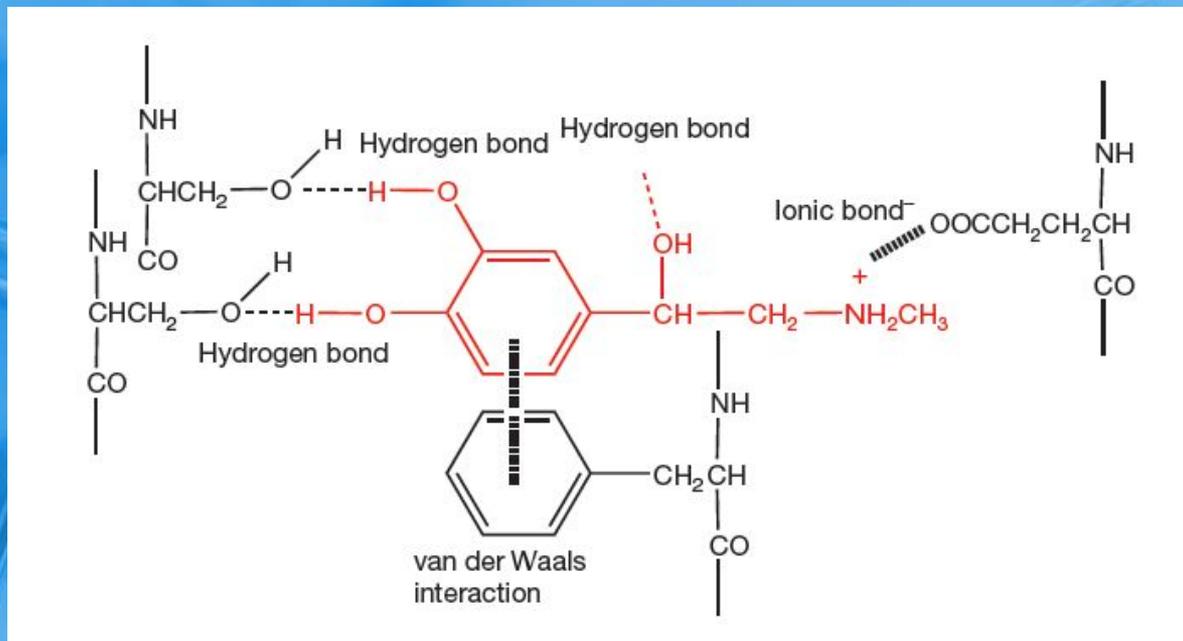
Отмечают 5 главных эффектов, оказываемых лекарственными средствами:

- подавляющее,
- стимулирующее,
- разрушающее клетки (цитотоксическое),
- раздражающее,
- замещающее недостающие вещества.

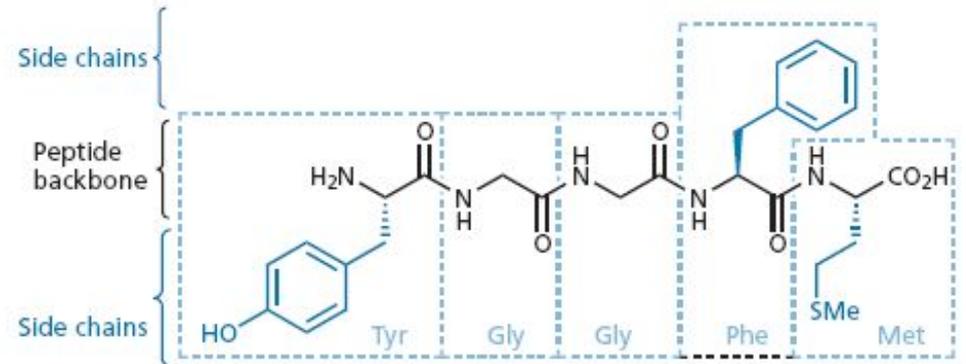
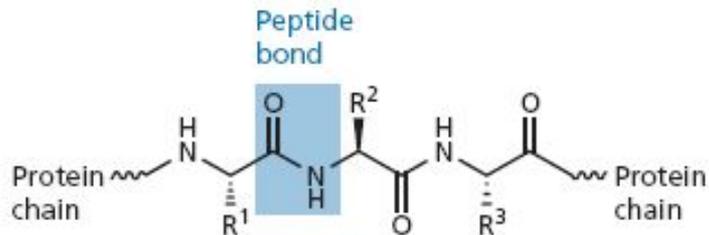


Молекулярная мишень — это молекула с центром связывания для лекарства. Эта молекула может содержать мембранные белки, распознающие гормоны или рецепторы, а также ионные каналы, нуклеиновые кислоты, молекулы-переносчики или ферменты.





БЕЛКИ. ПЕРВИЧНАЯ СТРУКТУРА



H-Tyr-Gly-Gly-Phe-Met-OH or YGGFM.



FIGURE 2.3 The planar peptide bond (bond rotation allowed for coloured bonds only).

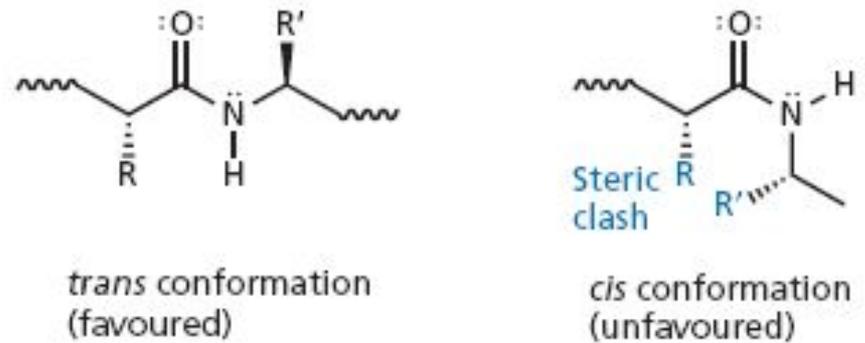
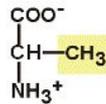


FIGURE 2.4 *Trans* and *cis* conformations of the peptide bond.

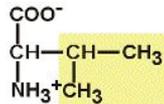
Неполярные

Алифатические

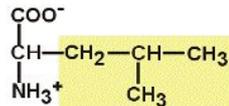
Аланин
Ала, А



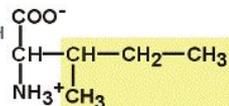
Валин
Вал, V



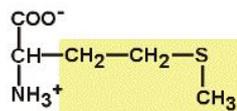
Лейцин
Лей, L



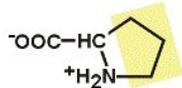
Изолейцин
Иле, J



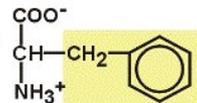
Метионин
Мет, M



Пролин
Про, P

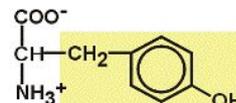


Фенилаланин
Фен, F

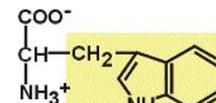


Ароматические

Тирозин
Тир, Y



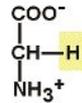
Триптофан
Три, W



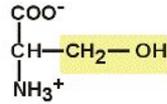
Полярные

Незаряженные

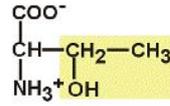
Глицин
Гли, G



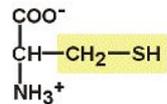
Серин
Сер, S



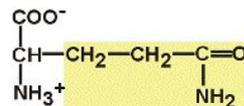
Треонин
Тре, T



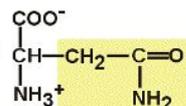
Цистеин
Цис, C



Глутамин
Глн, Q

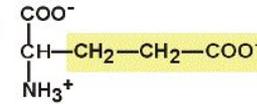


Аспарагин
Асн, N

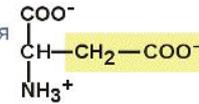


Отрицательно заряженные

Глутаминовая
кислота
Глу, E

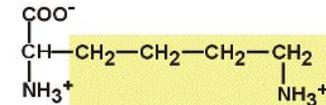


Аспарагиновая
кислота
Асп, D

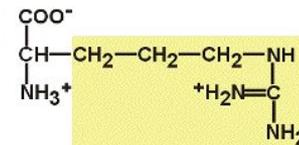


Положительно заряженные

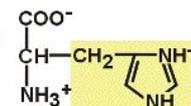
Лизин
Лиз, K



Аргинин
Арг, R



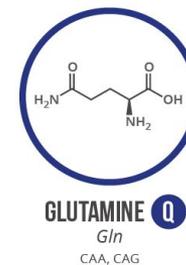
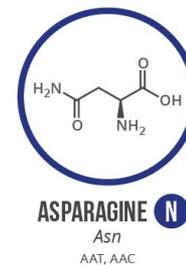
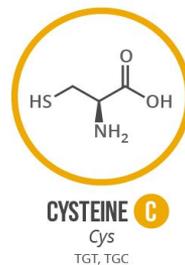
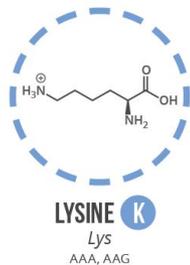
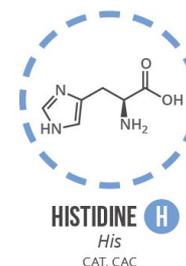
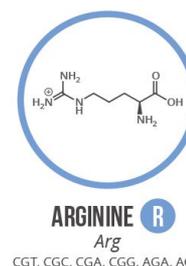
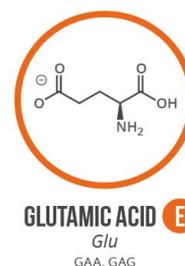
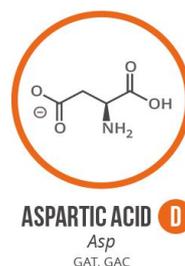
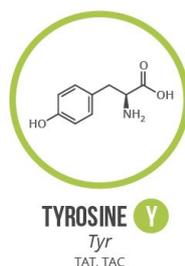
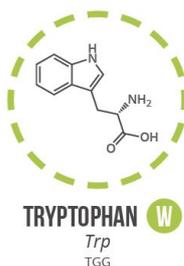
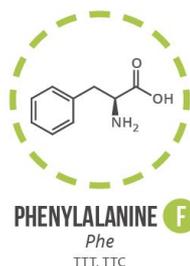
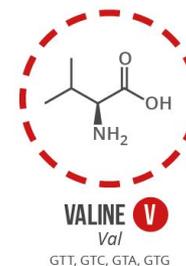
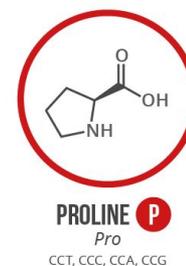
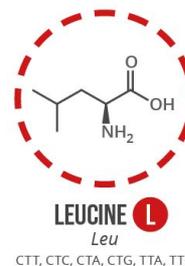
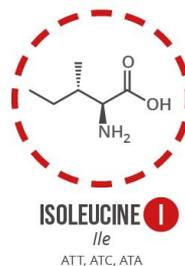
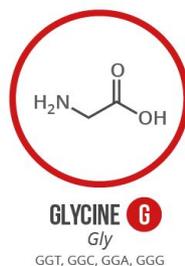
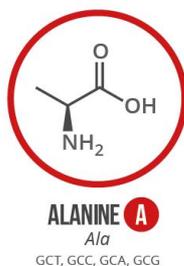
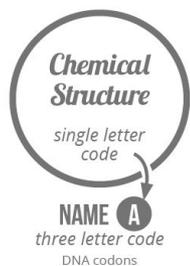
Гистидин
Гис, H



A GUIDE TO THE TWENTY COMMON AMINO ACIDS

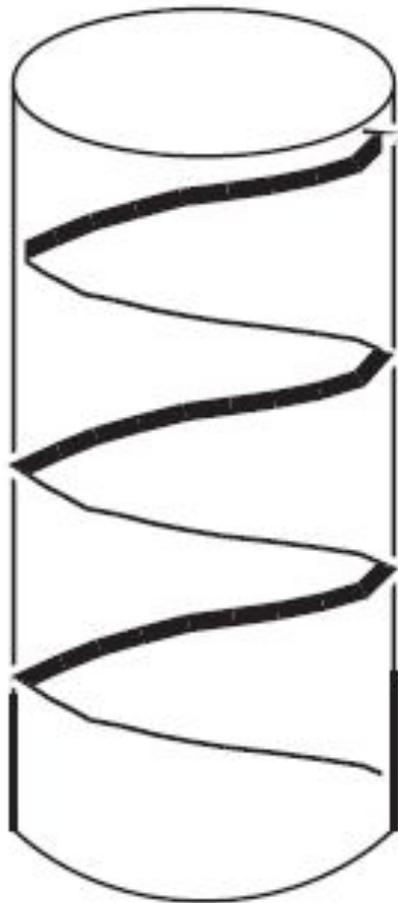
AMINO ACIDS ARE THE BUILDING BLOCKS OF PROTEINS IN LIVING ORGANISMS. THERE ARE OVER 500 AMINO ACIDS FOUND IN NATURE - HOWEVER, THE HUMAN GENETIC CODE ONLY DIRECTLY ENCODES 20. 'ESSENTIAL' AMINO ACIDS MUST BE OBTAINED FROM THE DIET, WHILST NON-ESSENTIAL AMINO ACIDS CAN BE SYNTHESISED IN THE BODY.

Chart Key: ● ALIPHATIC ● AROMATIC ● ACIDIC ● BASIC ● HYDROXYLIC ● ● SULFUR-CONTAINING ● AMIDIC ○ NON-ESSENTIAL ○ ESSENTIAL

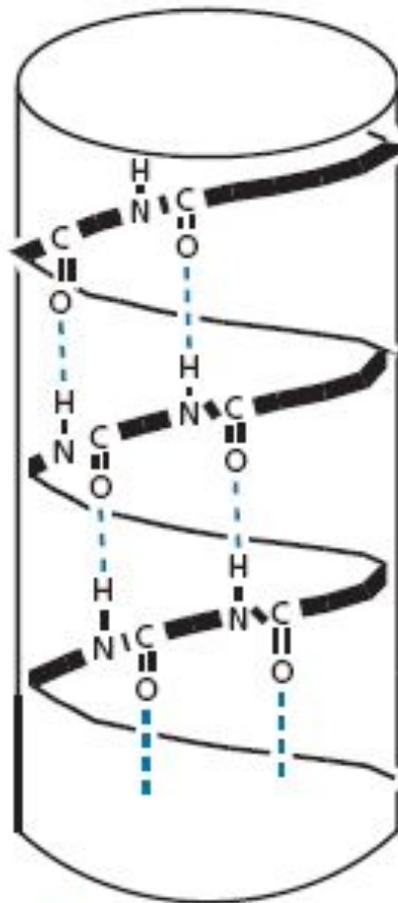


Note: This chart only shows those amino acids for which the human genetic code directly codes for. Selenocysteine is often referred to as the 21st amino acid, but is encoded in a special manner. In some cases, distinguishing between asparagine/aspartic acid and glutamine/glutamic acid is difficult. In these cases, the codes asx (B) and glx (Z) are respectively used.

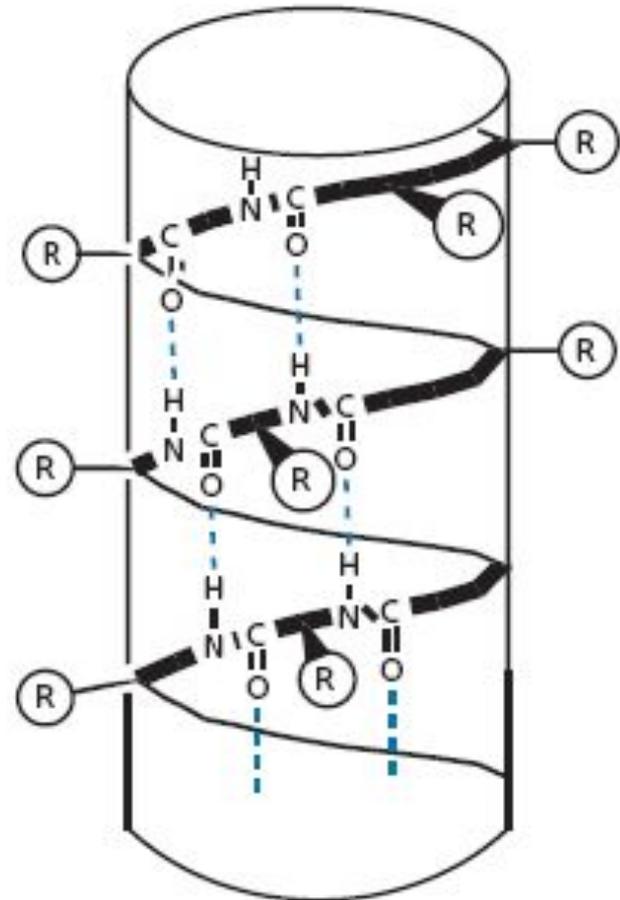
БЕЛКИ. ВТОРИЧНАЯ СТРУКТУРА



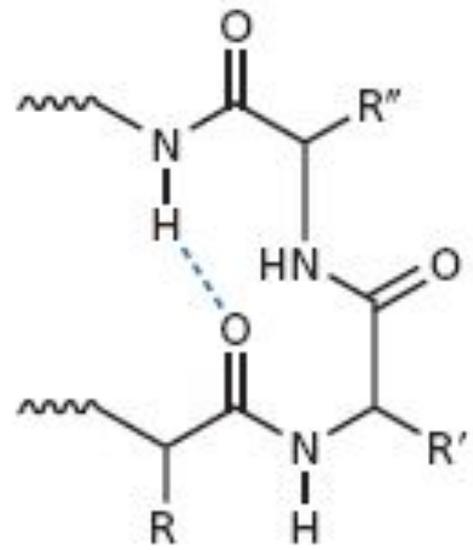
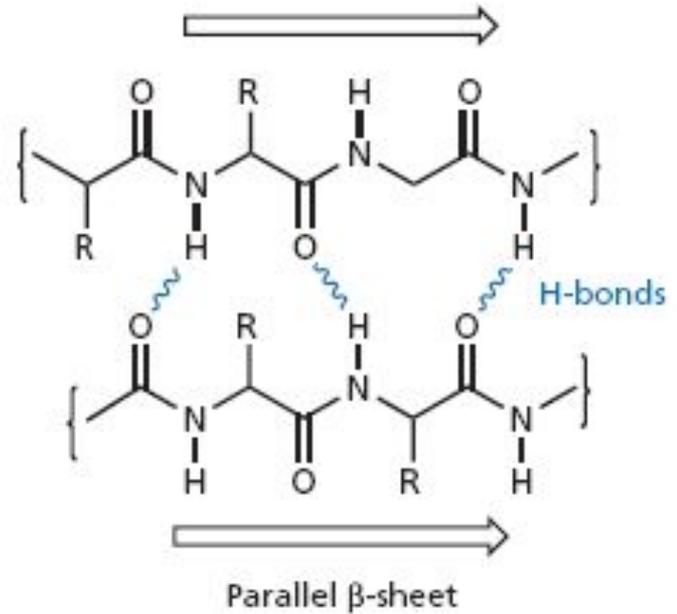
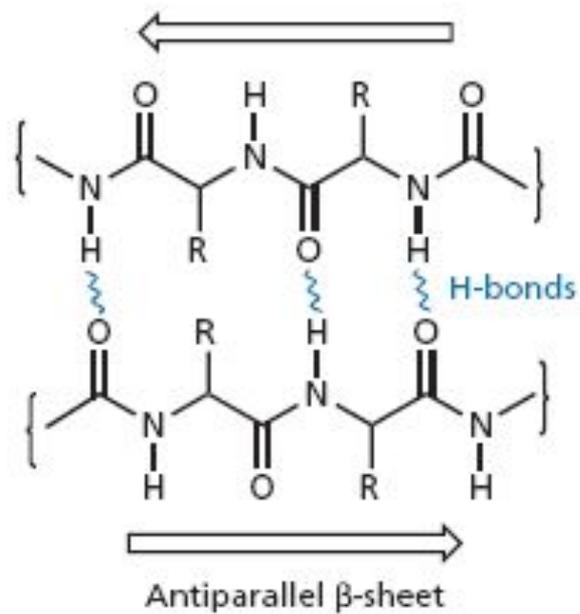
α -Helical backbone



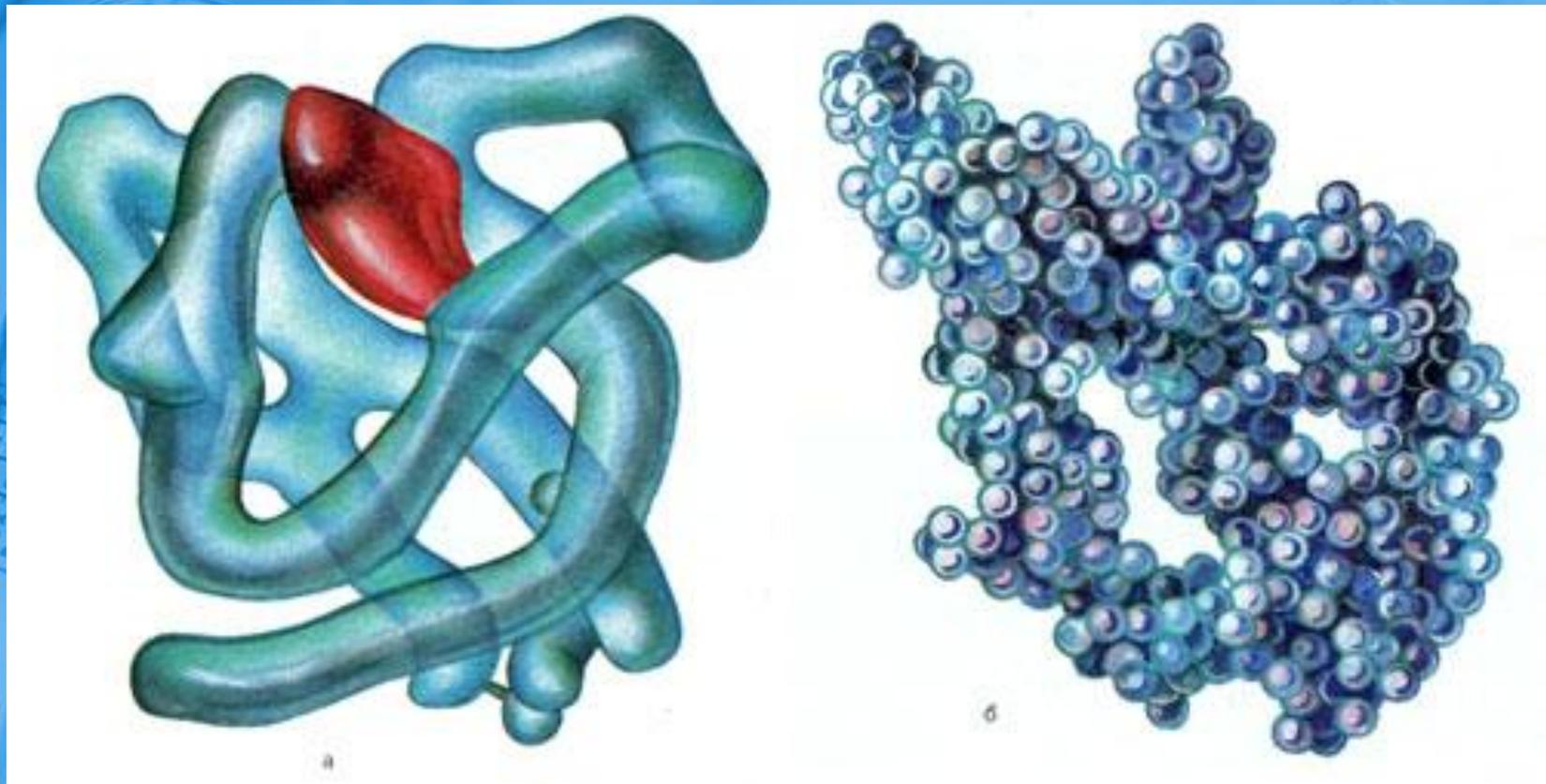
Hydrogen bonding
between peptide bonds

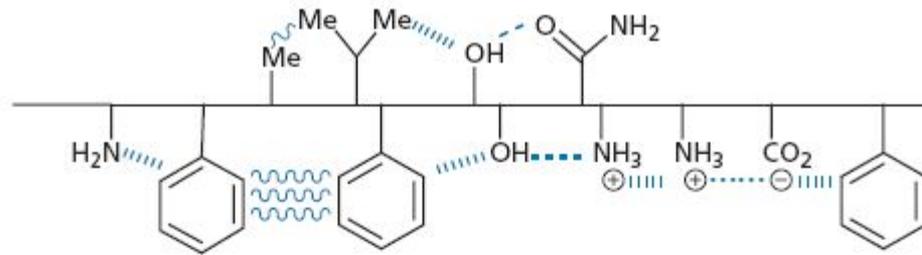


Position of side chains

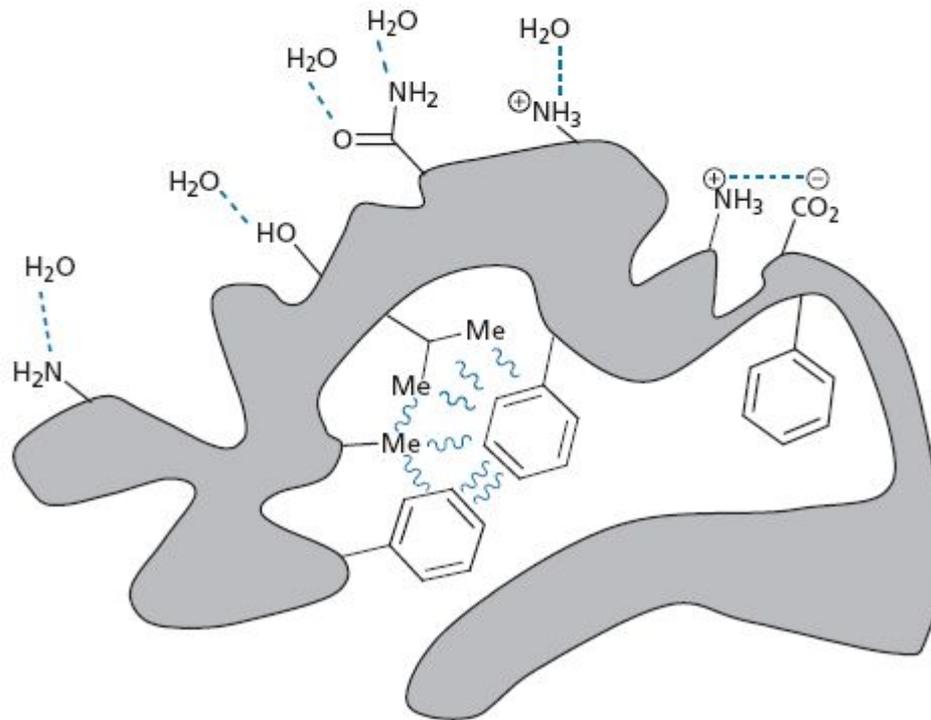


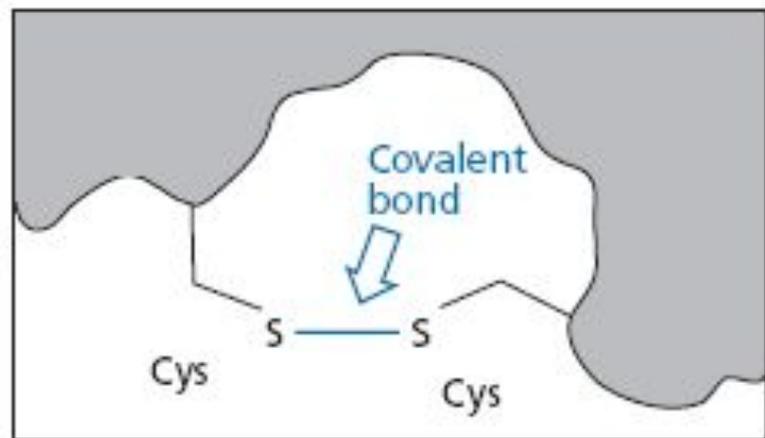
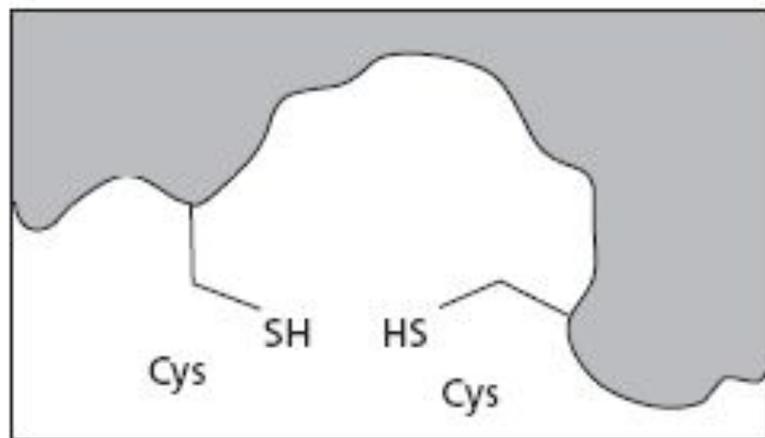
БЕЛКИ. ТРЕТИЧНАЯ СТРУКТУРА

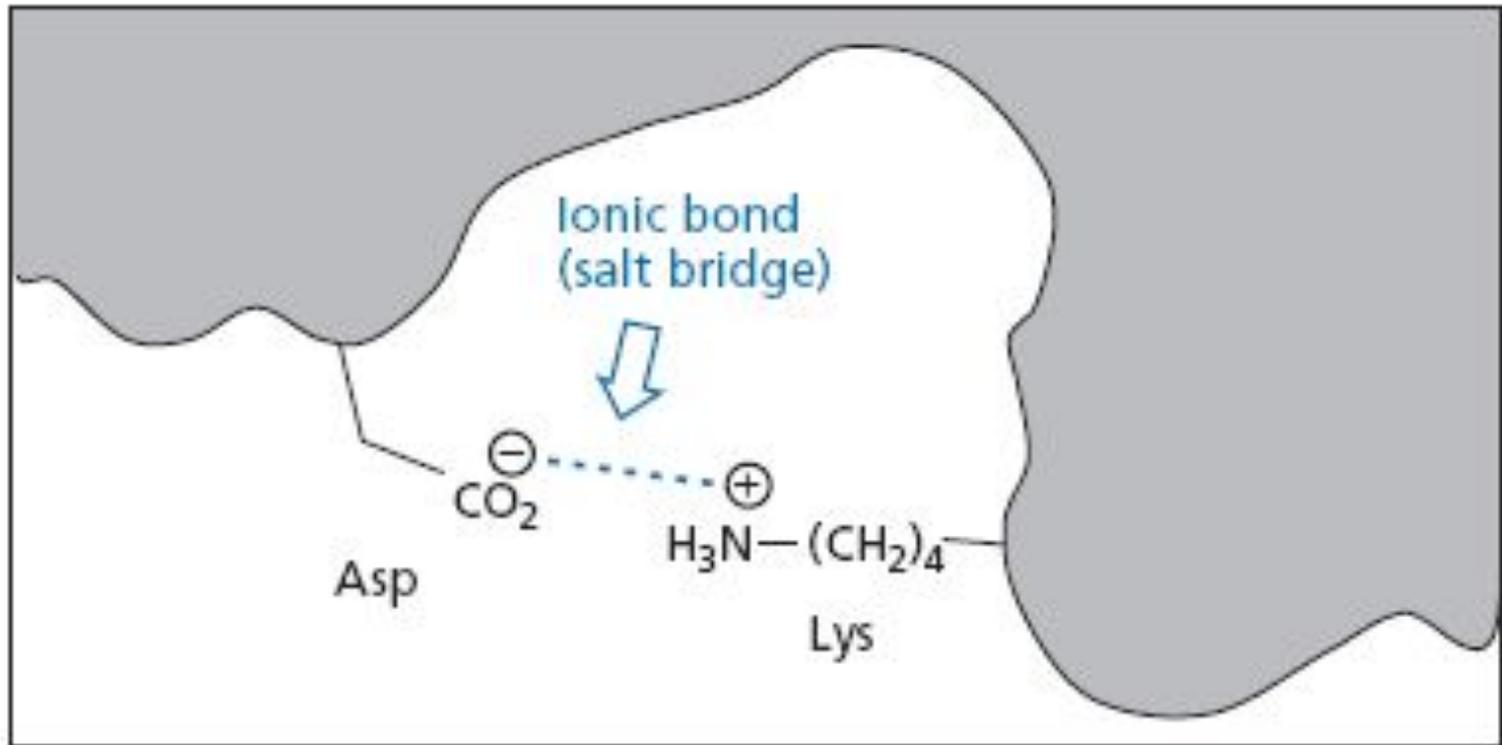


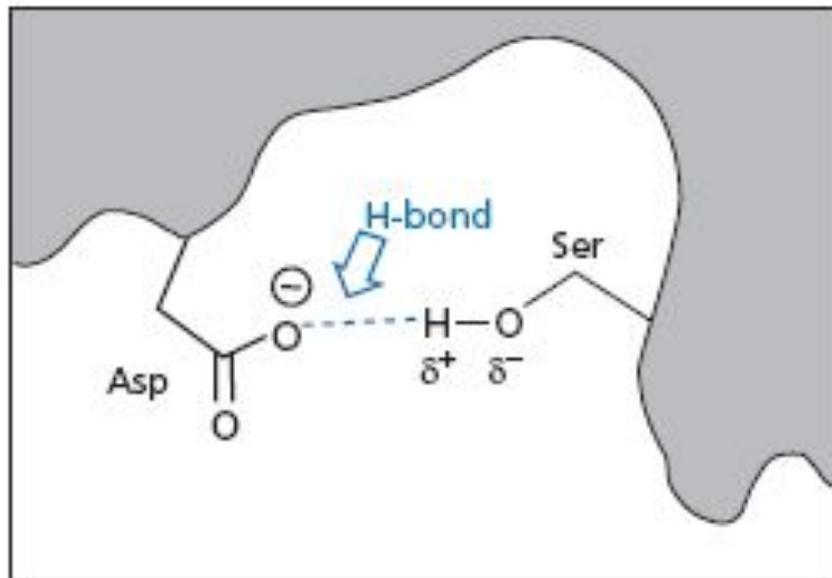
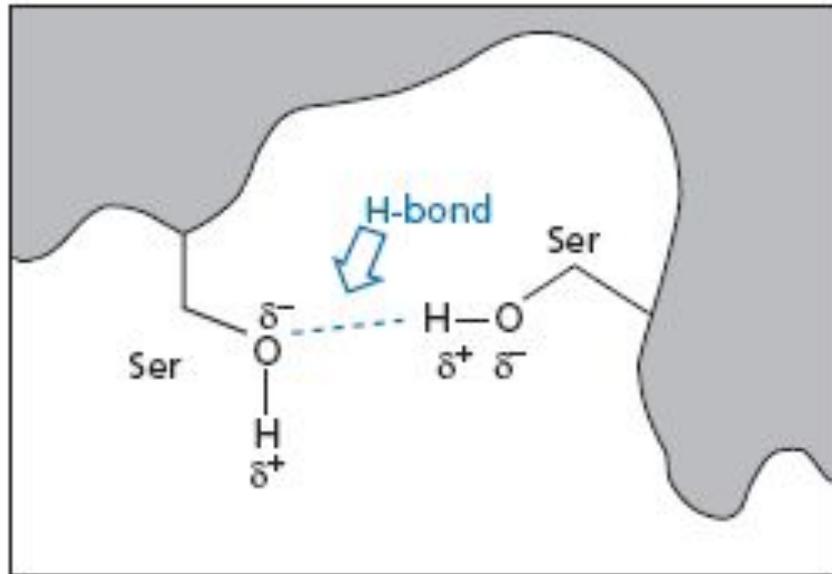


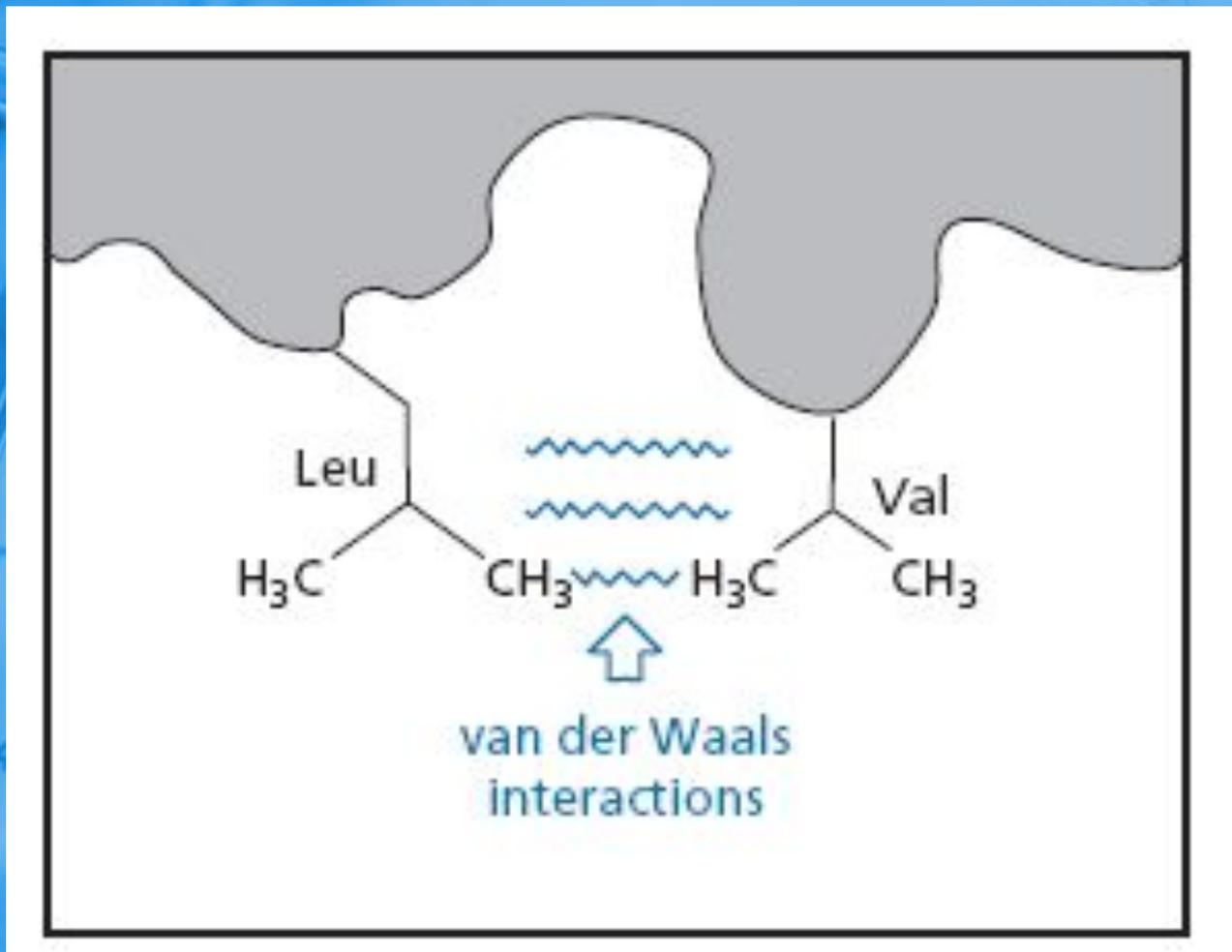
..... Repulsive interactions ~~~~~ van der Waals interactions
 ----- Hydrogen bonding interactions
 Ionic bonding interactions

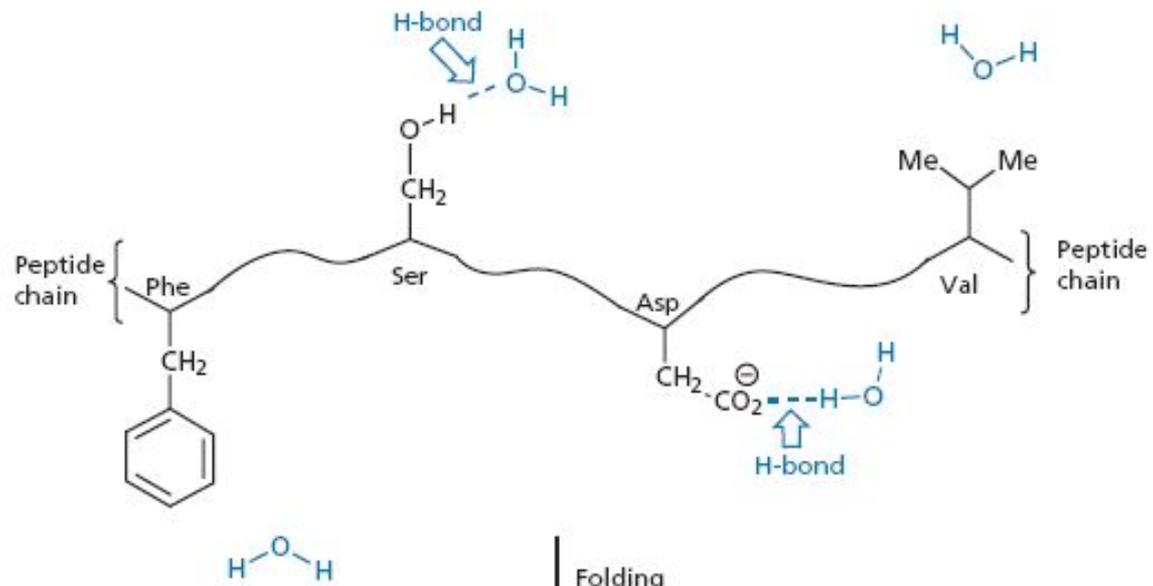




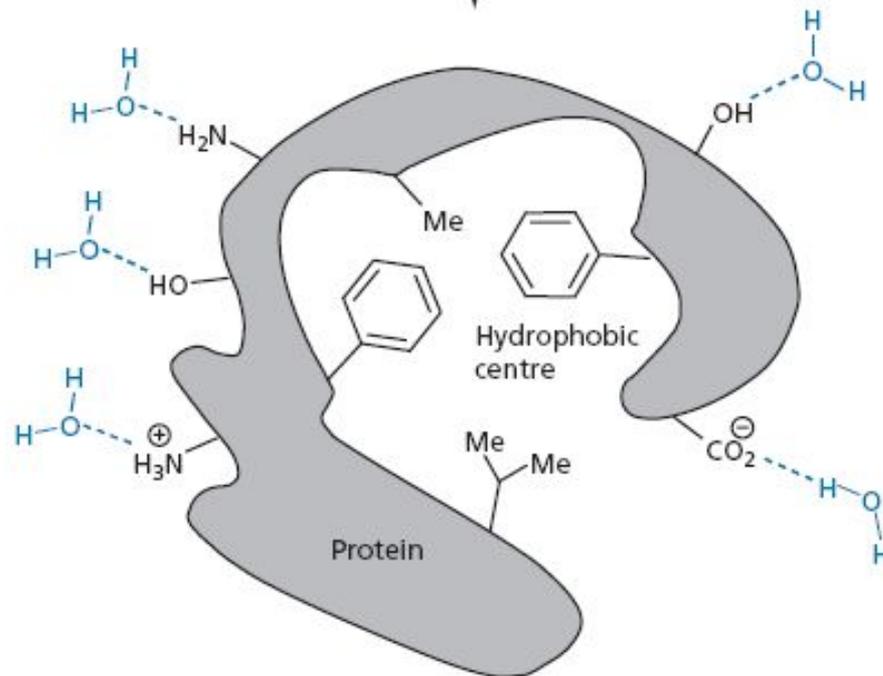


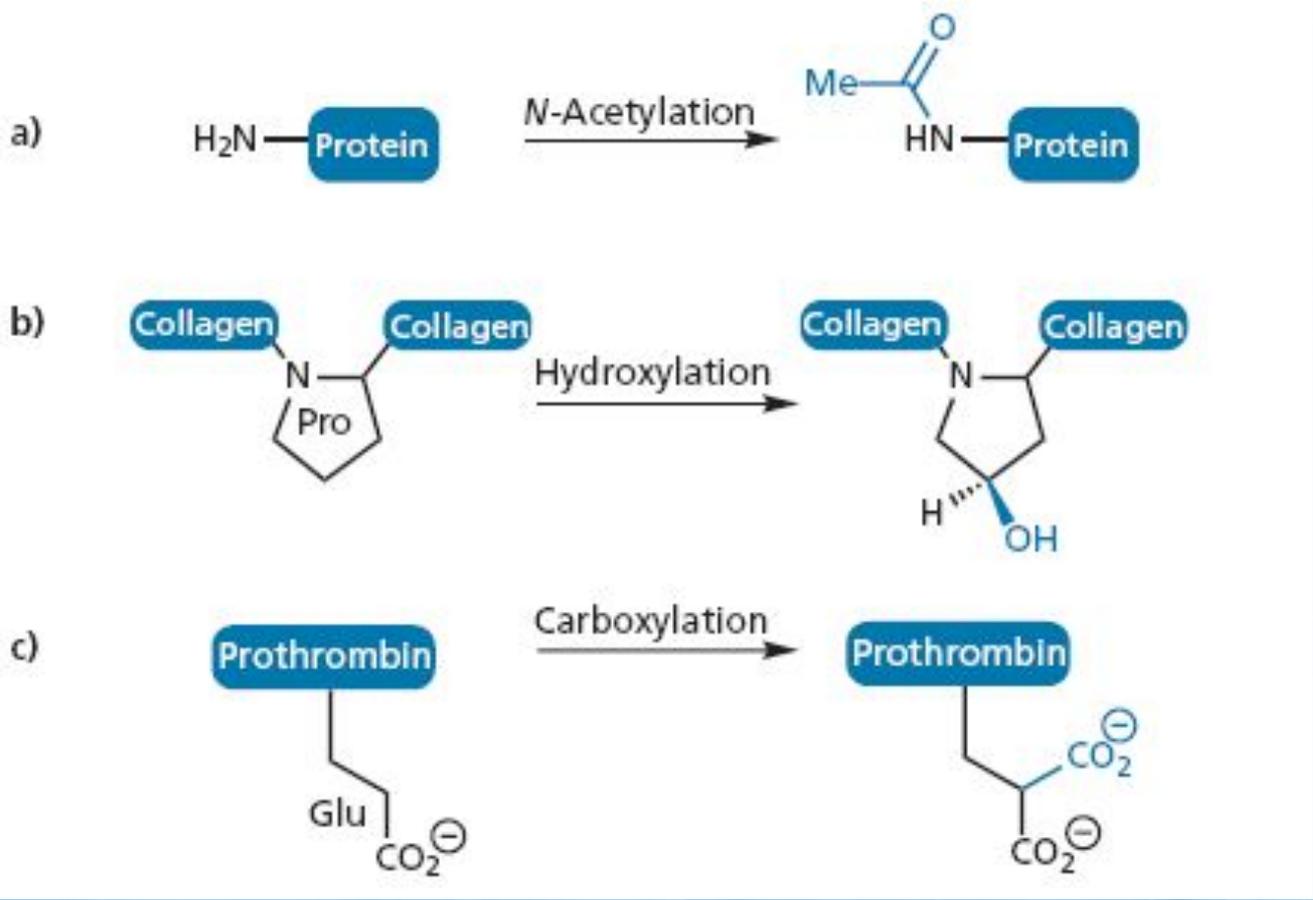




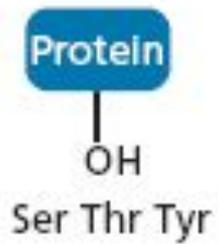


Folding

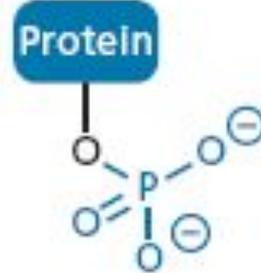




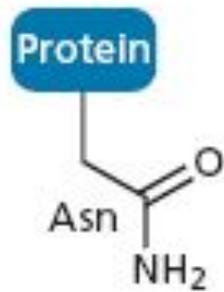
d)



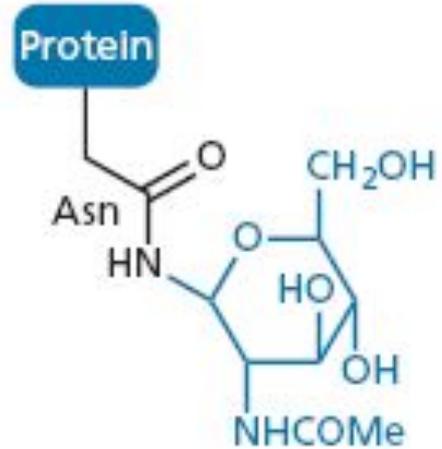
Phosphorylation



e)



Glycosylation



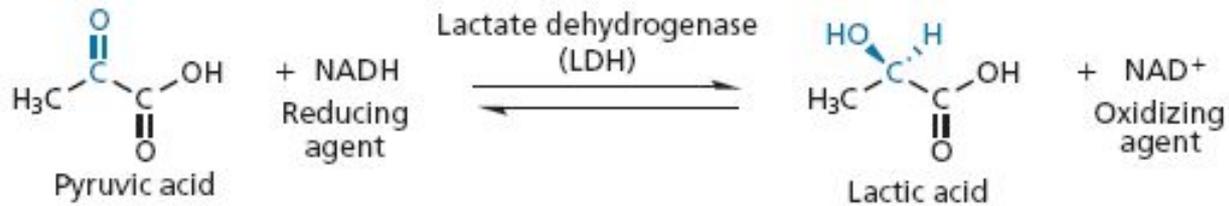
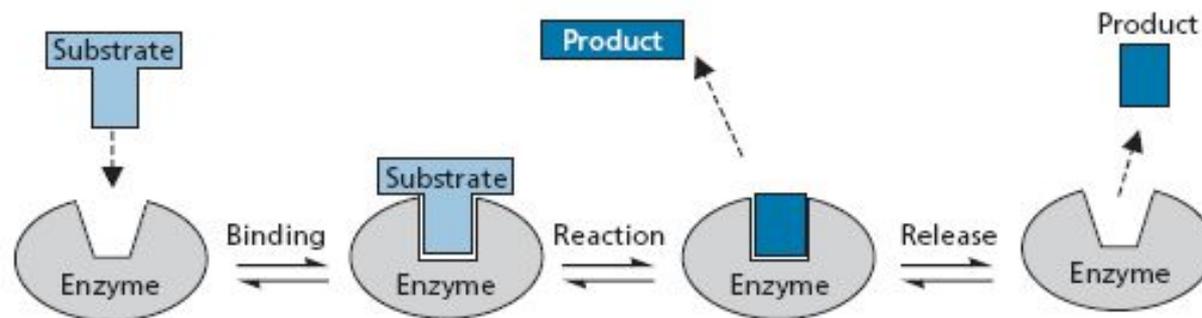
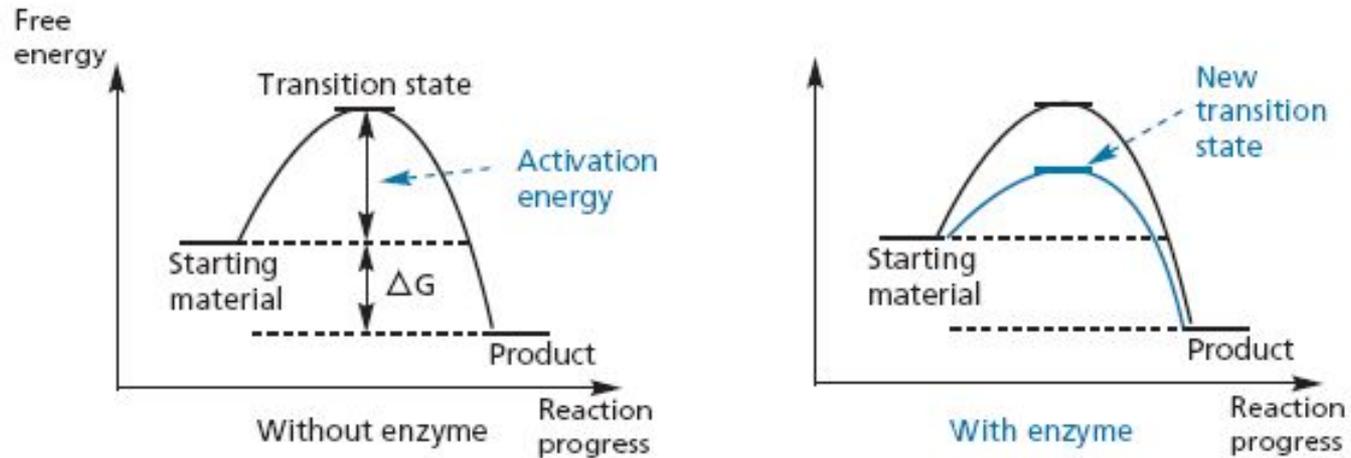
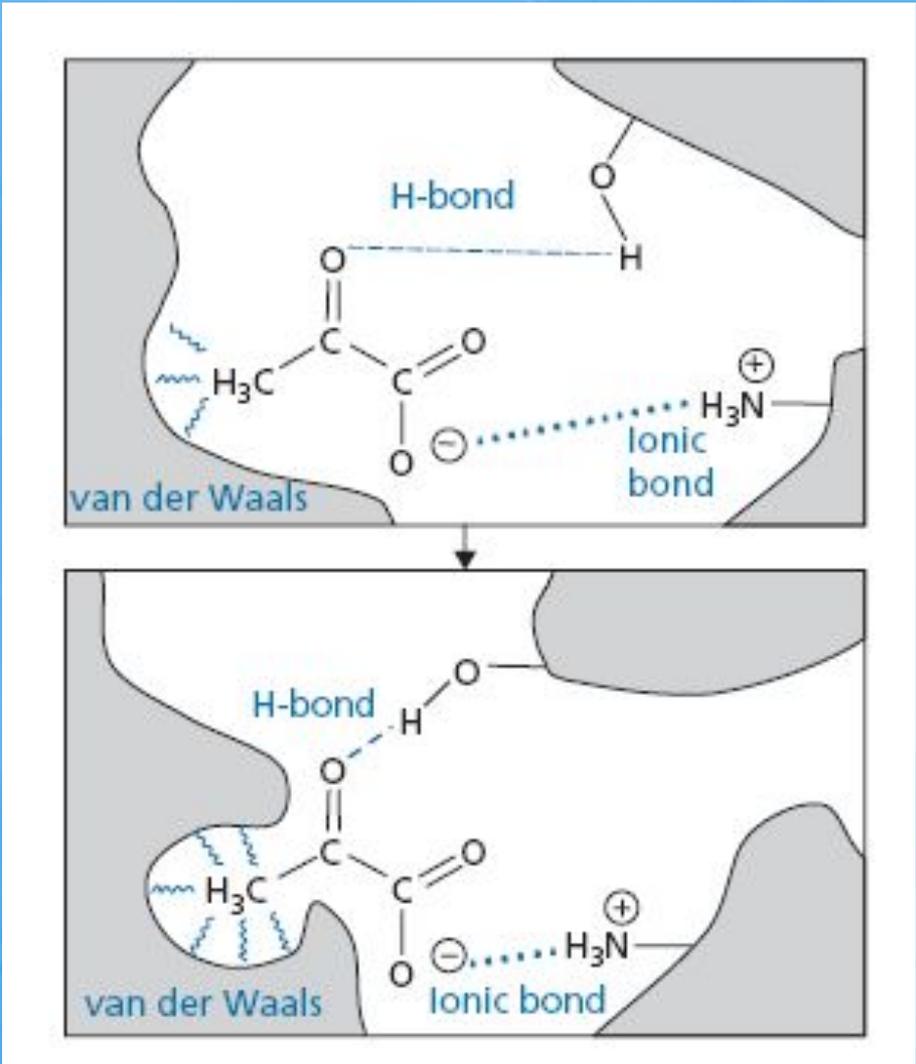
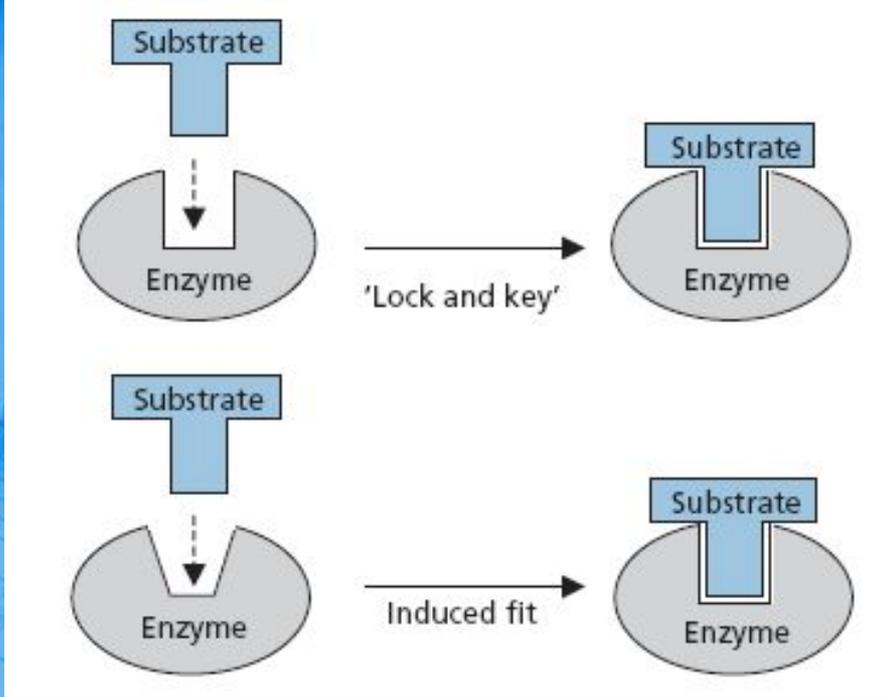
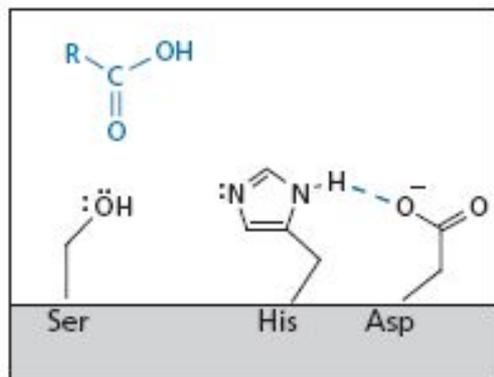
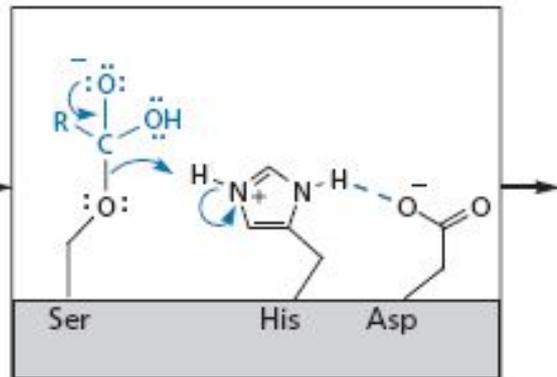
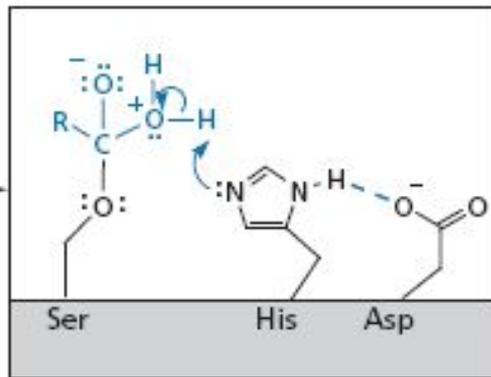
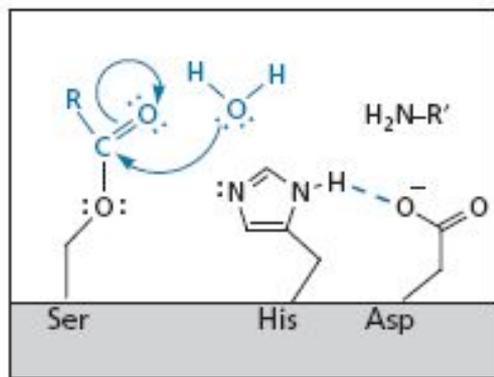
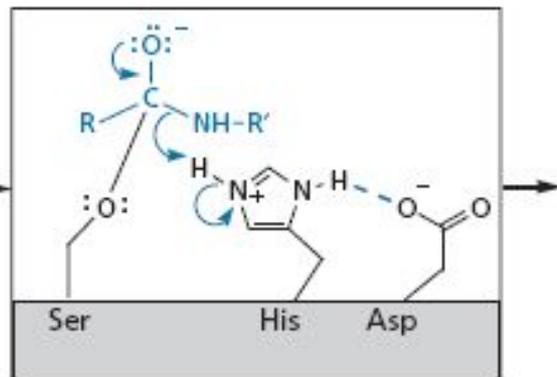
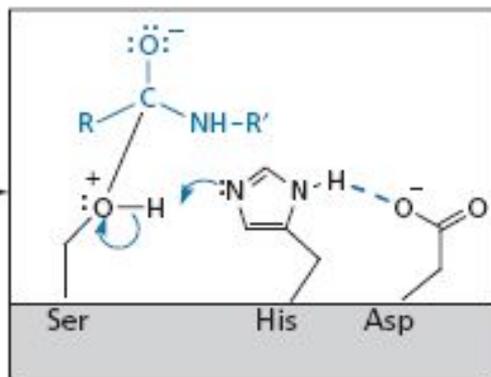
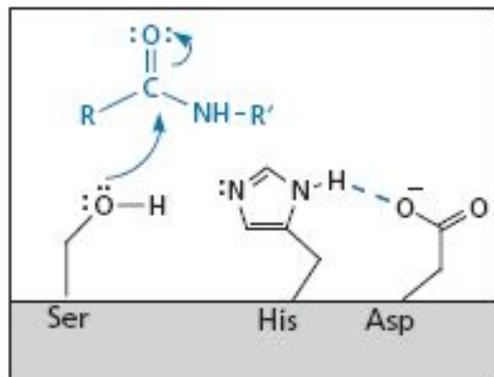
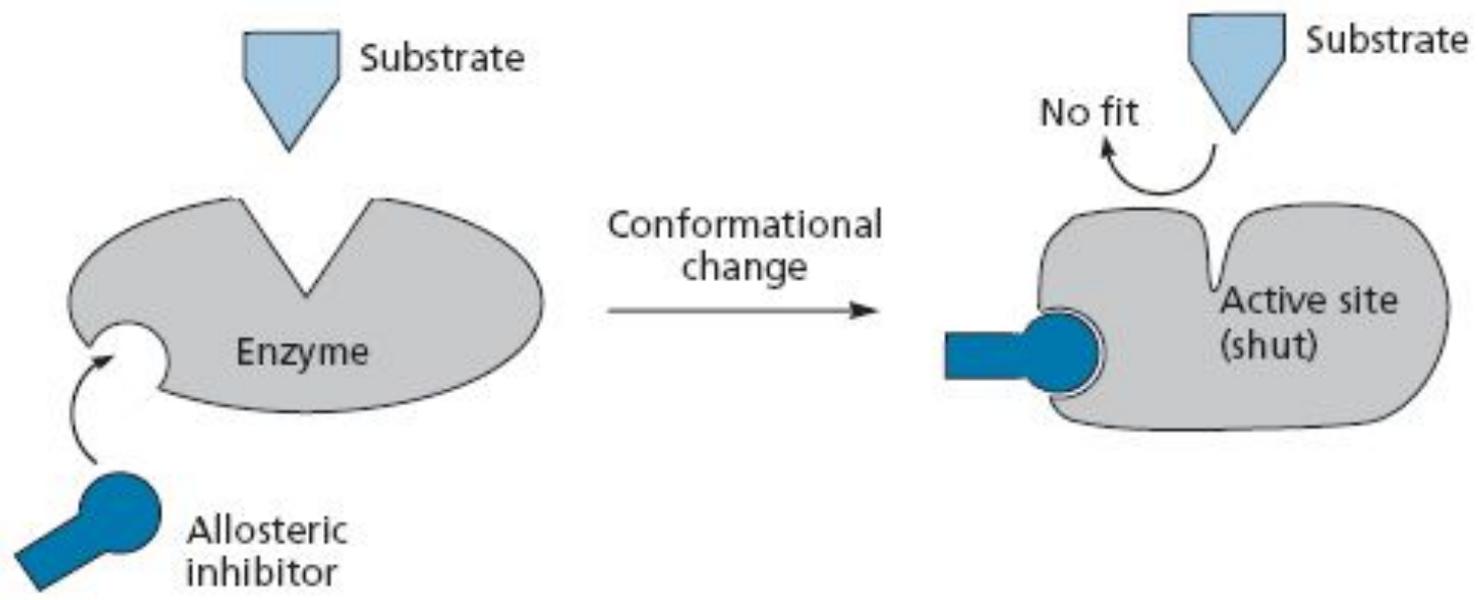


FIGURE 3.1 Reaction catalysed by lactate dehydrogenase.



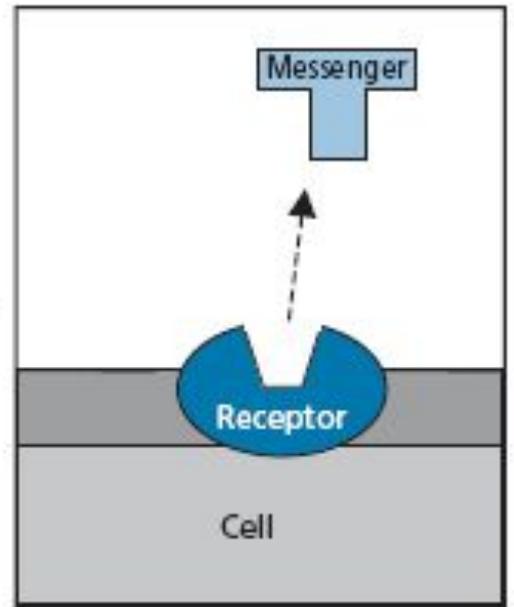
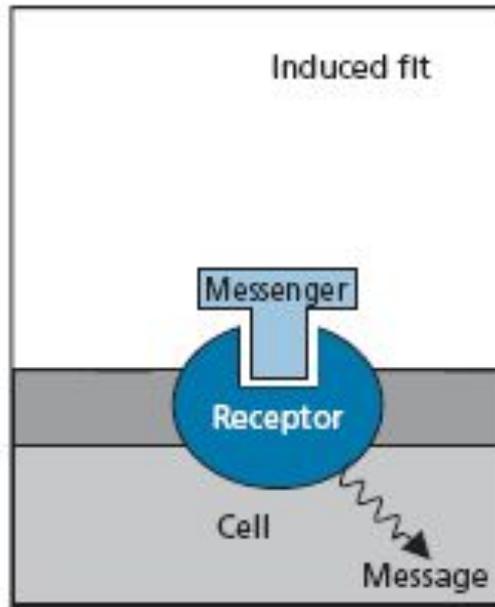
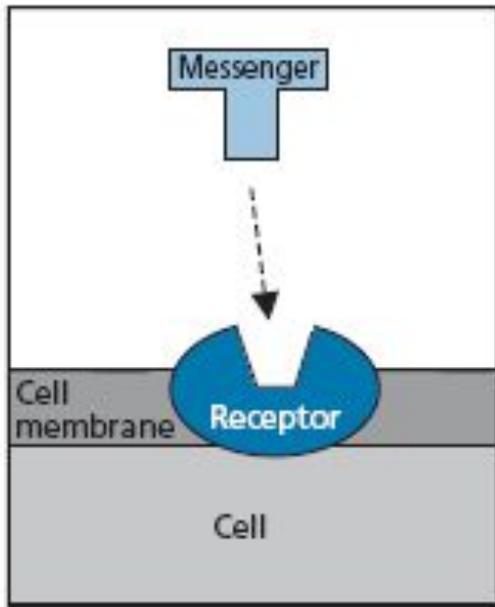


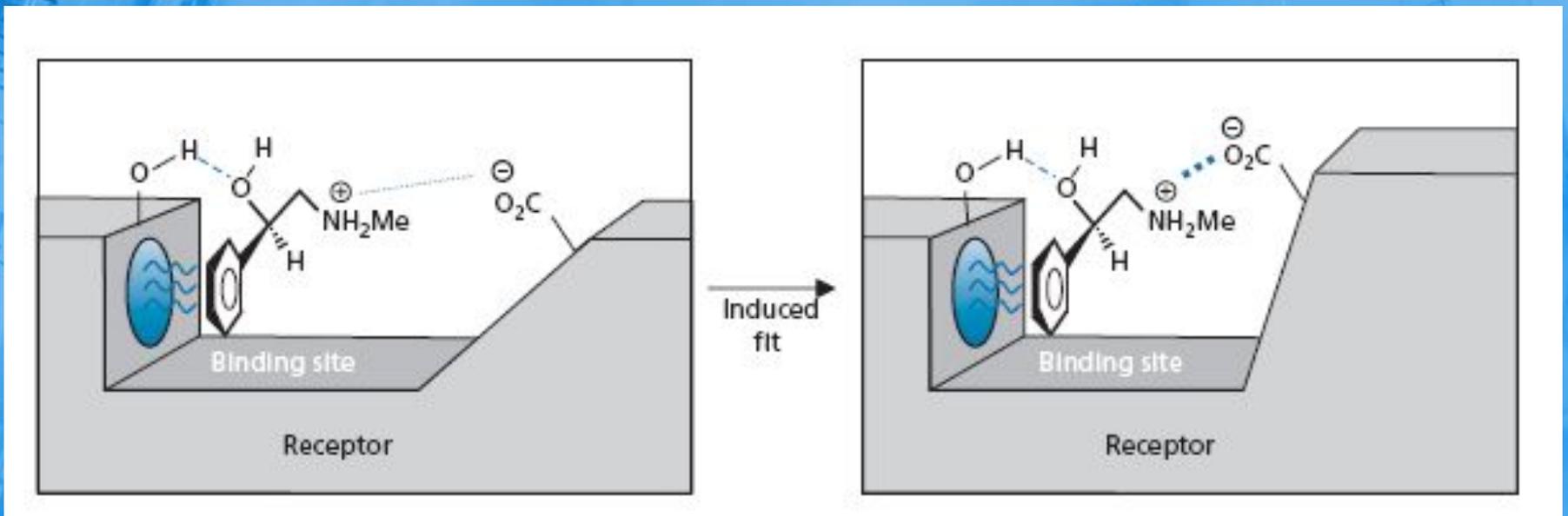
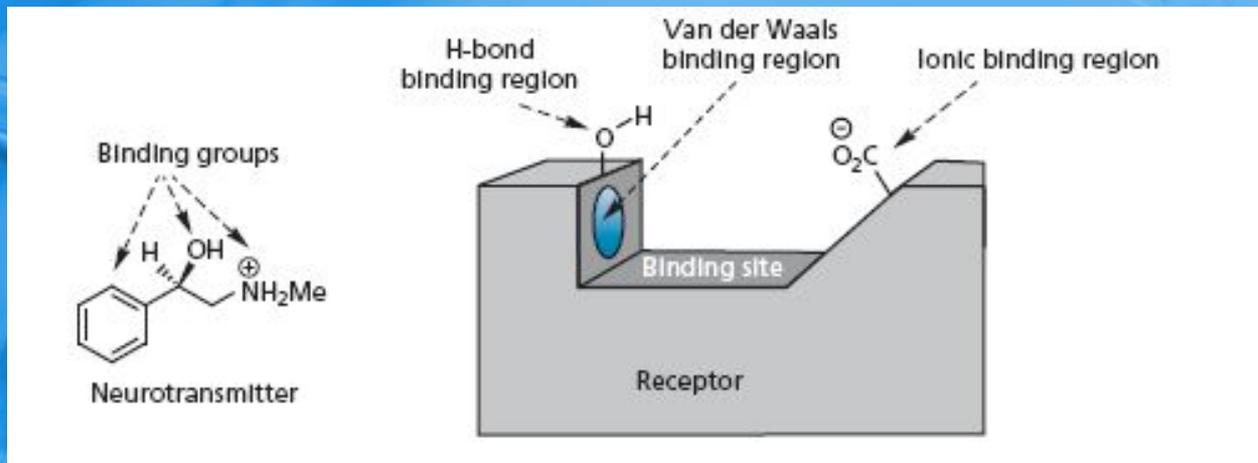


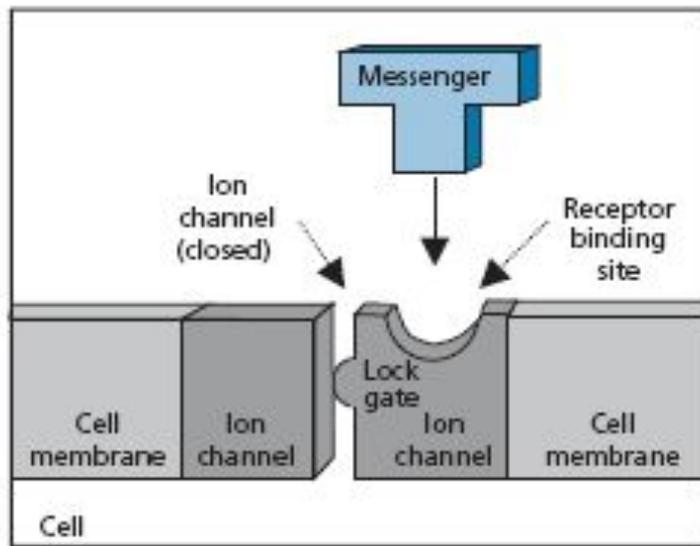


Клеточный рецептор — молекула (обычно белок или гликопротеид) на поверхности клетки, клеточных органелл или растворенная в цитоплазме. Специфично реагирует изменением своей пространственной конфигурации на присоединение к ней молекулы определённого химического вещества, передающего внешний регуляторный сигнал и, в свою очередь, передает этот сигнал внутрь клетки или клеточной органеллы, нередко при помощи так называемых вторичных посредников или трансмембранных ионных токов.

Вещество, специфически соединяющееся с рецептором, называется лигандом этого рецептора. Внутри организма это обычно гормон или нейромедиатор либо их искусственные заменители, применяемые в качестве лекарственных средств и ядов (агонисты). Некоторые лиганды, напротив, блокируют рецепторы (антагонисты).







Induced fit and opening of ion channel

