21 基因的分子生物学

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Outline

21.1 遗传物质是 DNA 的证明

21.2 DNA复制

21.3 遗传信息流是从DNA到RNA到蛋白质

21.4 基因突变

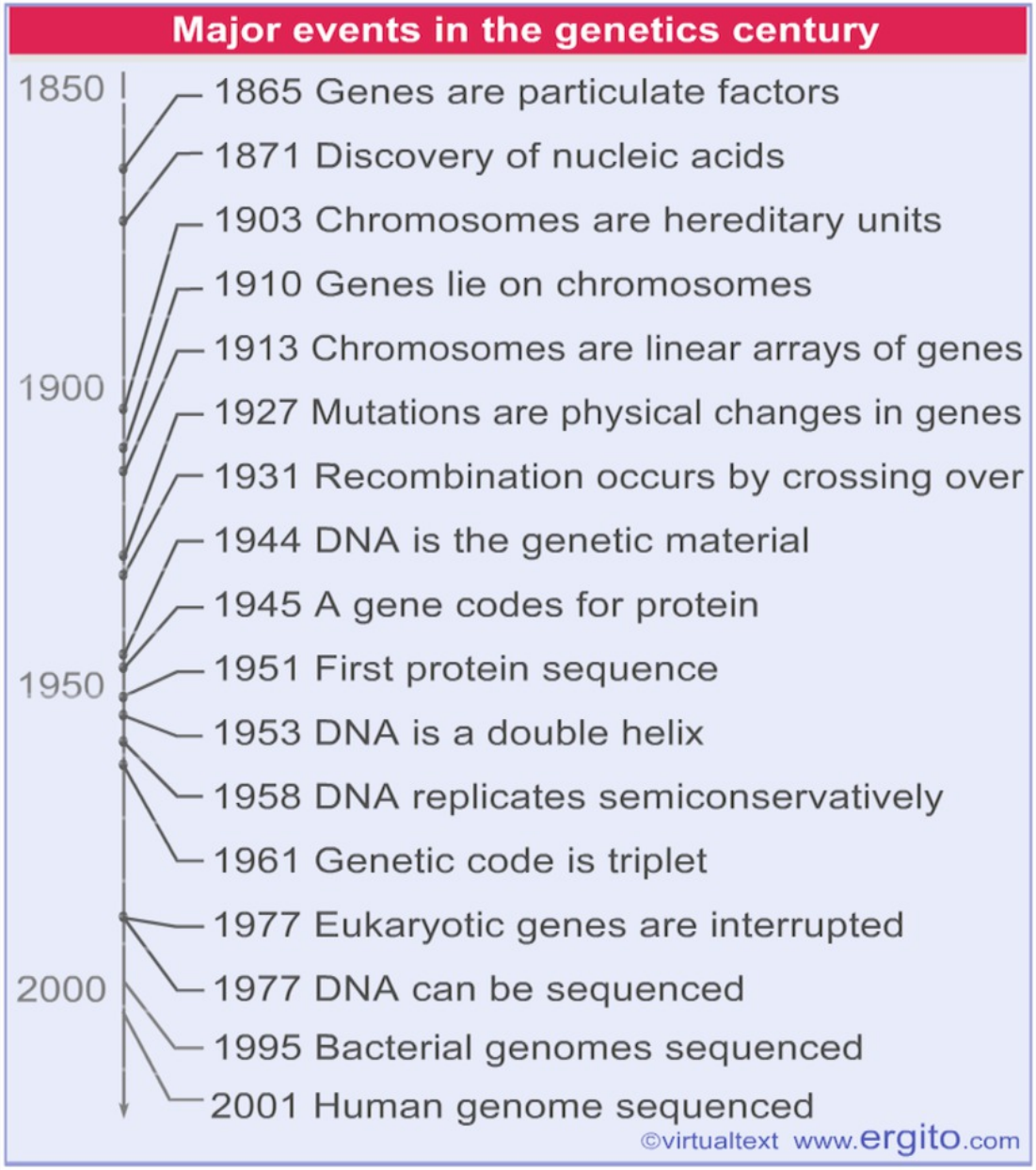
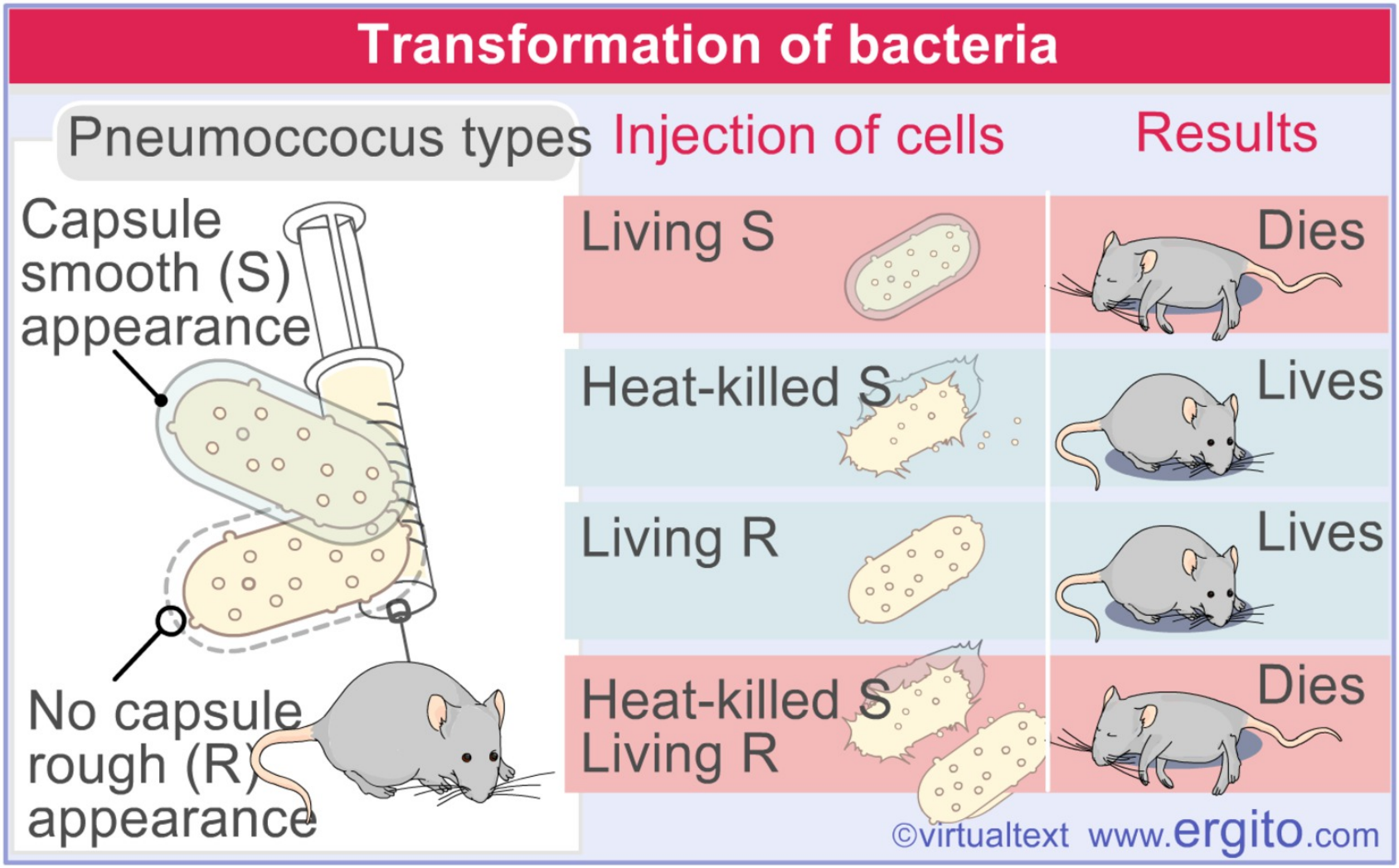


Figure 1. 遗传学世纪的大事件

21.1 遗传物质是 DNA 的证明

21.1.1 肺炎链球菌转化实验



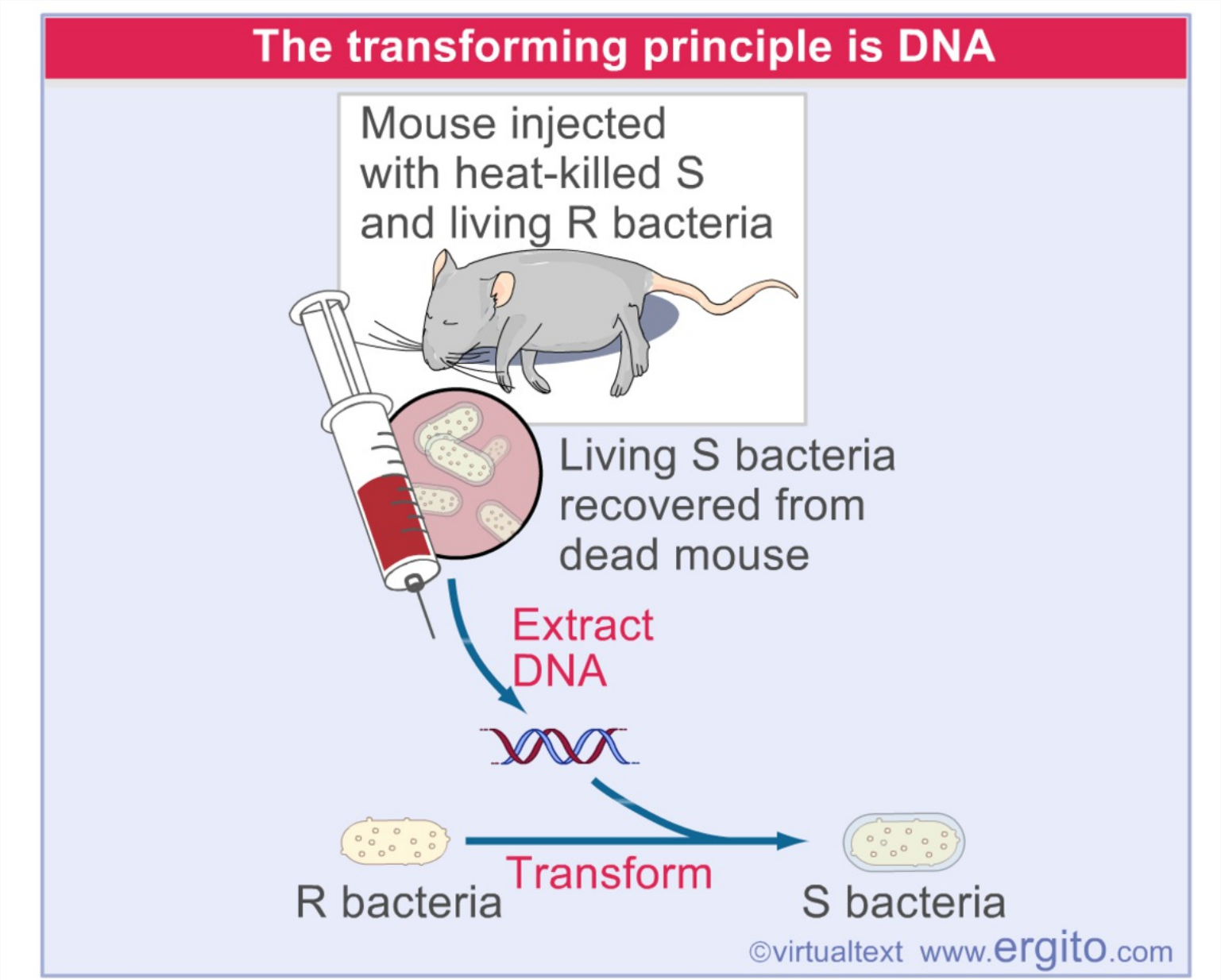


Figure 2. 转化因子是 DNA

21.1.2 T2 噬菌体感染实验

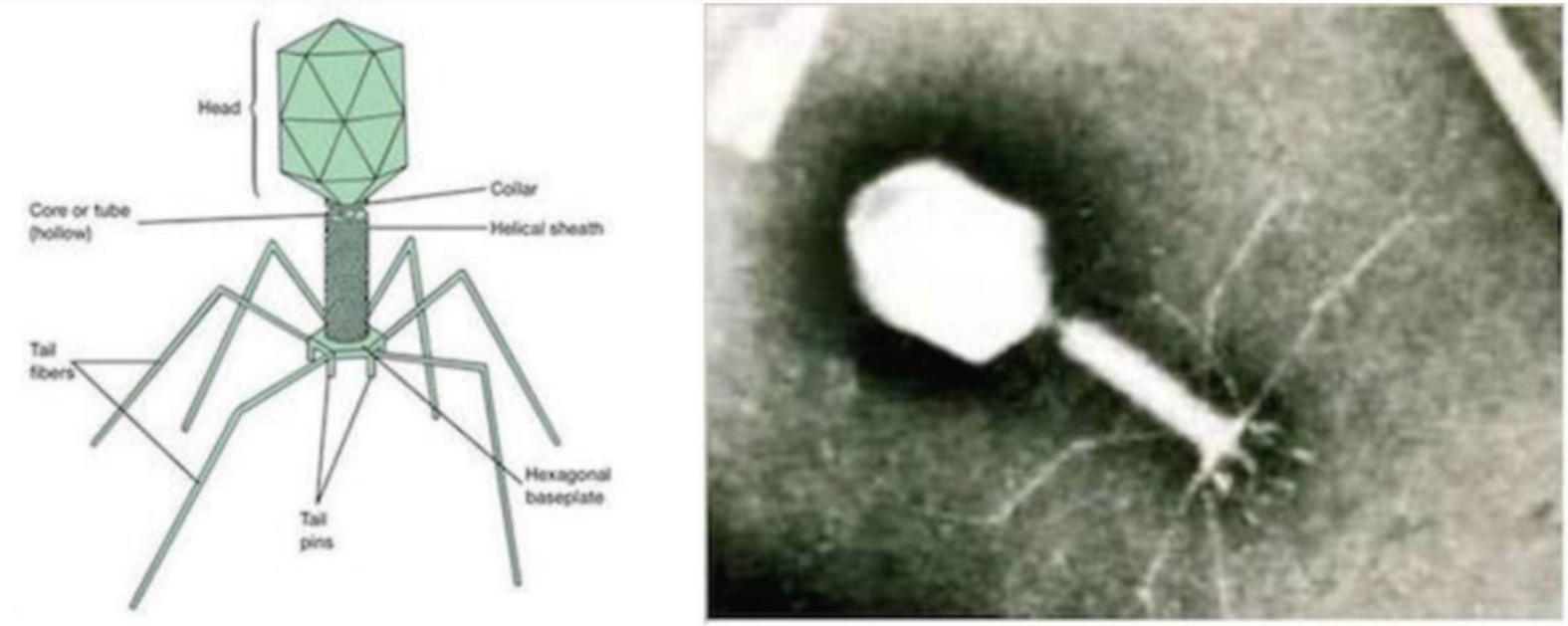


Figure 3. T2 噬菌体. 左: 结构示意图; 右: 透射电镜照片.

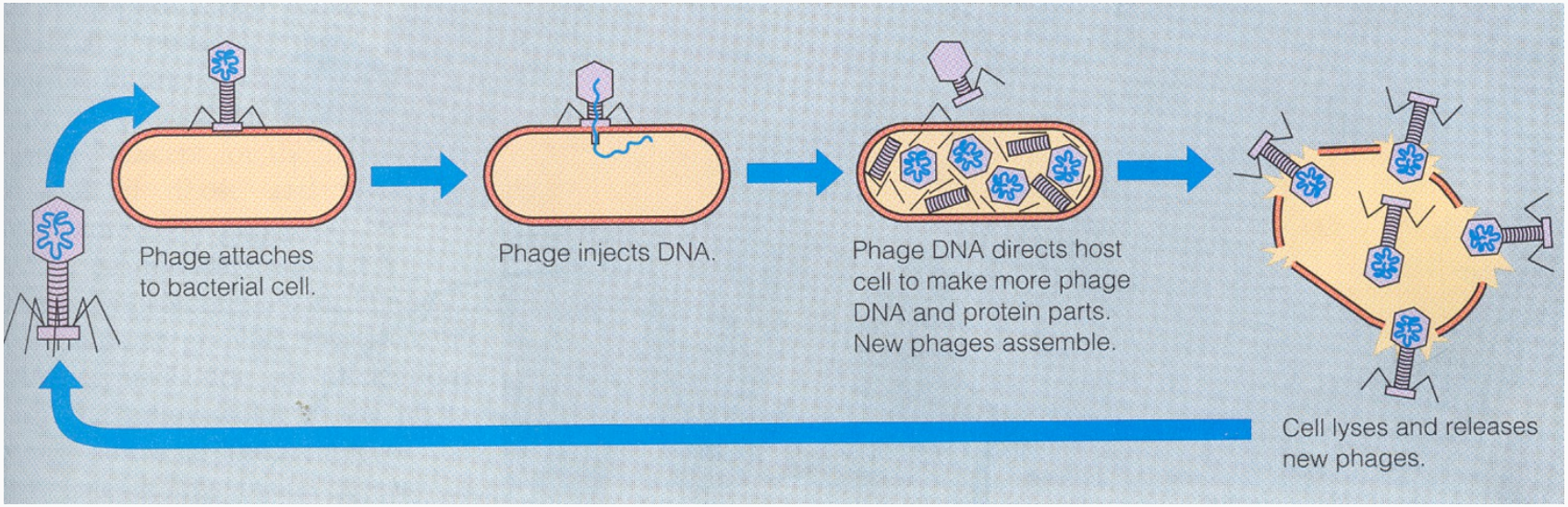


Figure 4. 噬菌体繁殖

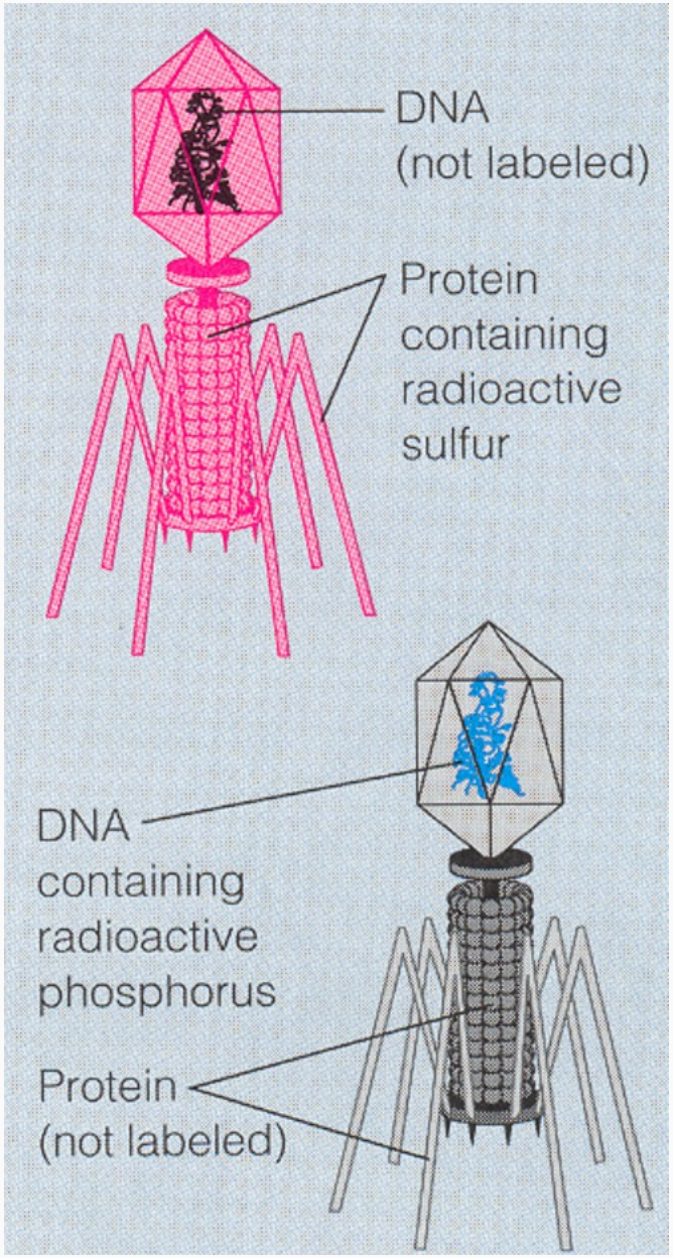


Figure 5. 放射性标记 T2 噬菌体

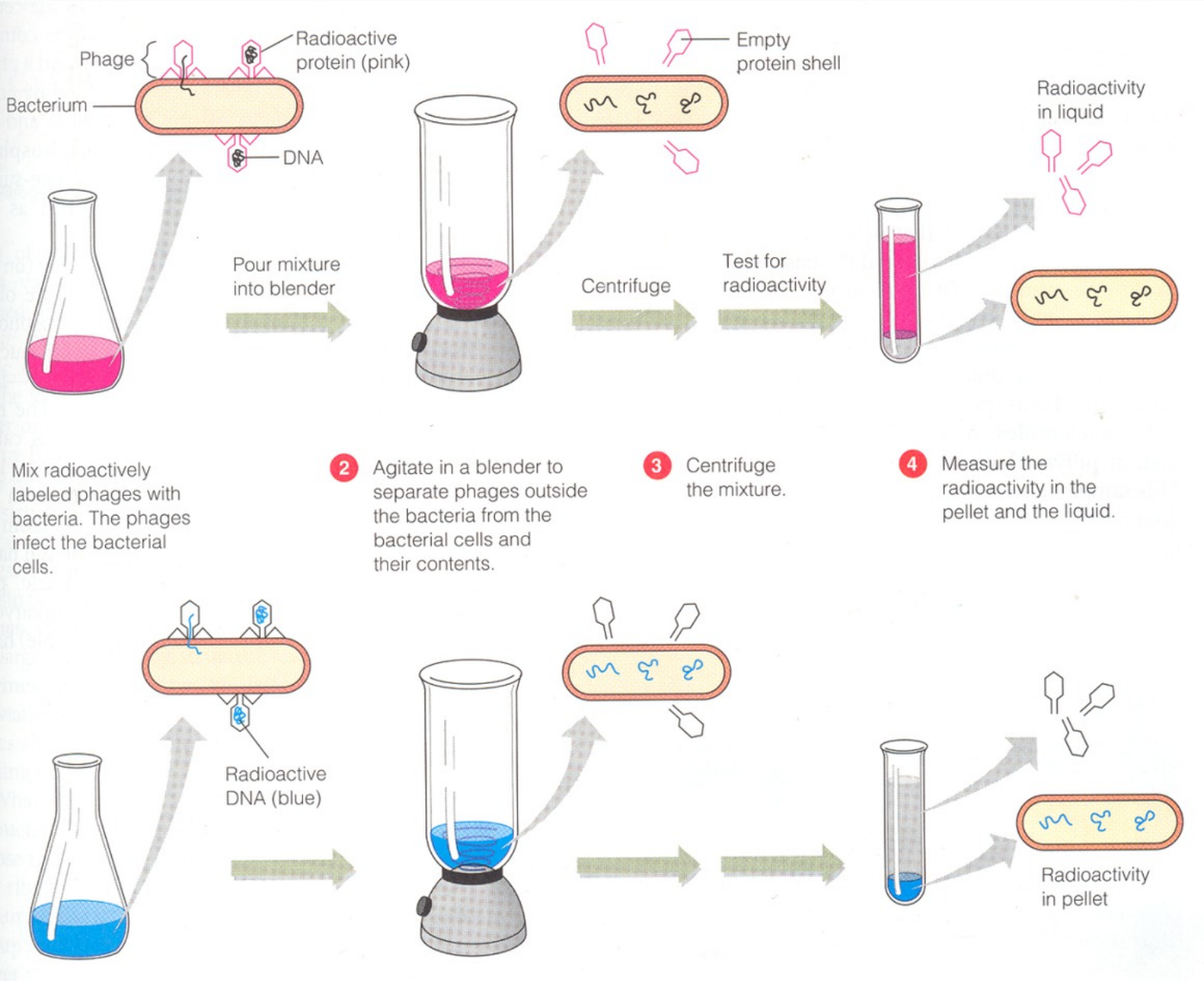


Figure 6. 赫尔希–蔡斯关于 T2 噬菌体的感染实验

21.1.3 DNA 与 RNA 是多核苷酸的聚合体

1. Chargaff 法则
    - [A]=[T] [G]=[C]
2. DNA 与 RNA 是多核苷酸的聚合体
    - 核苷
    - 核苷酸
    - DNA 分子的**一级**结构

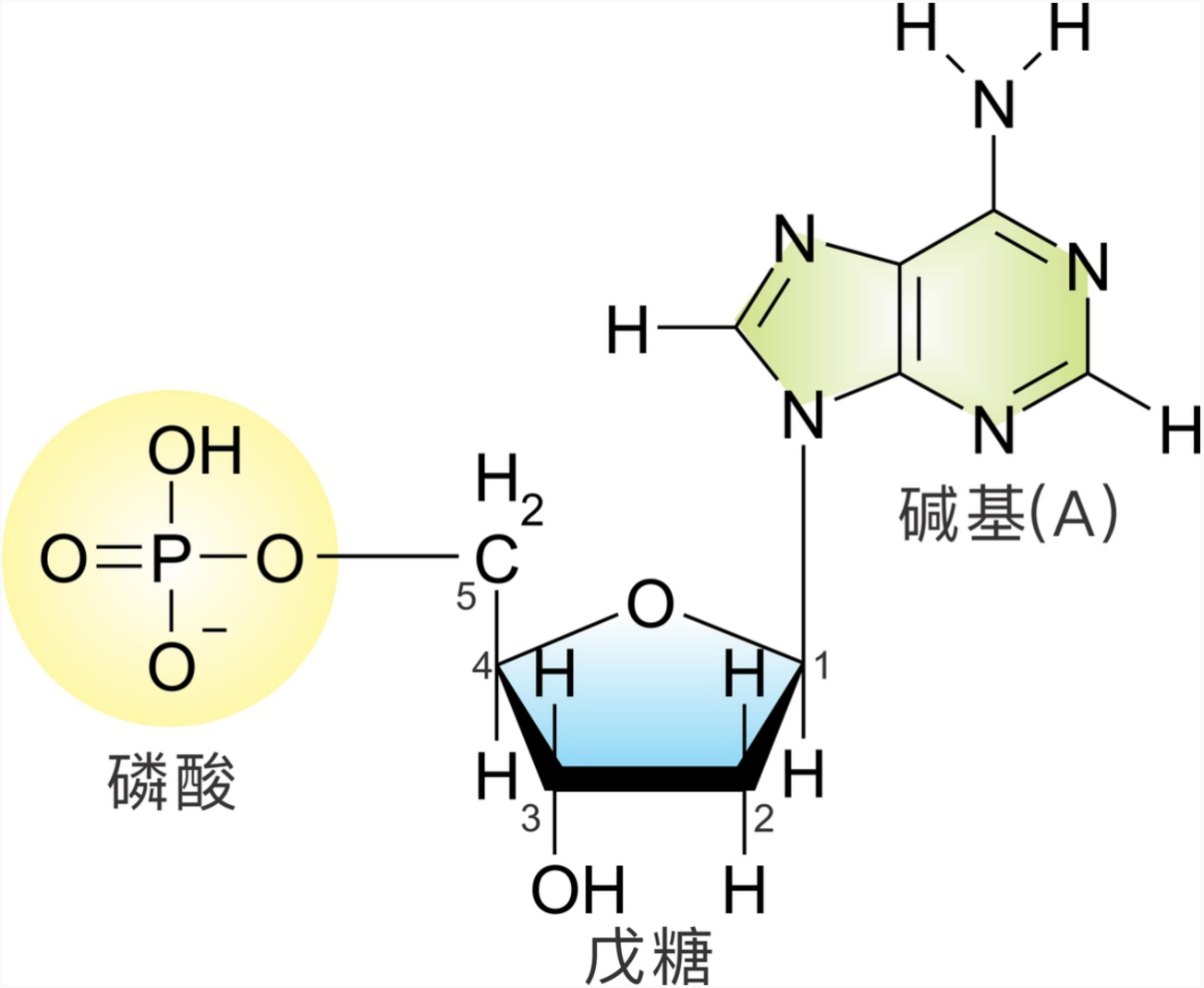


Figure 7. 核苷酸

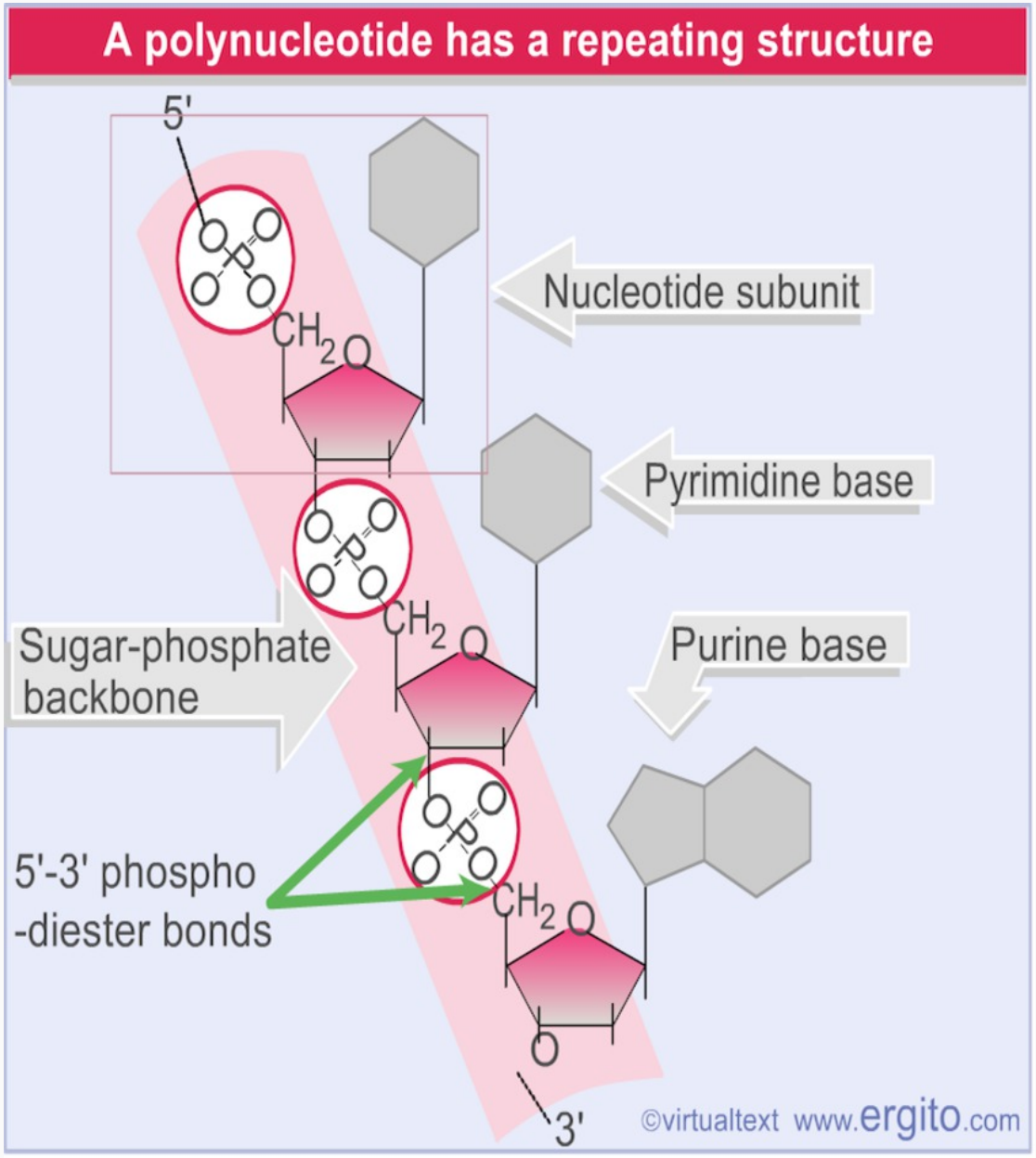


Figure 8. 多核苷酸中的重复结构

21.1.4 DNA — 不朽的双螺旋

- Watson 和 Crick.
- DNA 分子由两条互补核苷酸单链组成; 两条核苷酸链总是按碱基 A 与 T, G 与 C 互补配对, 成反向平行, 通过氢键形成稳定的双螺旋结构.

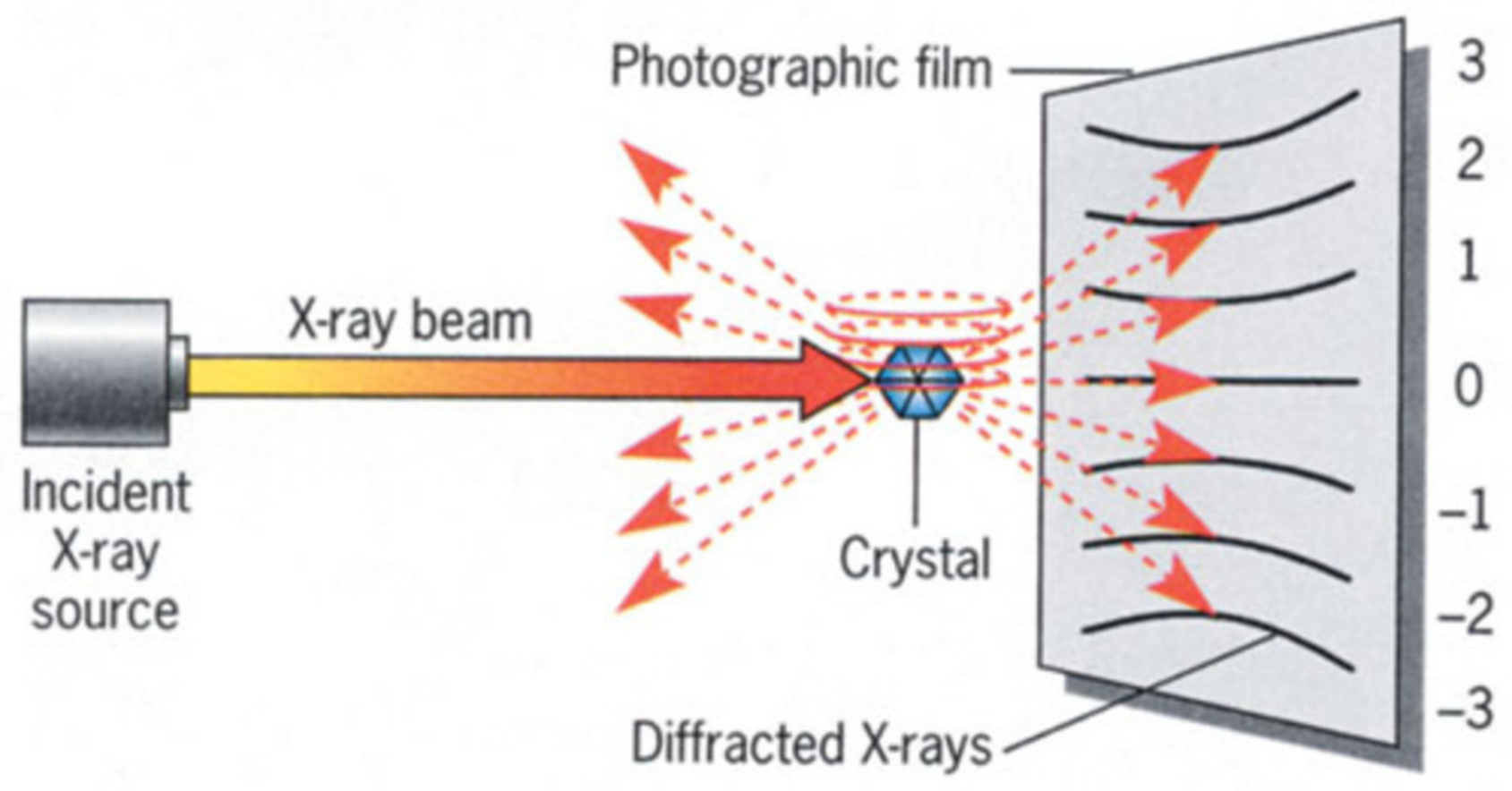


Figure 9. X-射线衍射实验

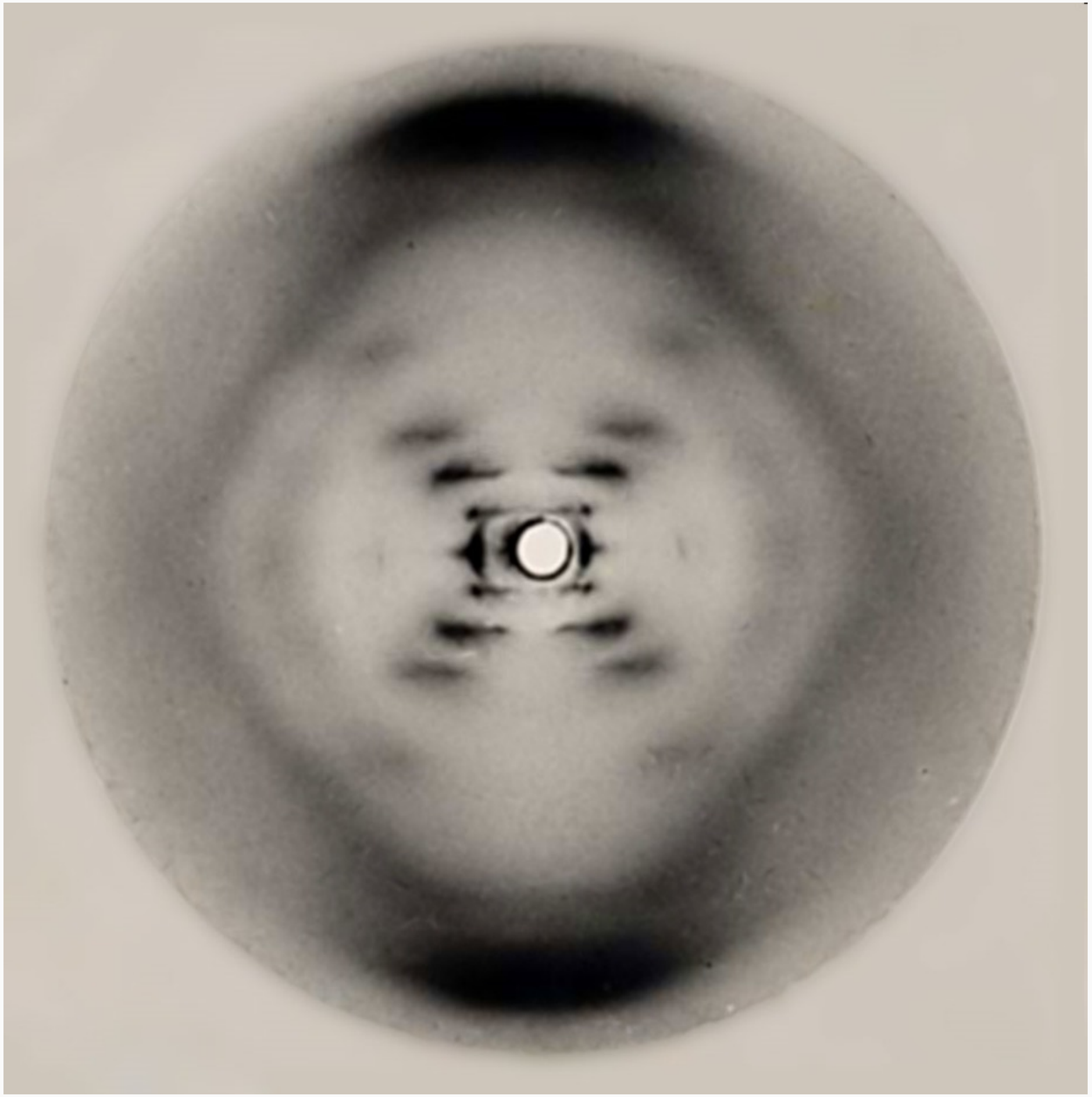


Figure 10. DNA 晶体的 X-射线衍射照片

(a) Rosalind Franklin

(b) Maurice Wilkins

Figure 11. 研究 DNA 晶体的科学家

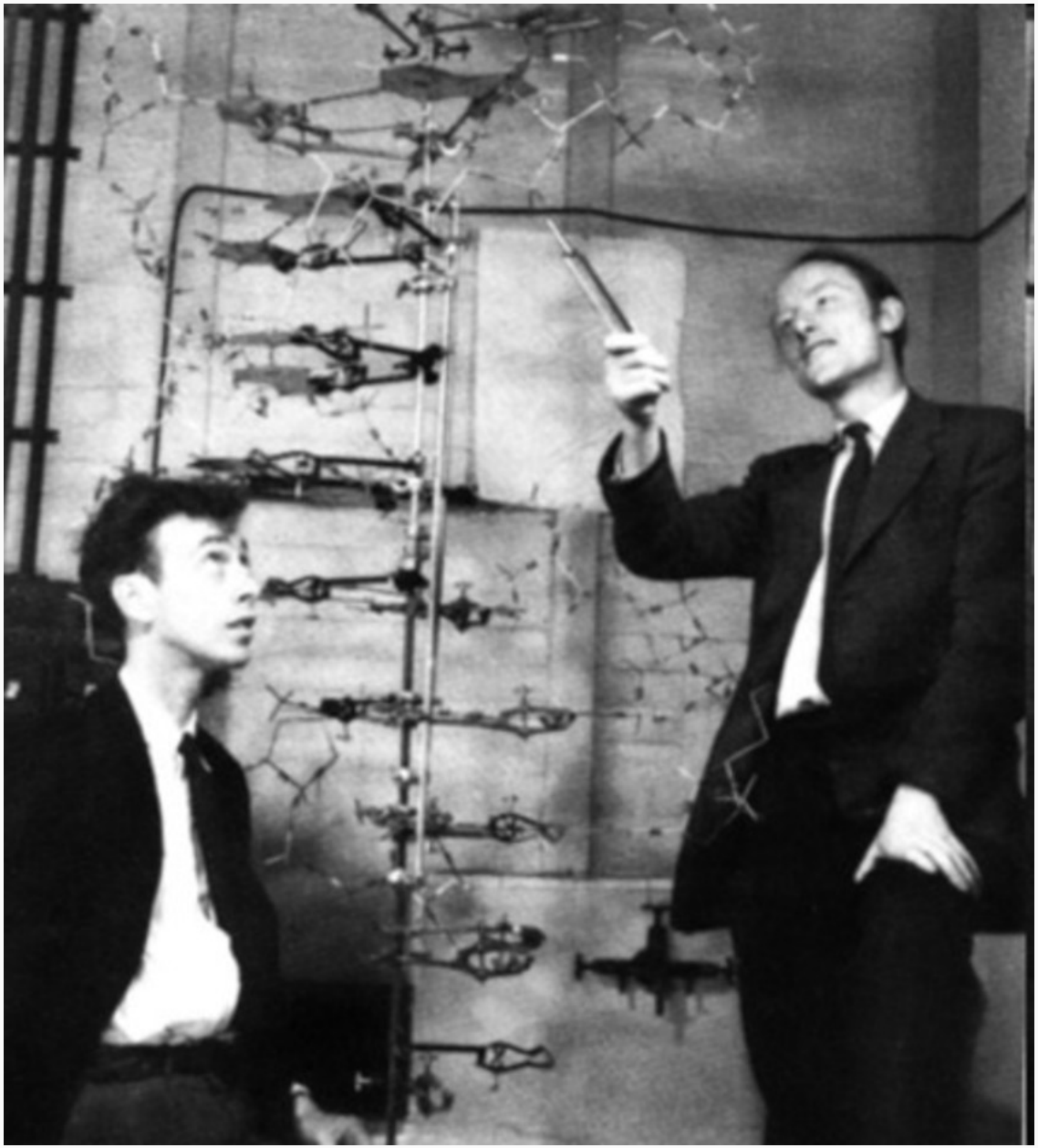


Figure 12. Watson 和 Crick

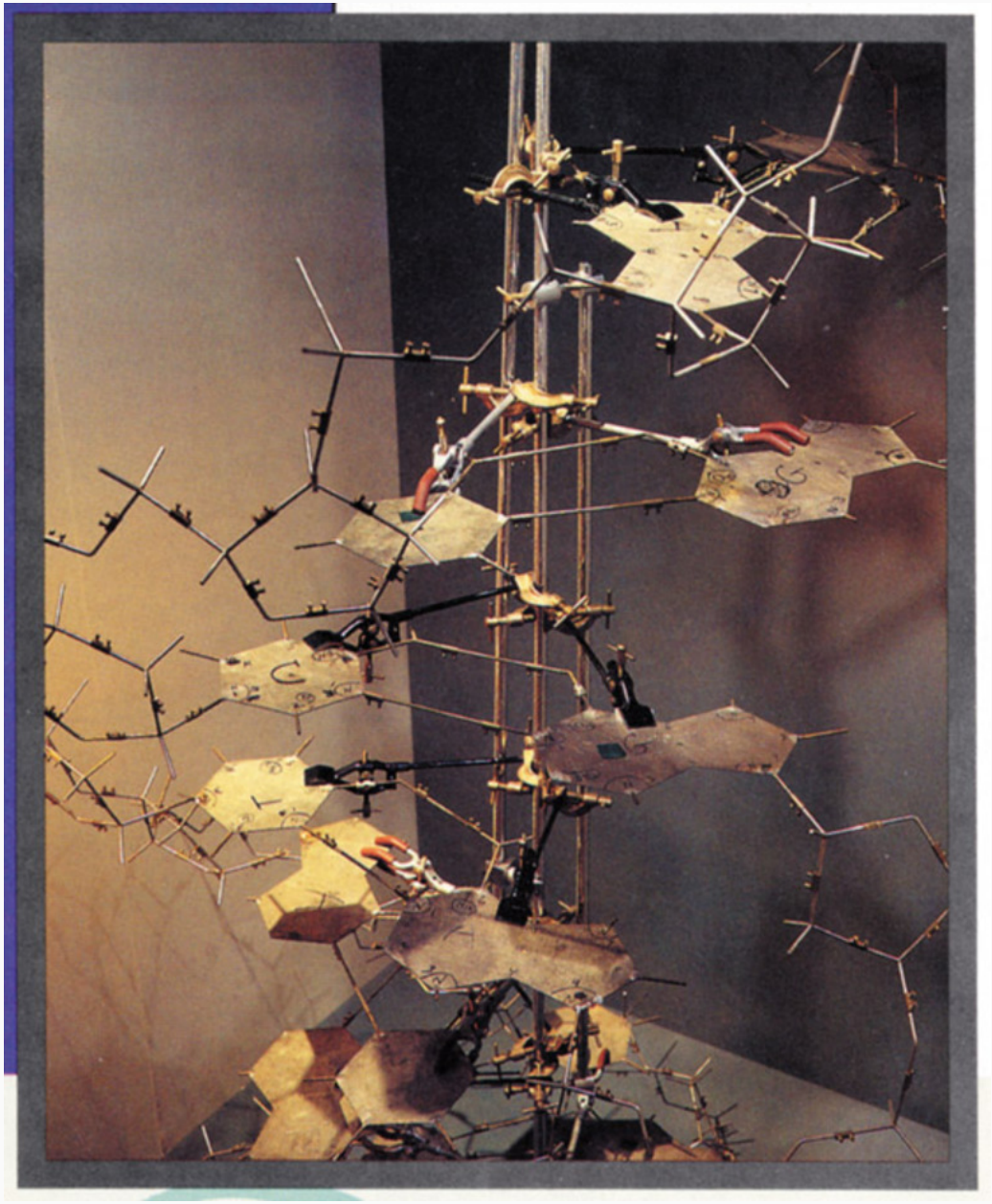


Figure 13. Model of DNA built by James Watson and Francis Crick at Cambridge University

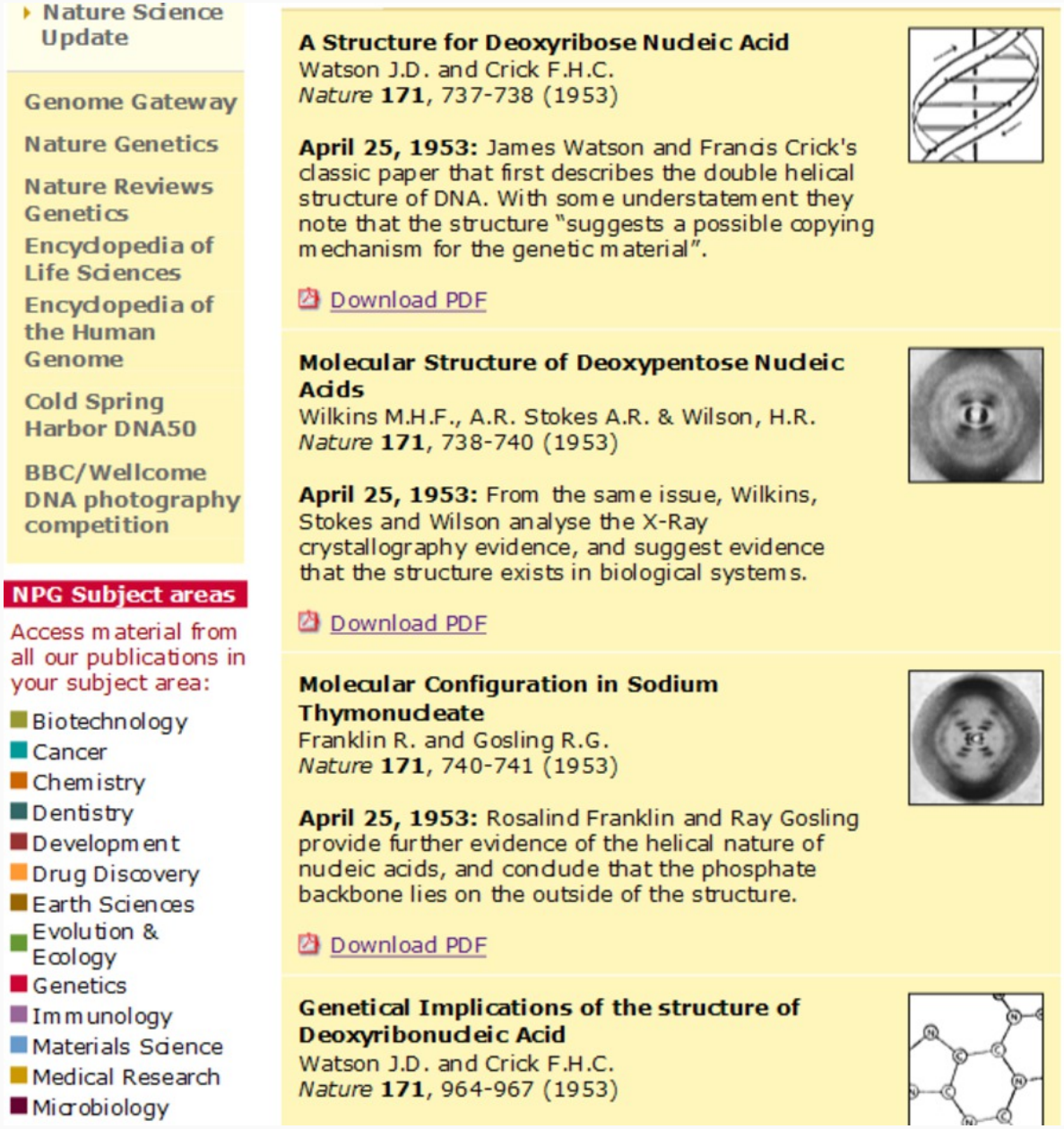


Figure 14. http://www.nature.com/nature/dna50/archive.html

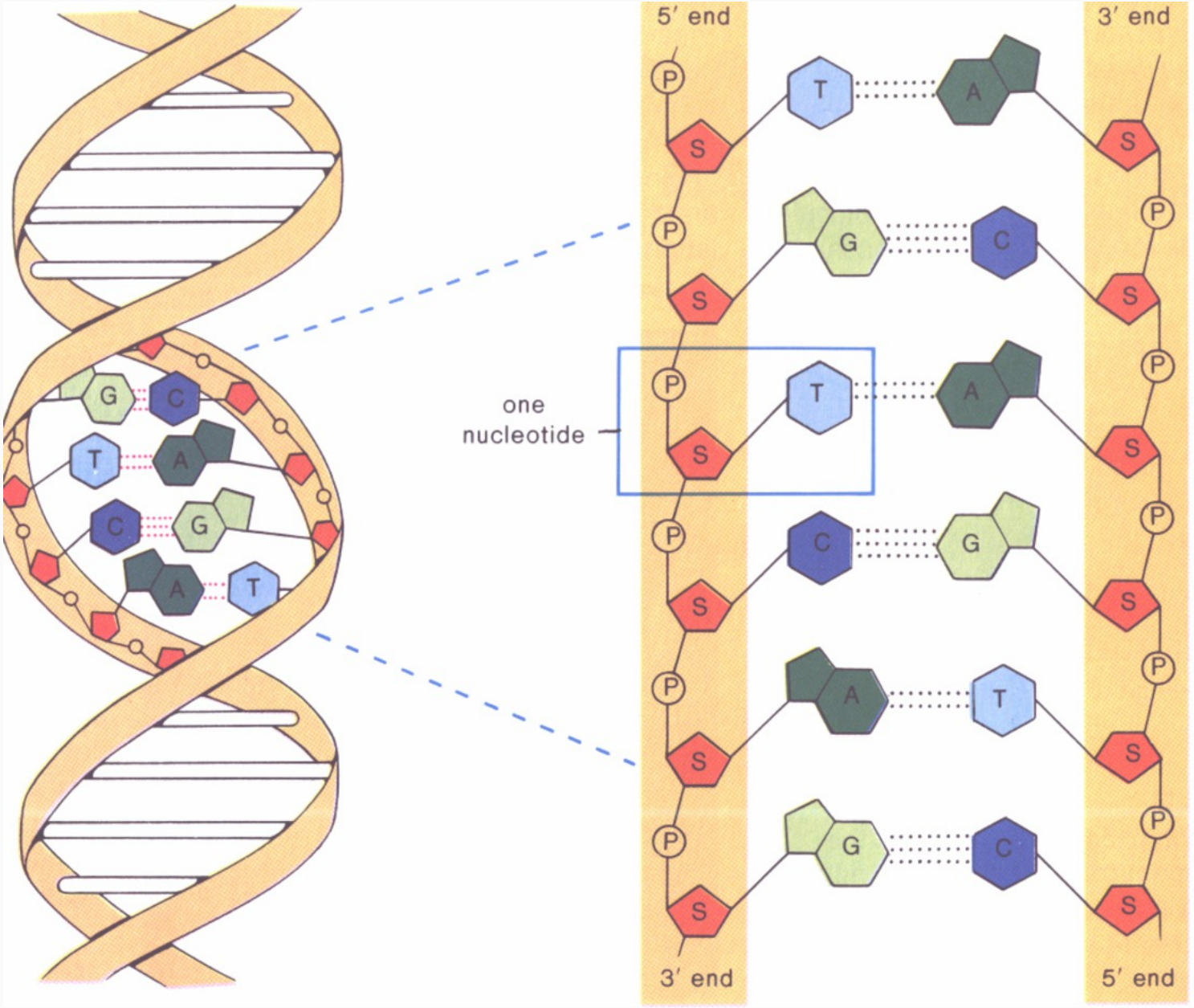


Figure 15. DNA 双螺旋结构

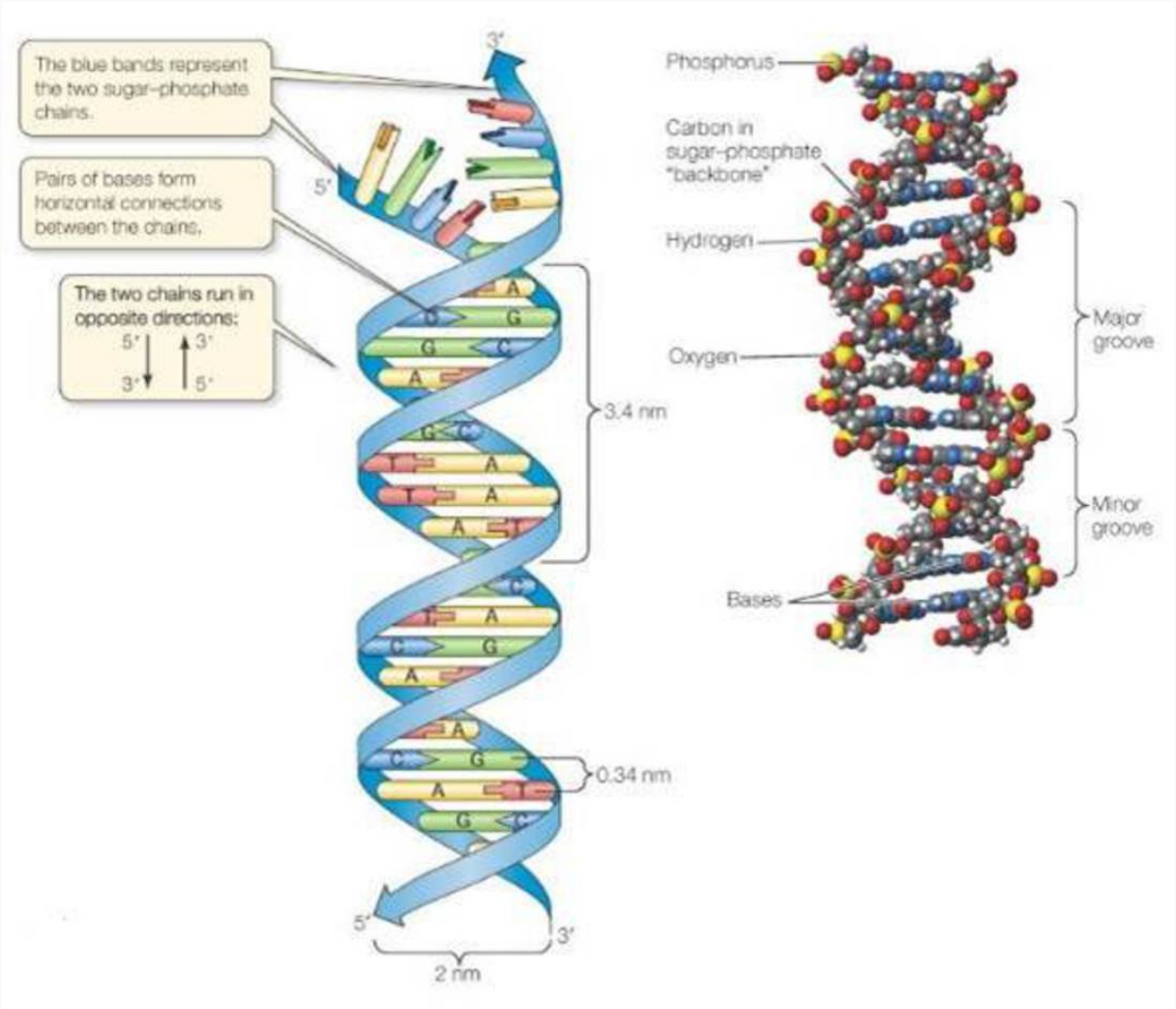


Figure 16. DNA 双螺旋结构

21.2 DNA复制

21.2.1 DNA复制依赖于碱基配对

A 与 T, G 与 C 配对.

21.2.2 DNA复制是半保留式的

DNA 复制形成的两个 DNA 分子, 每个都由一条新链和一条旧链组成.

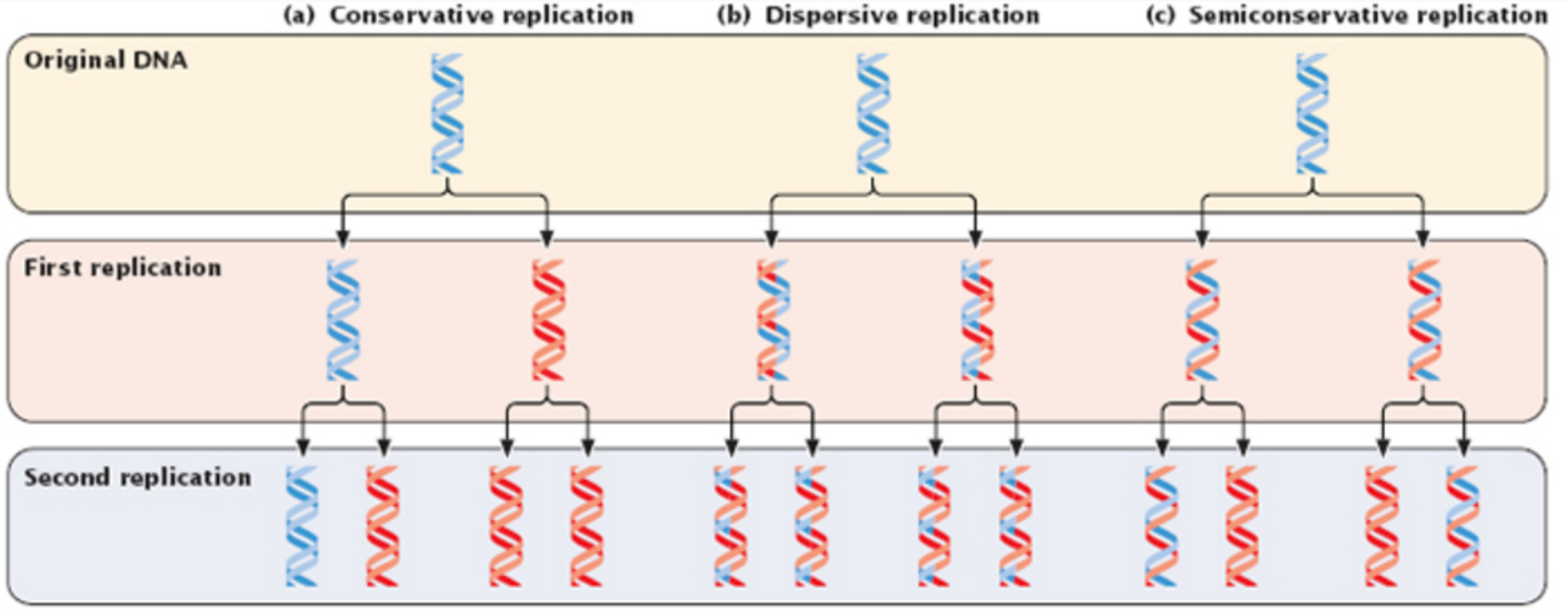


Figure 17. Three alternate schemes of replication

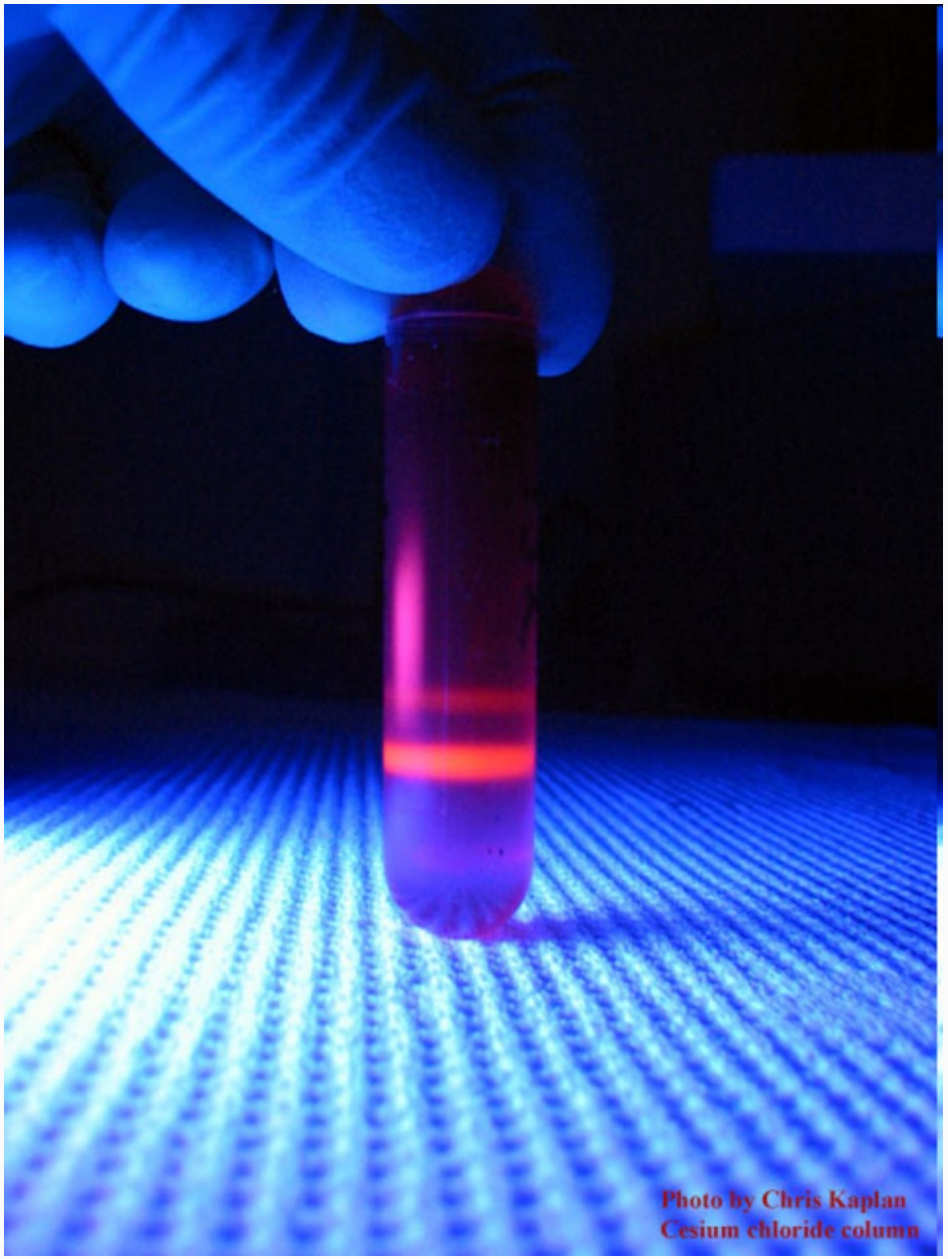


Figure 18. DNA 密度梯度离心 (CsCl, 氯化铯)

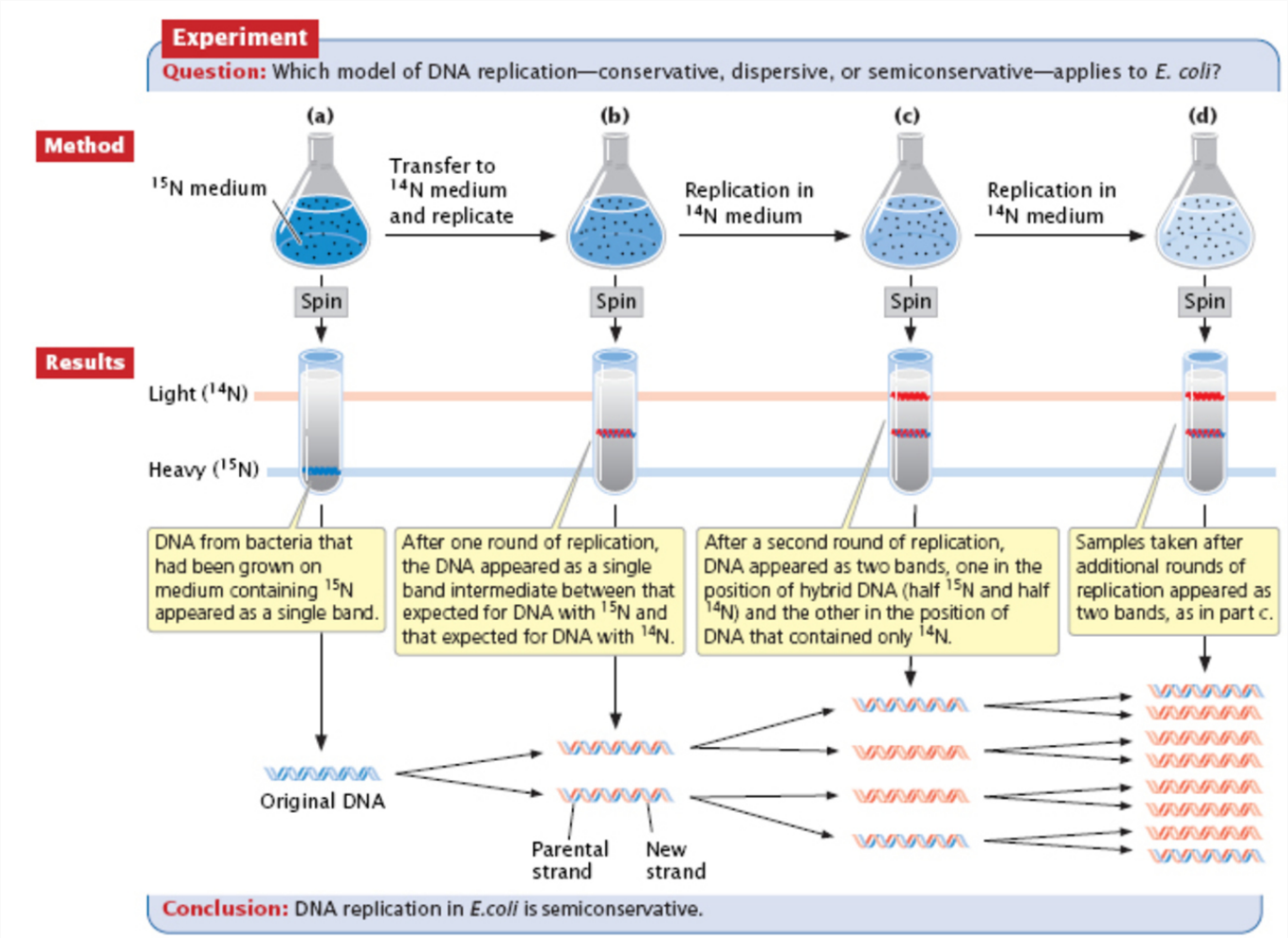


Figure 19. 大肠杆菌中的 DNA 复制[1]

[1] Meselson, M. & Stahl, F. W. The Replication of DNA in Escherichia Coli. *Proceedings of the National Academy of Sciences* **44,** 671–682 (1958)

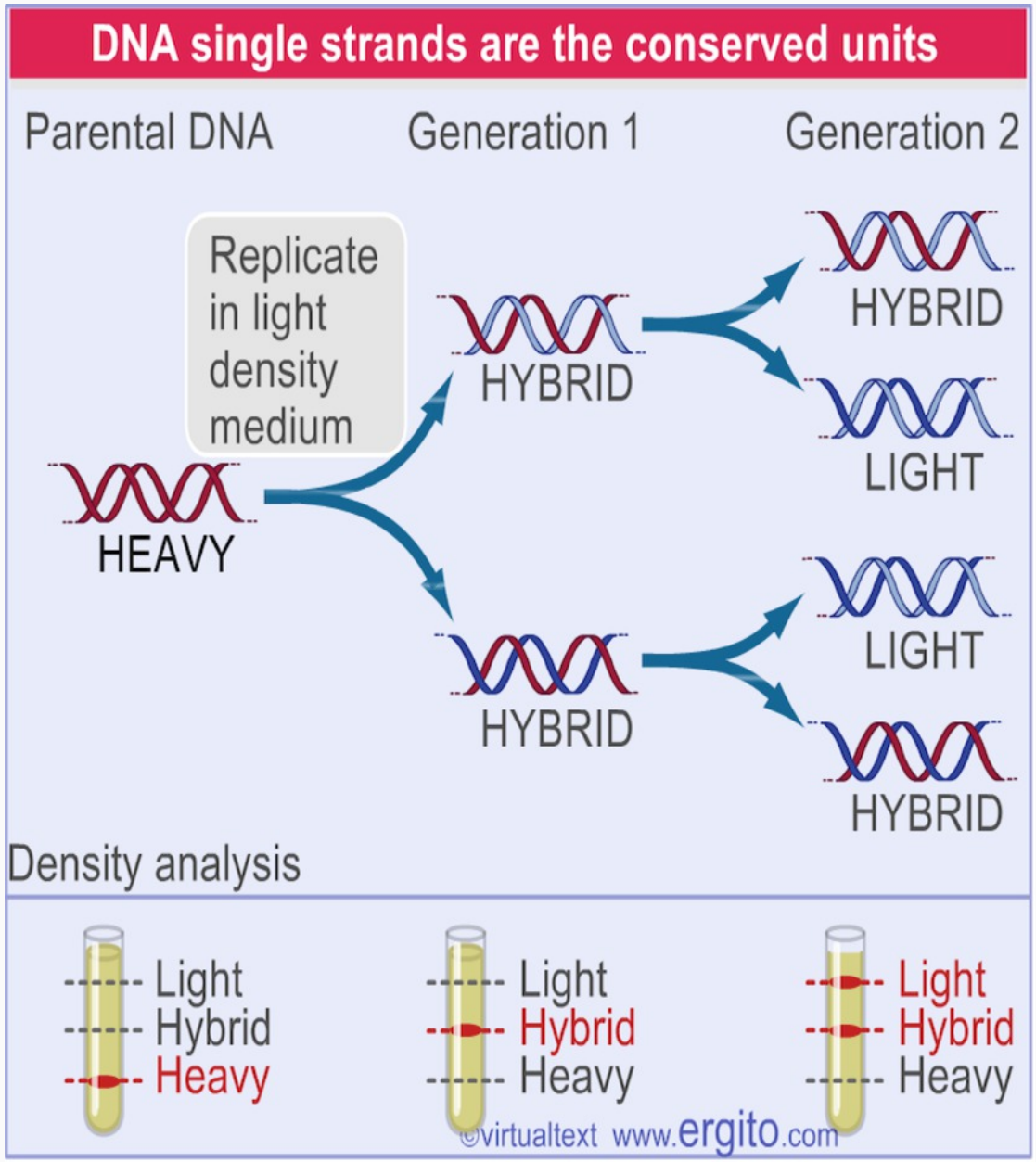


Figure 20. DNA 单链是保留的单元

Figure 21. DNA 半保留复制

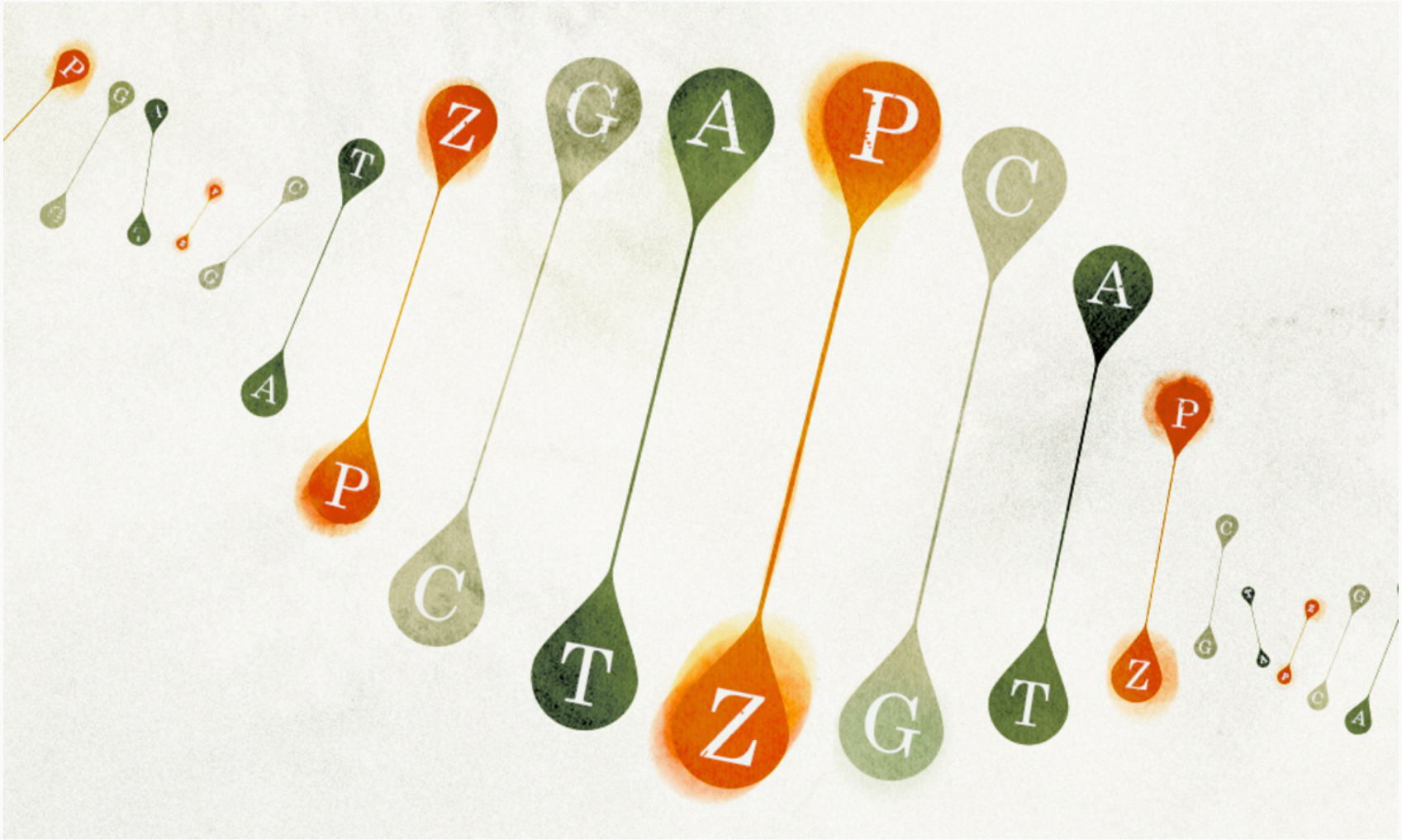


Figure 22. 合成的核苷酸 P 和 Z

21.2.3 复制的半不连续性

- DNA 聚合酶**只能**使核苷酸按 $5' \to 3'$ 方向连接成链
- 而 DNA 的两条链的方向相反, 这相反的一条链, DNA 聚合酶是通过冈崎片段来合成它的互补链的.

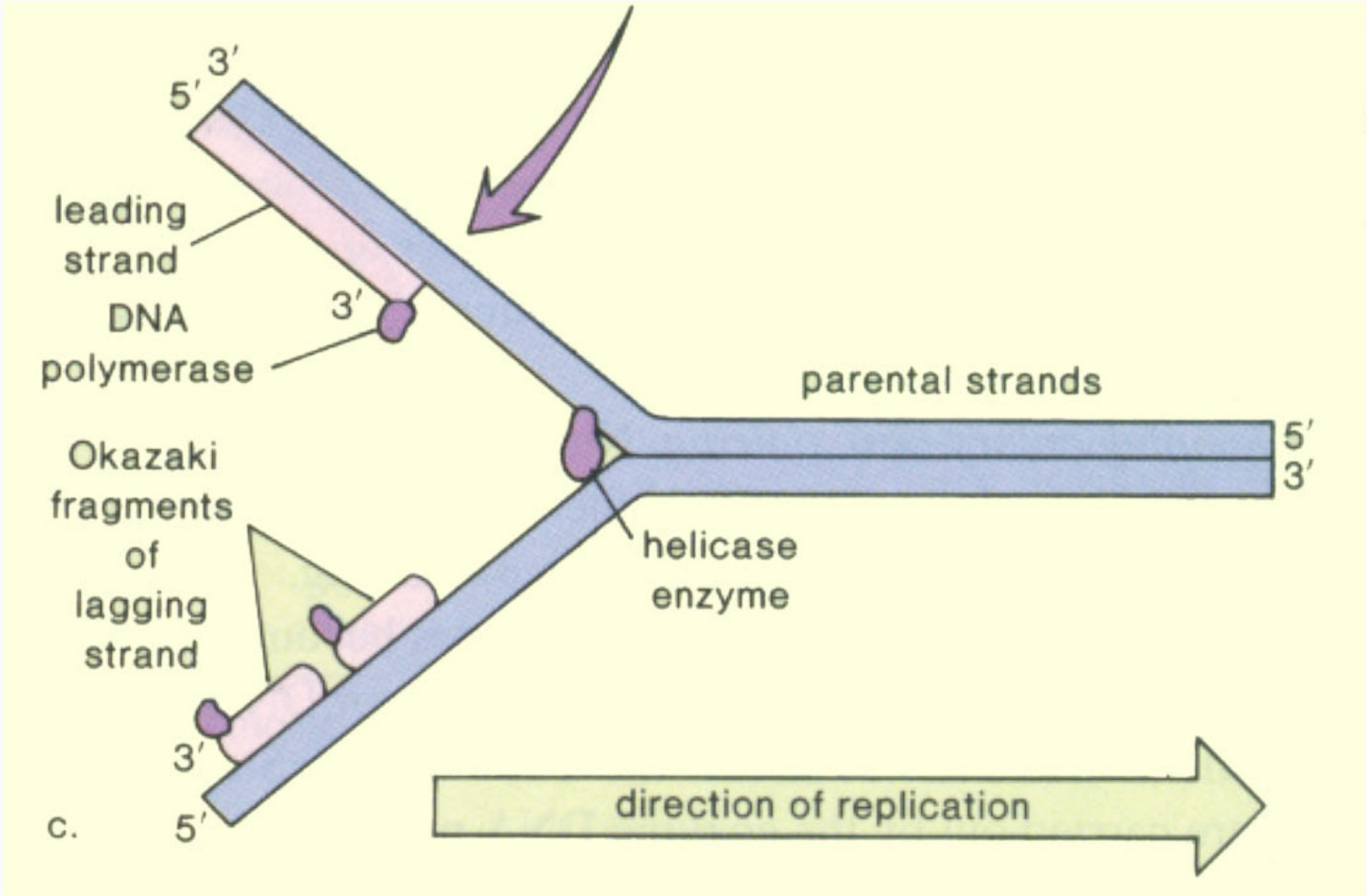


Figure 23. 复制叉

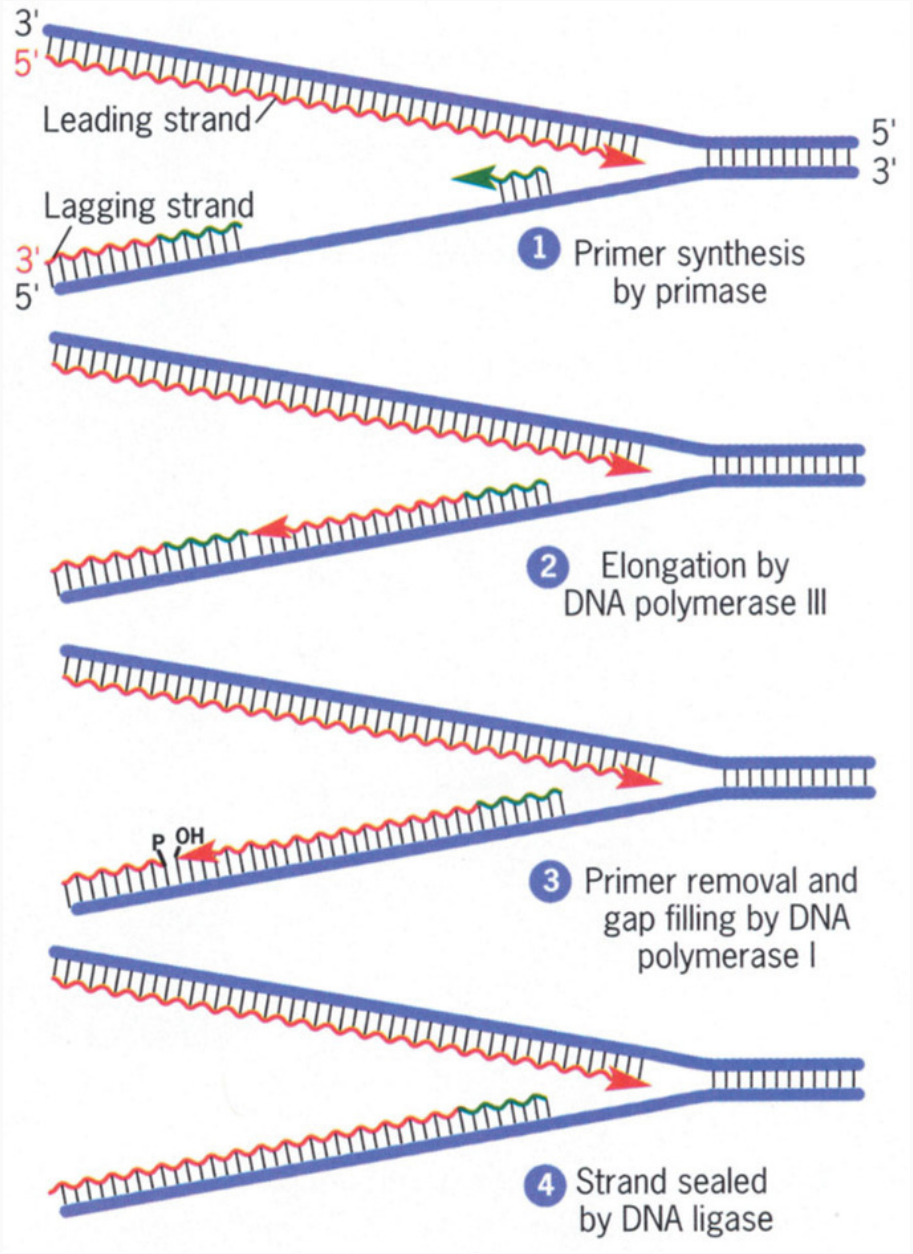


Figure 24. RNA 引物的去除

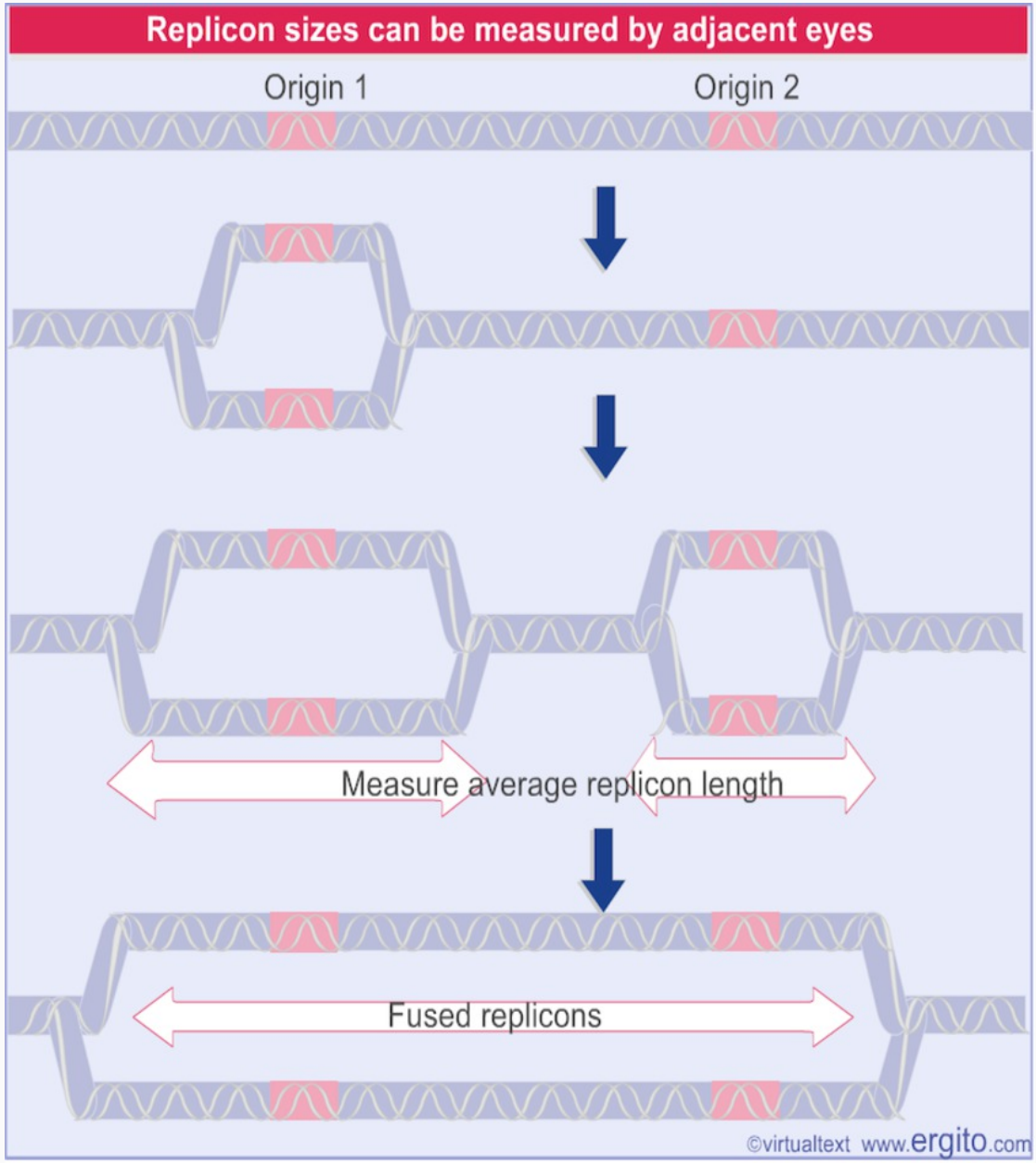


Figure 25. 真核生物的复制起始位点

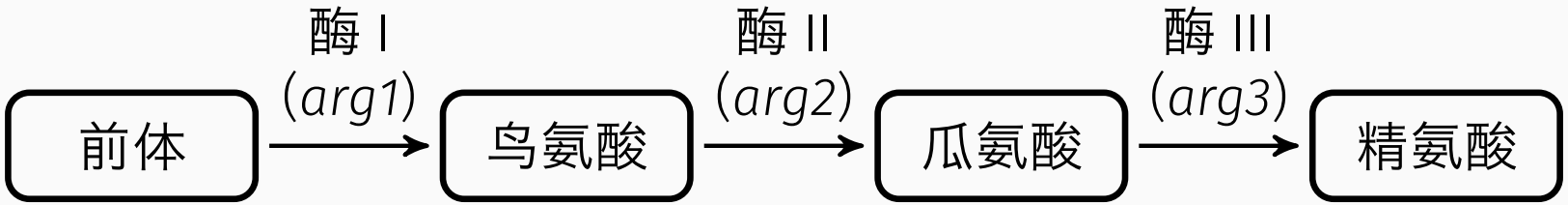
21.3 遗传信息流是从DNA到RNA到蛋白质

21.3.1 蛋白质是表型特征的分子基础

- 1909年, A. Garrod 尿黑酸症
  - 黑色尿(性状) — 酶 — 基因
- 1940年代, George Beadle 和 Edward Taturm
  - 一个基因一个酶
  - 一个基因一条多肽

Table 1. 粗糙脉孢菌 3 种精氨酸依赖型

突变型	生长所需氨基酸
1	精氨酸或瓜氨酸或鸟氨酸
2	精氨酸或瓜氨酸
3	精氨酸



21.3.2 DNA 与蛋白质的合成

1. RNA 的结构与功能
   - 与 DNA 相比较, 其结构特点:
     - 单链
     - 戊糖是核糖
     - 尿嘧啶代替胸腺嘧啶
   - 功能
     - 信使 RNA (mRNA)
     - 核糖体 RNA (rRNA)
     - 转运 RNA (tRNA)
     - ...

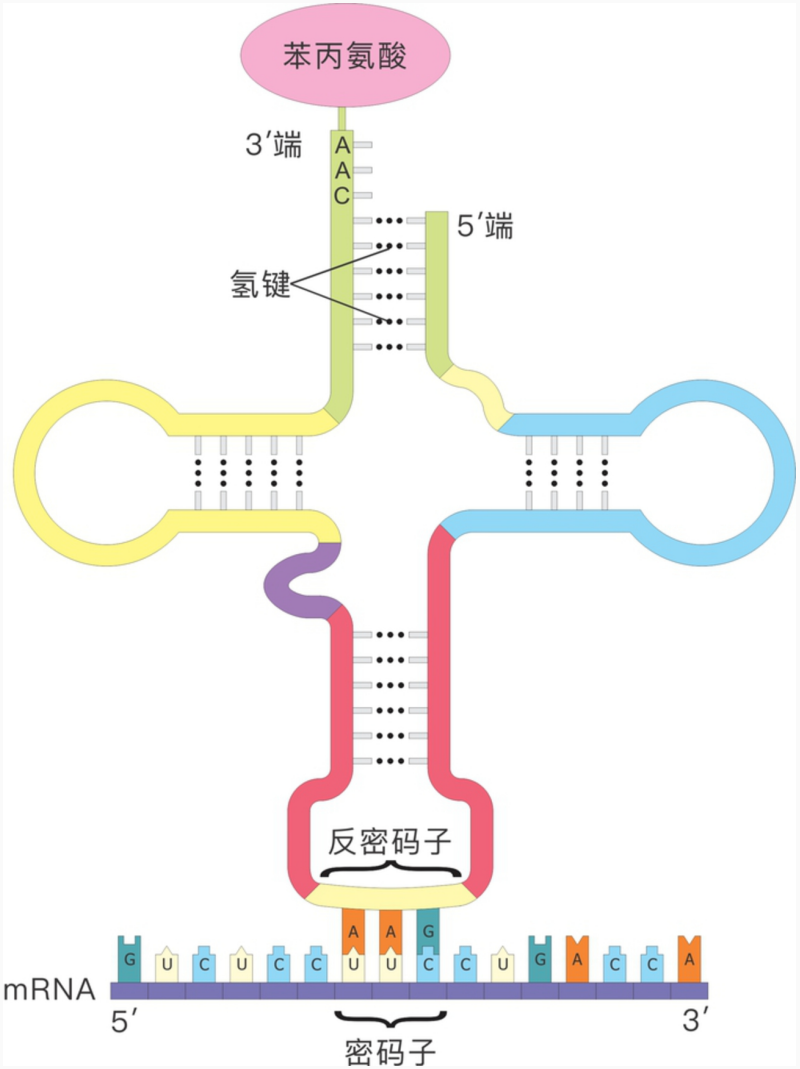


Figure 26. tRNA 结构

2. 转录 — 从 DNA 到 RNA

- 以 DNA 为模板, 通过 RNA 聚合酶使碱基互补配对合成 RNA 的过程.
- 过程: 转录启始, 延伸和终止.

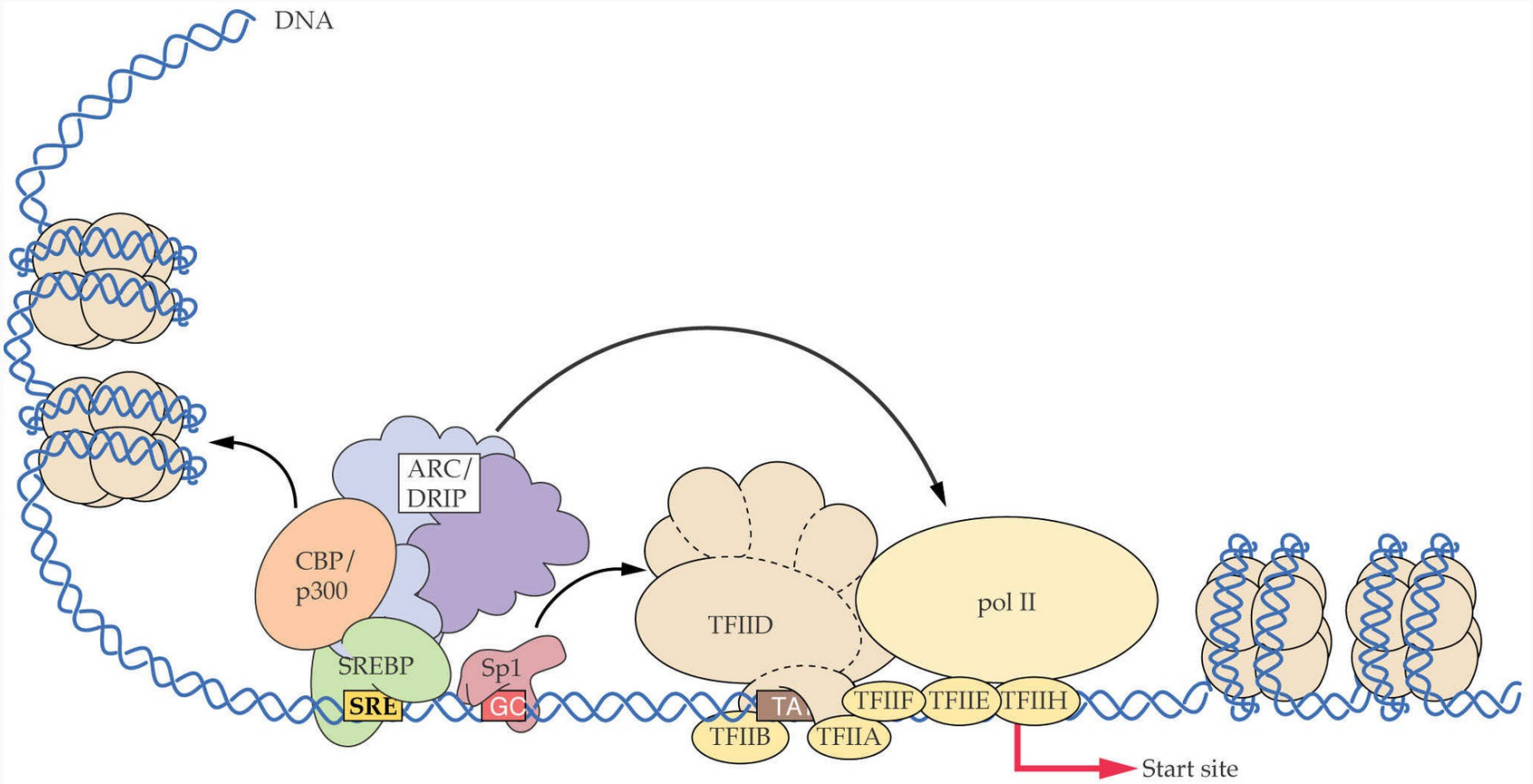


Figure 27. 基因转录起始

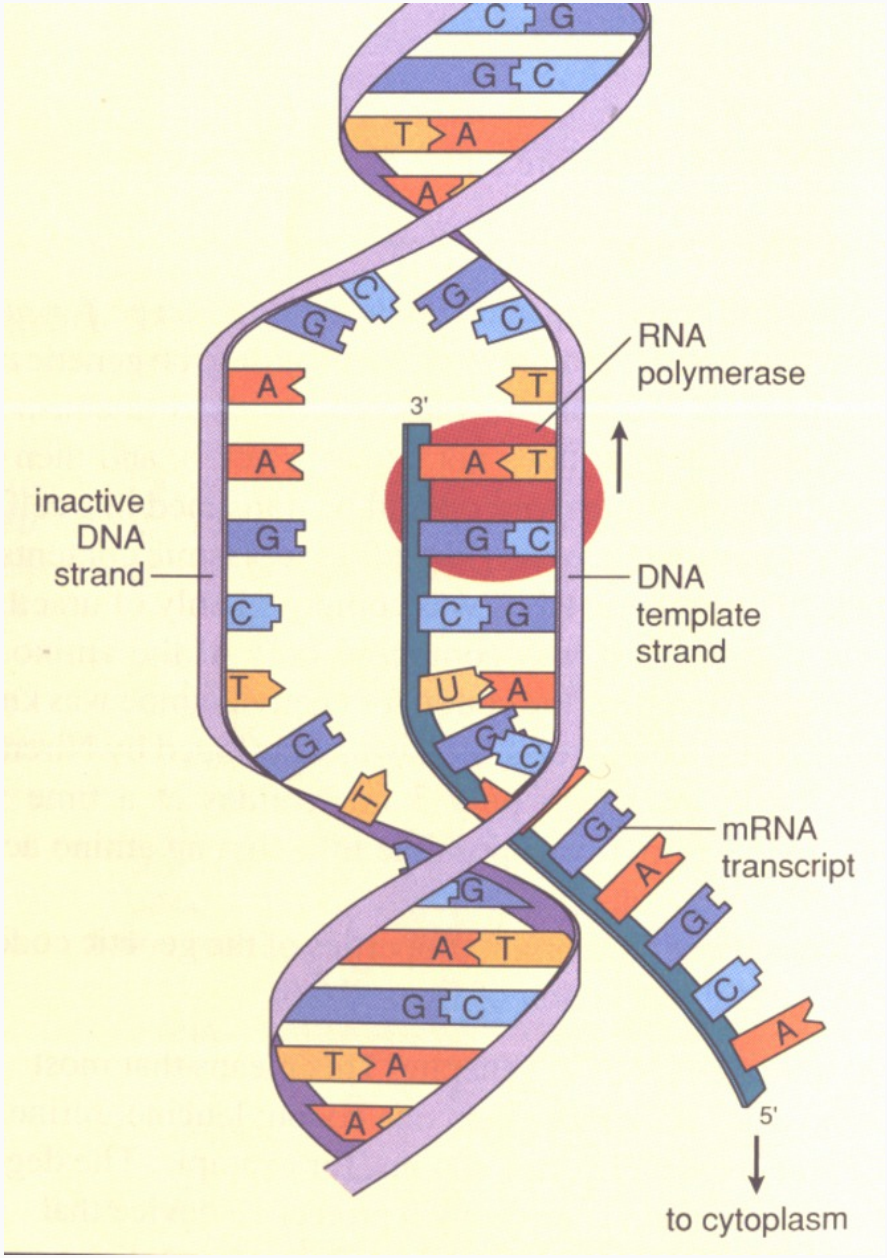

RNA
polymerase
3'
inactive
DNA
strand
DNA
template
strand
mRNA
transcript
5'
to cytoplasm

Figure 28. 转录

3. 遗传密码

- 三联体密码子
- 密码是连续的
- 密码的简并性

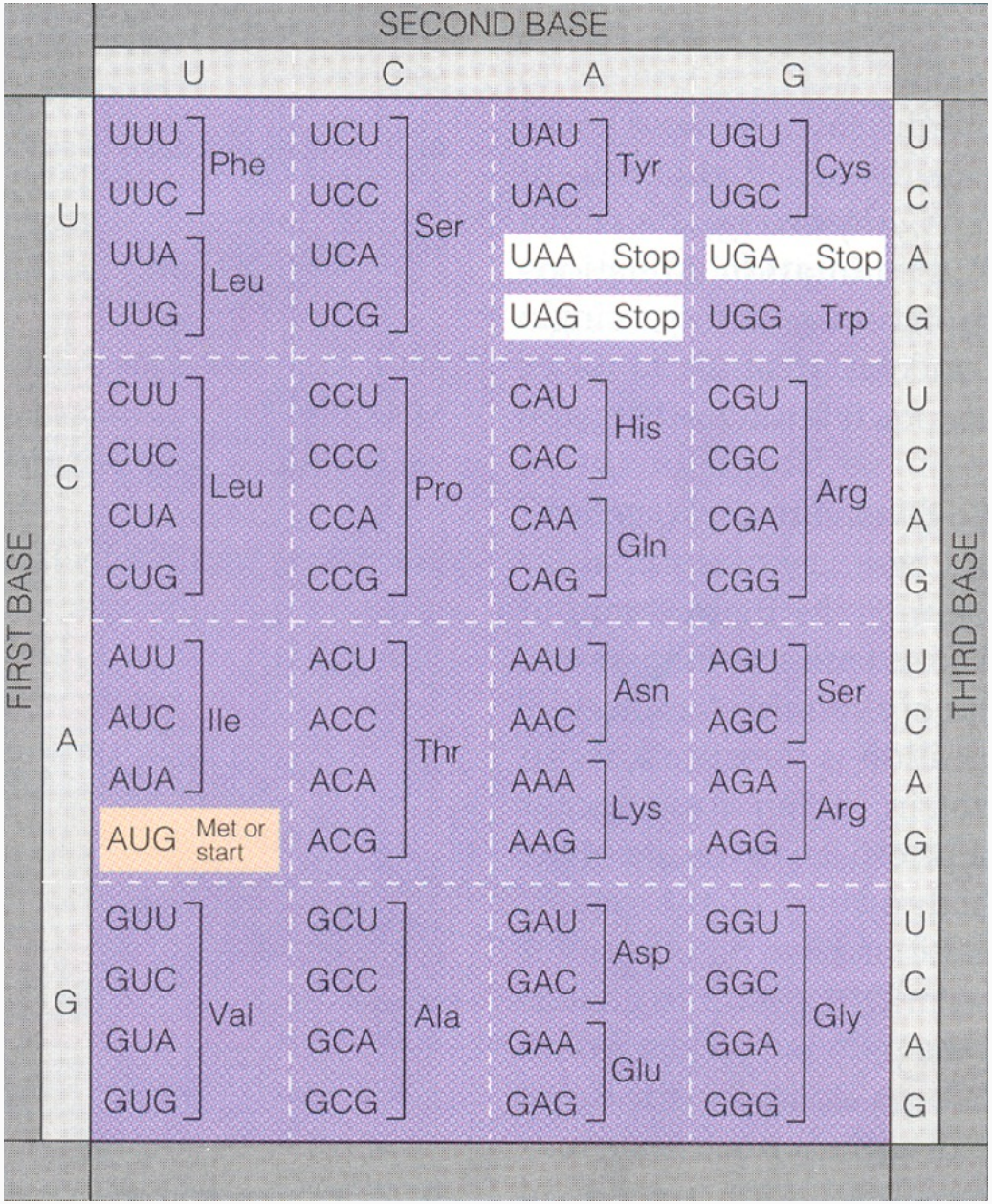


Figure 29. 遗传密码表

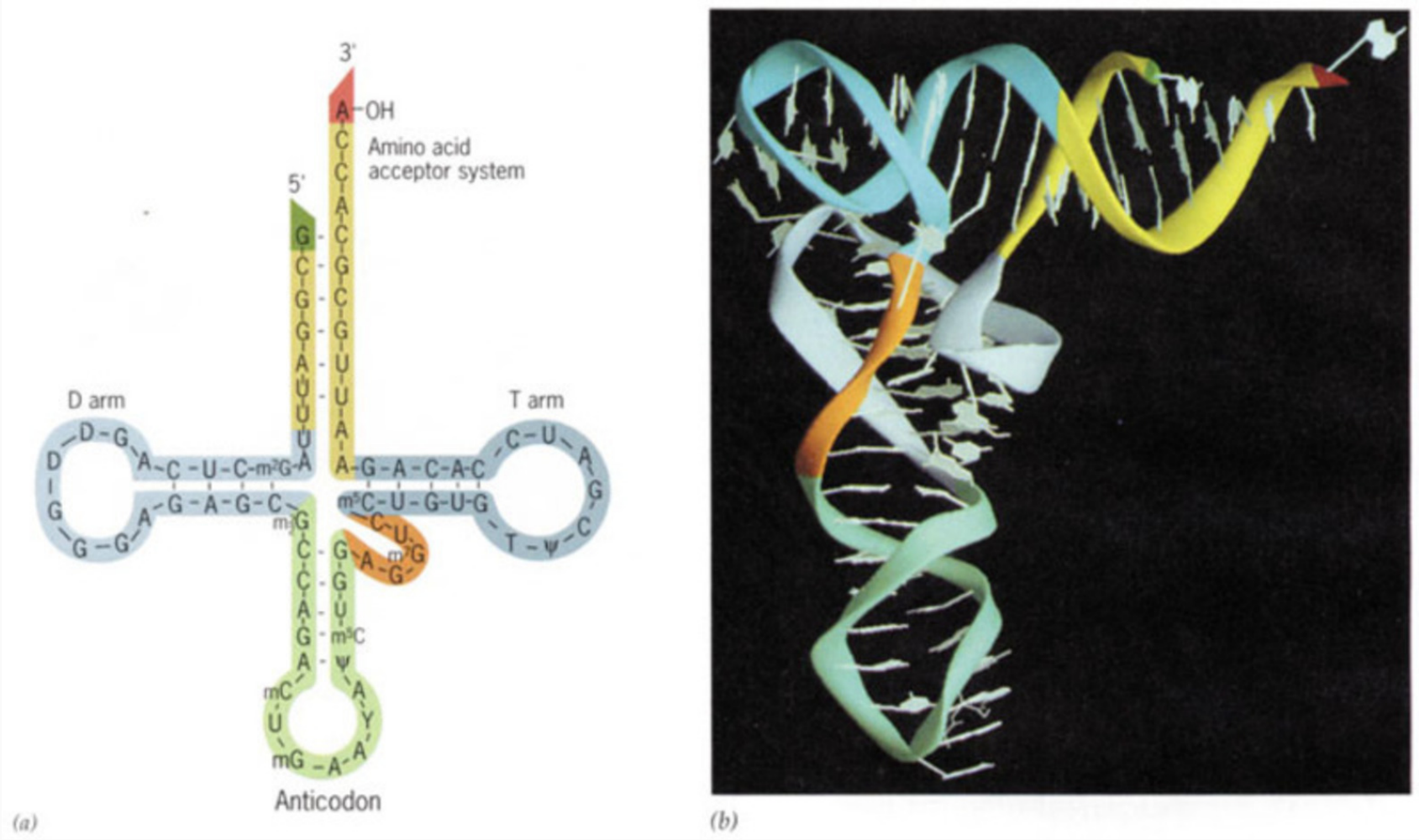


Figure 30. tRNA 三级结构

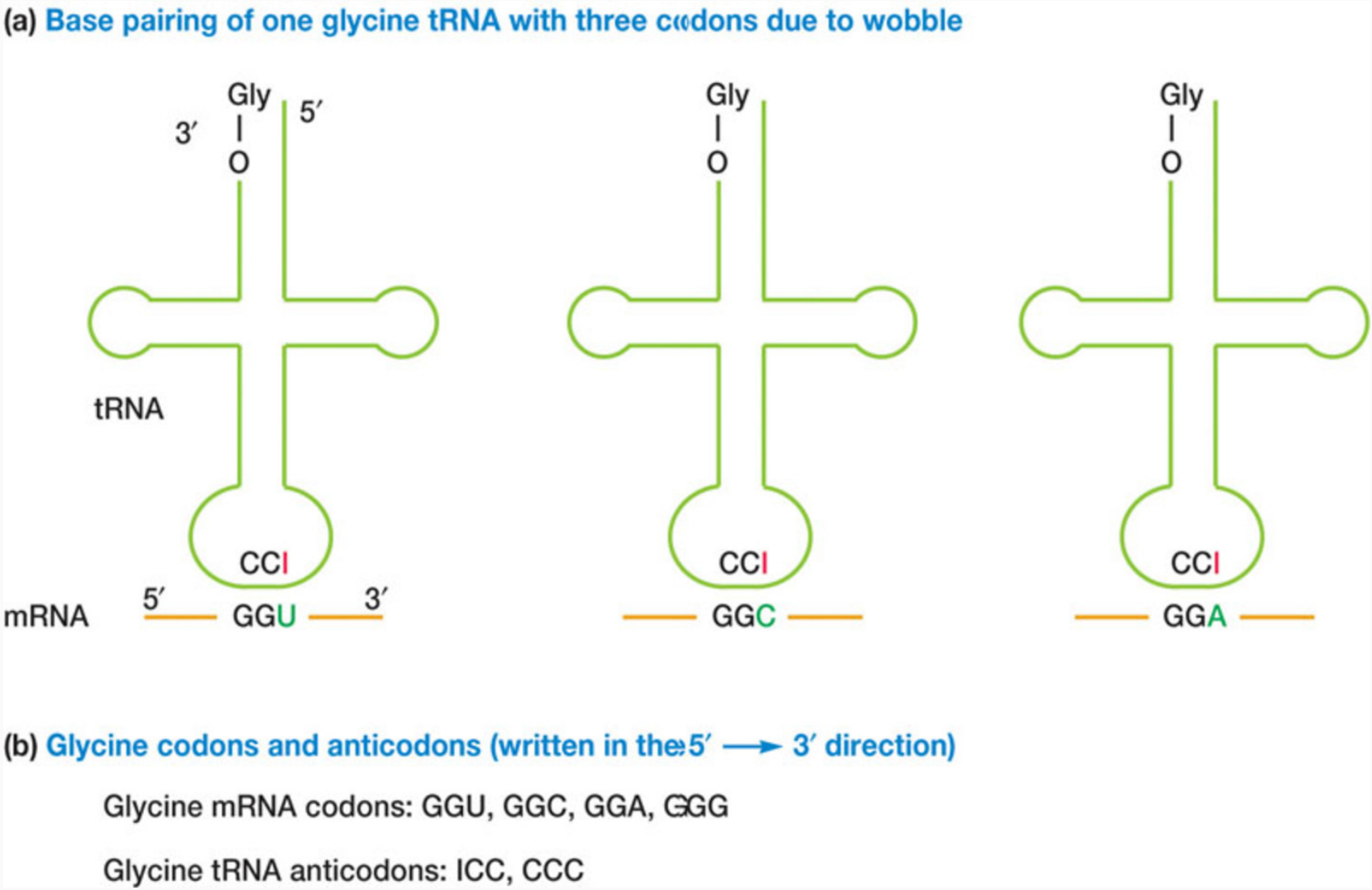


Figure 31. 摆动 (Wobble)

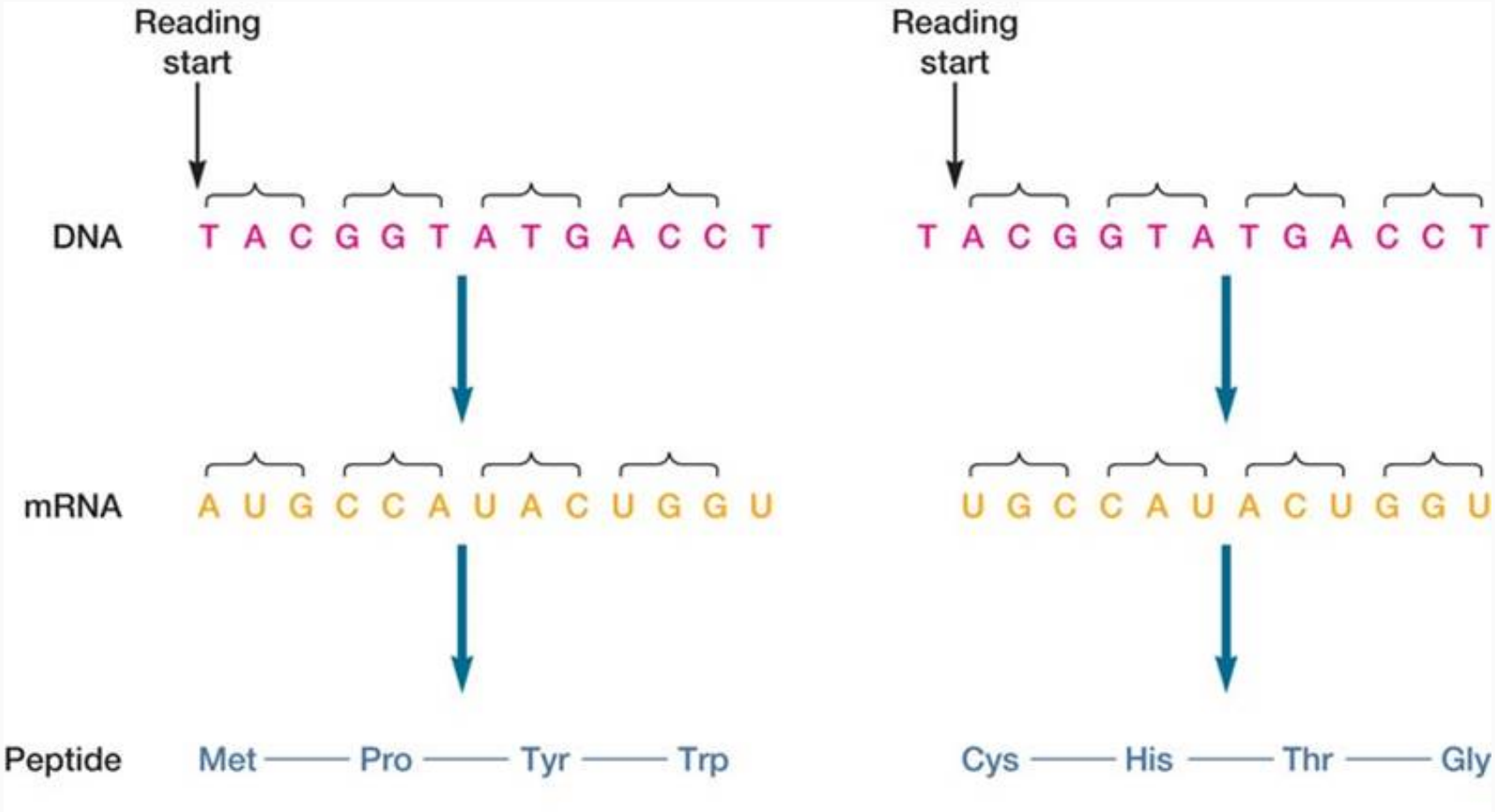


Figure 32. 阅读框及其重要性

21.3.3 遗传信息在细胞质中被翻译

1. tRNA 携带氨基酸
2. 核糖体 “阅读” 密码子, 氨基酸连成多肽
    - 核糖体
    - 翻译的起始和连接
    - 翻译的终止

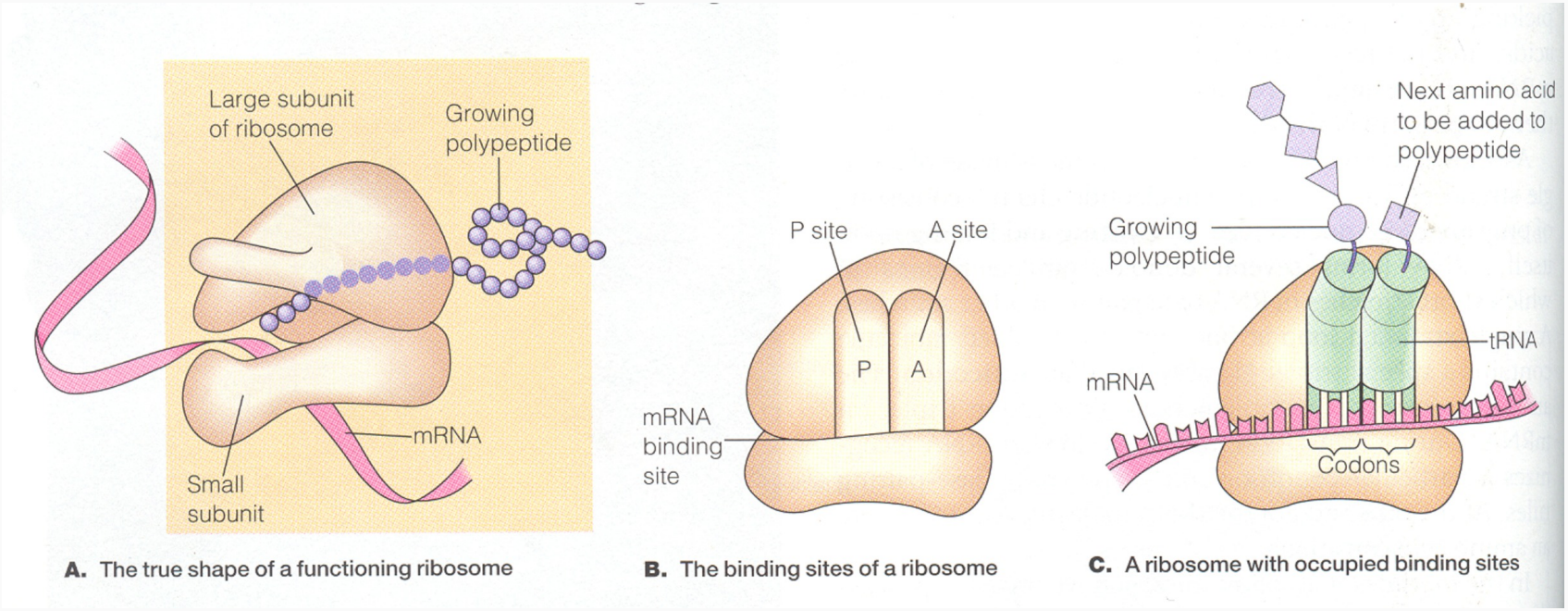


Figure 33. 核糖体

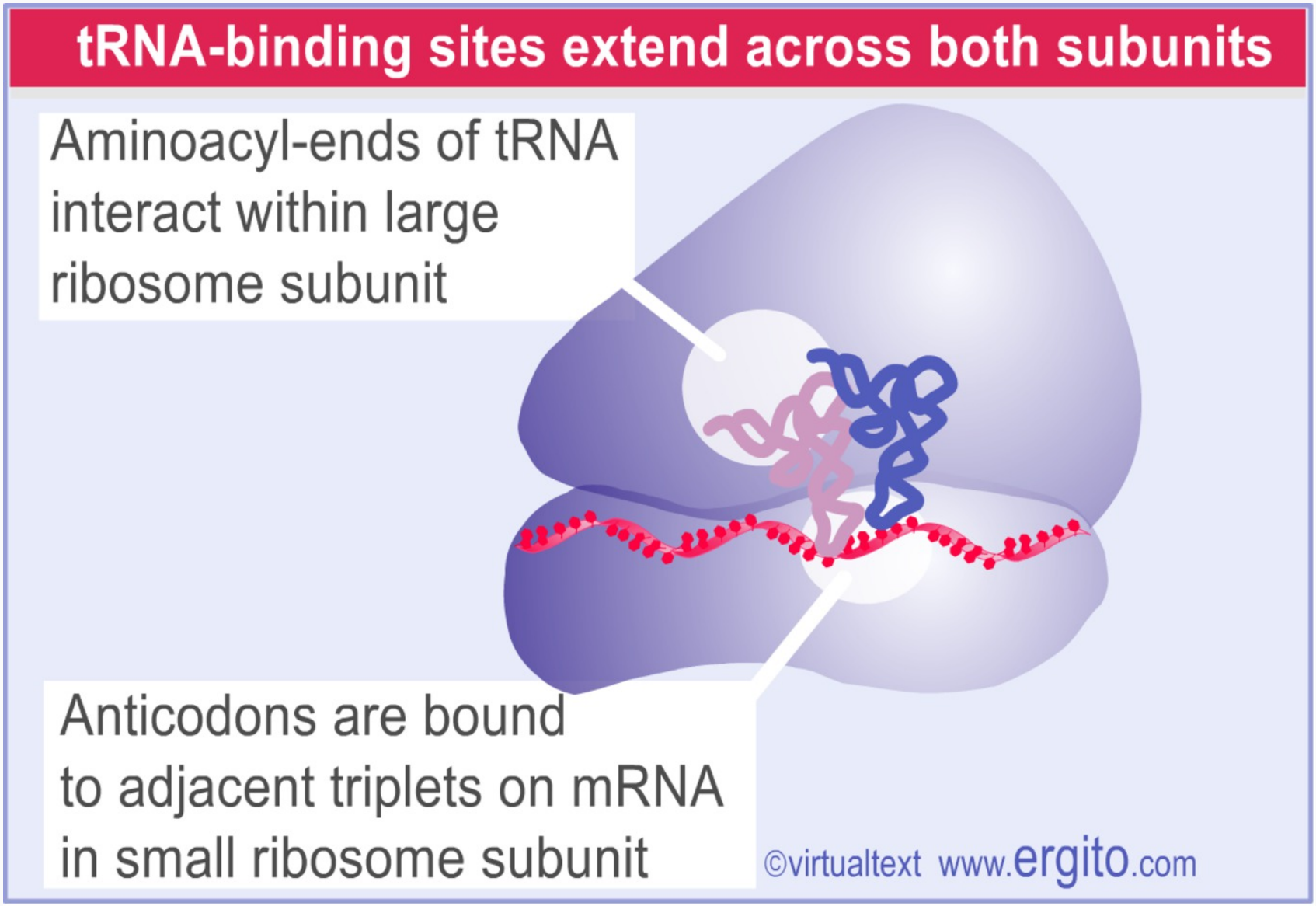


Figure 34. 核糖体中的 tRNA 结合位点

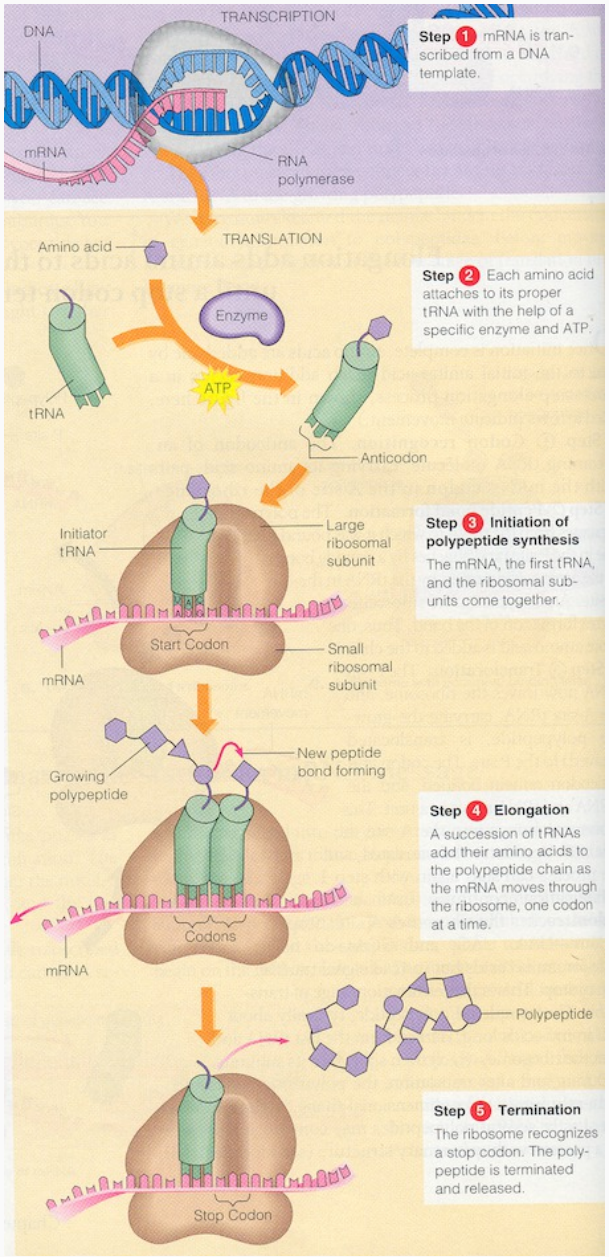


Figure 35. 转录和翻译

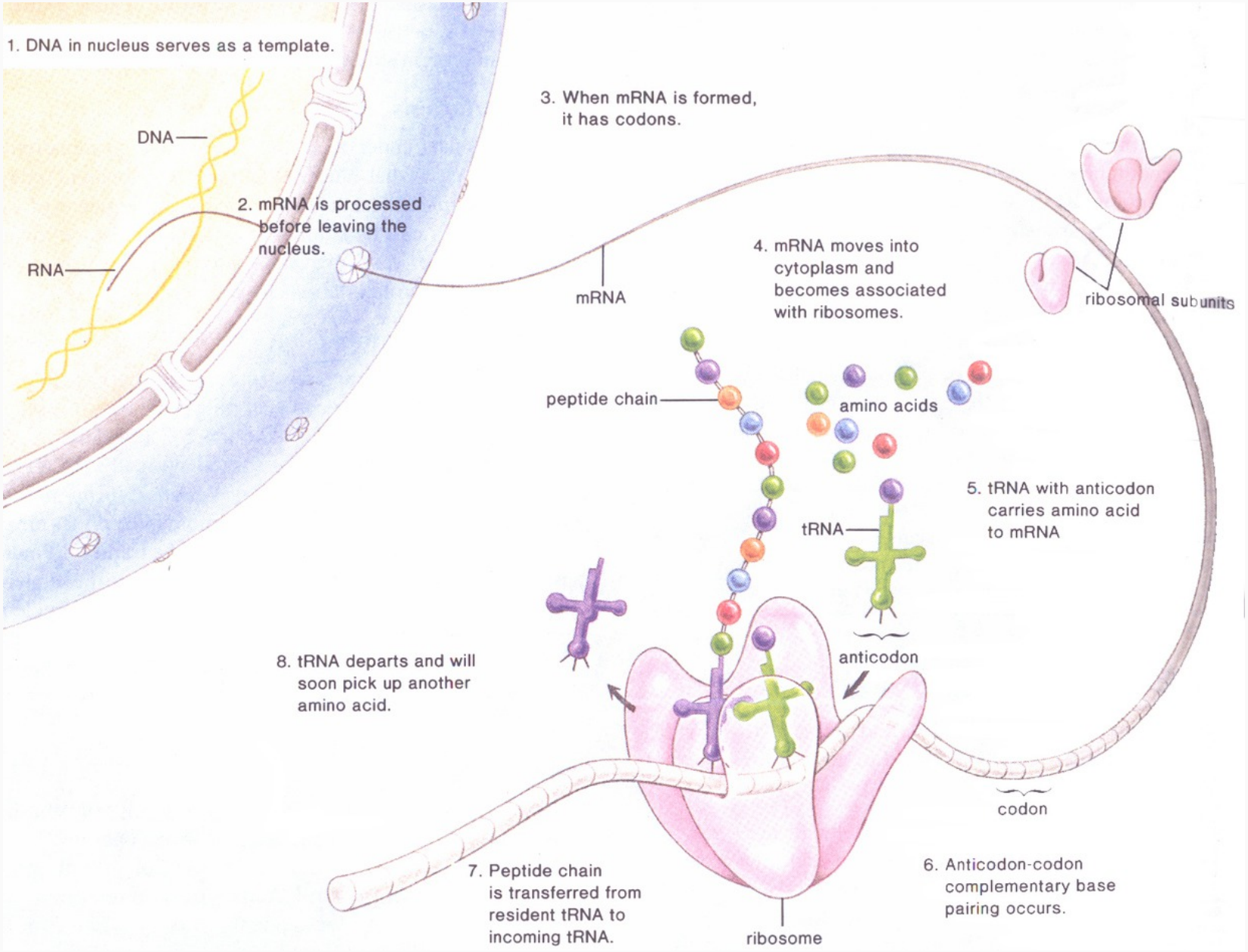
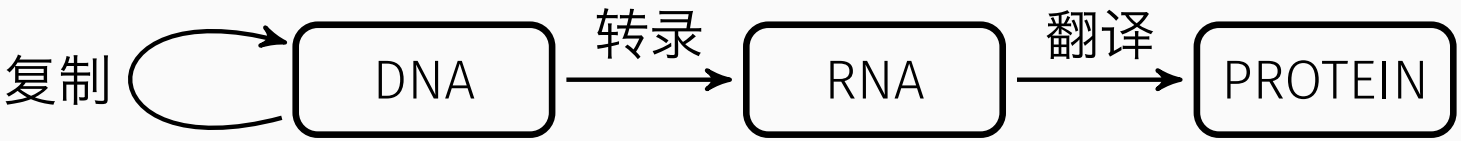
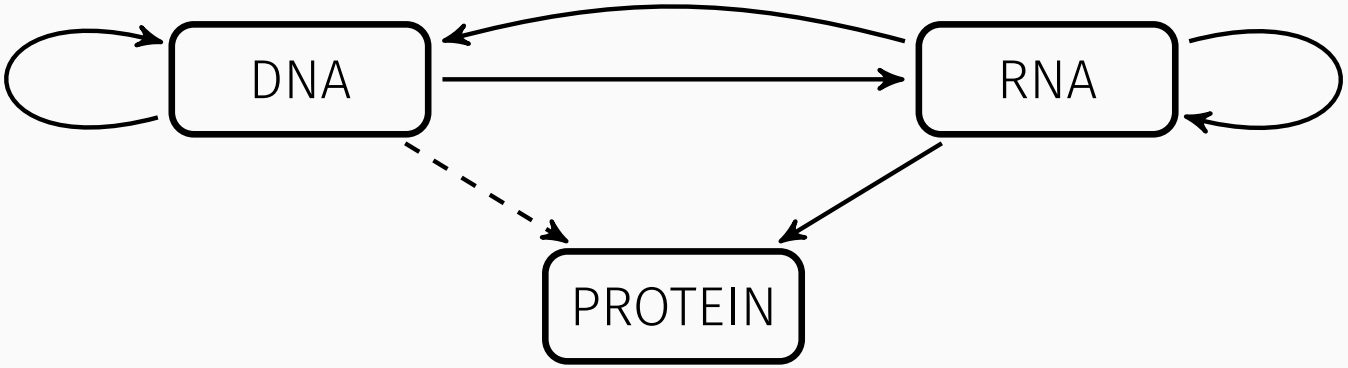


Figure 36. 转录和翻译

21.3.4 中心法则

- 遗传信息从 DNA 到 RNA 到蛋白质




DNA
RNA
PROTEIN

- 朊粒与中心法则
  - 新型克 – 雅氏病 (nv–CJD), 库鲁病 (Kuru), 牛海绵状脑病 (BSE), 羊摩擦症 (scrapie)
  - 朊粒 (prion)
  - *PrP*
  - PrP^{c}, PrP^{sc}

21.4 基因突变

21.4.1 碱基置换

- 置换 (substitution)
  - 转换 (transition)
  - 颠换 (transversion)
- 镰刀形贫血症 (GAG $\rightarrow$ GUG)

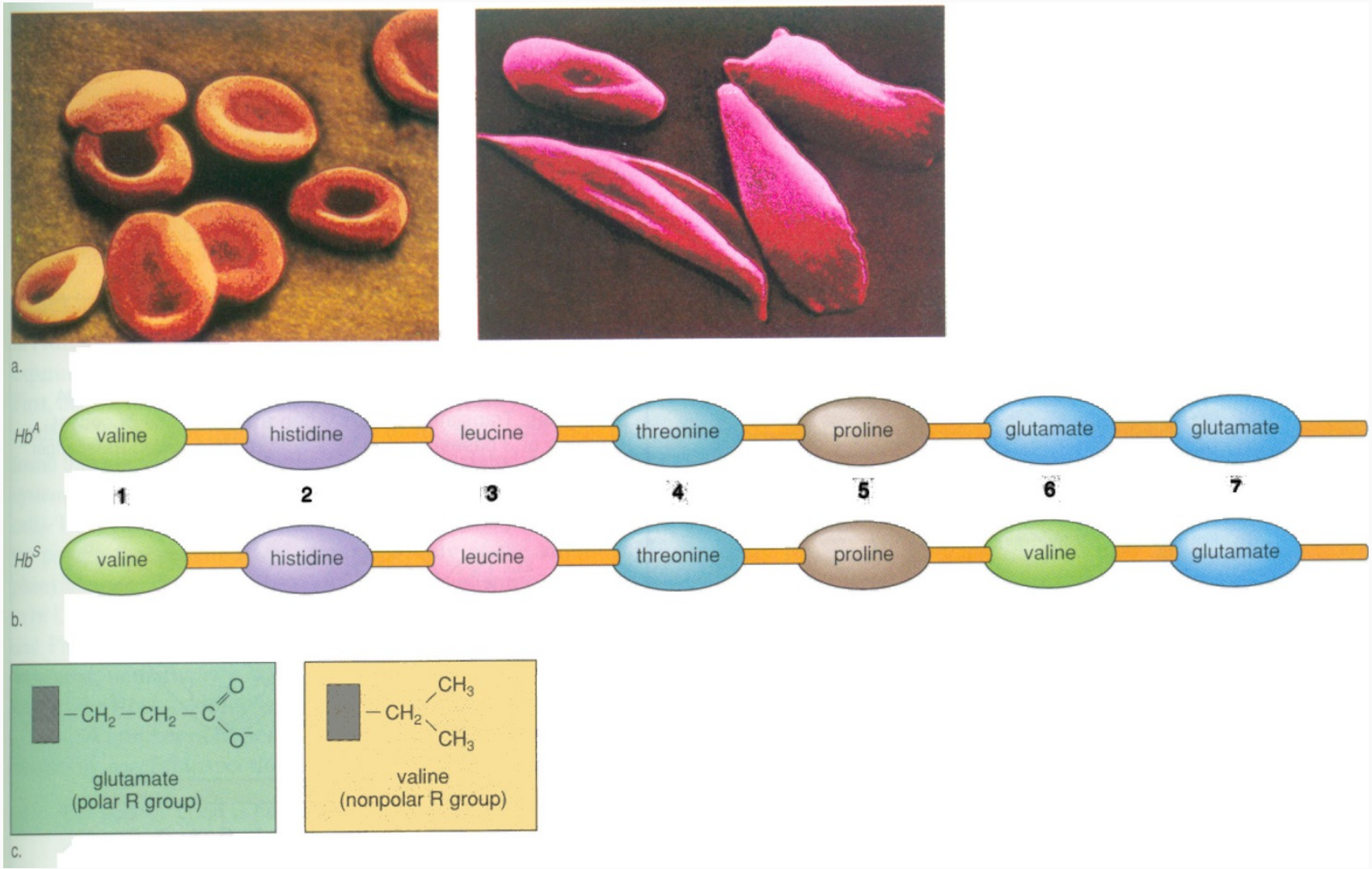


Figure 37. 镰刀形贫血症

21.4.2 移码突变

- 插入 (insertion)
- 缺失 (deletion)
- 基因的编码区非3的整倍数插入/缺失, 称为移码突变

21.4.3 DNA 损伤修复

- 突变的诱发
  - 辐射
  - 化学诱变剂
  - 其他诱变因素
    - 温度
    - DNA 修复系统发生错误
- 损伤修复
  - 切除修复
  - 同源重组修复

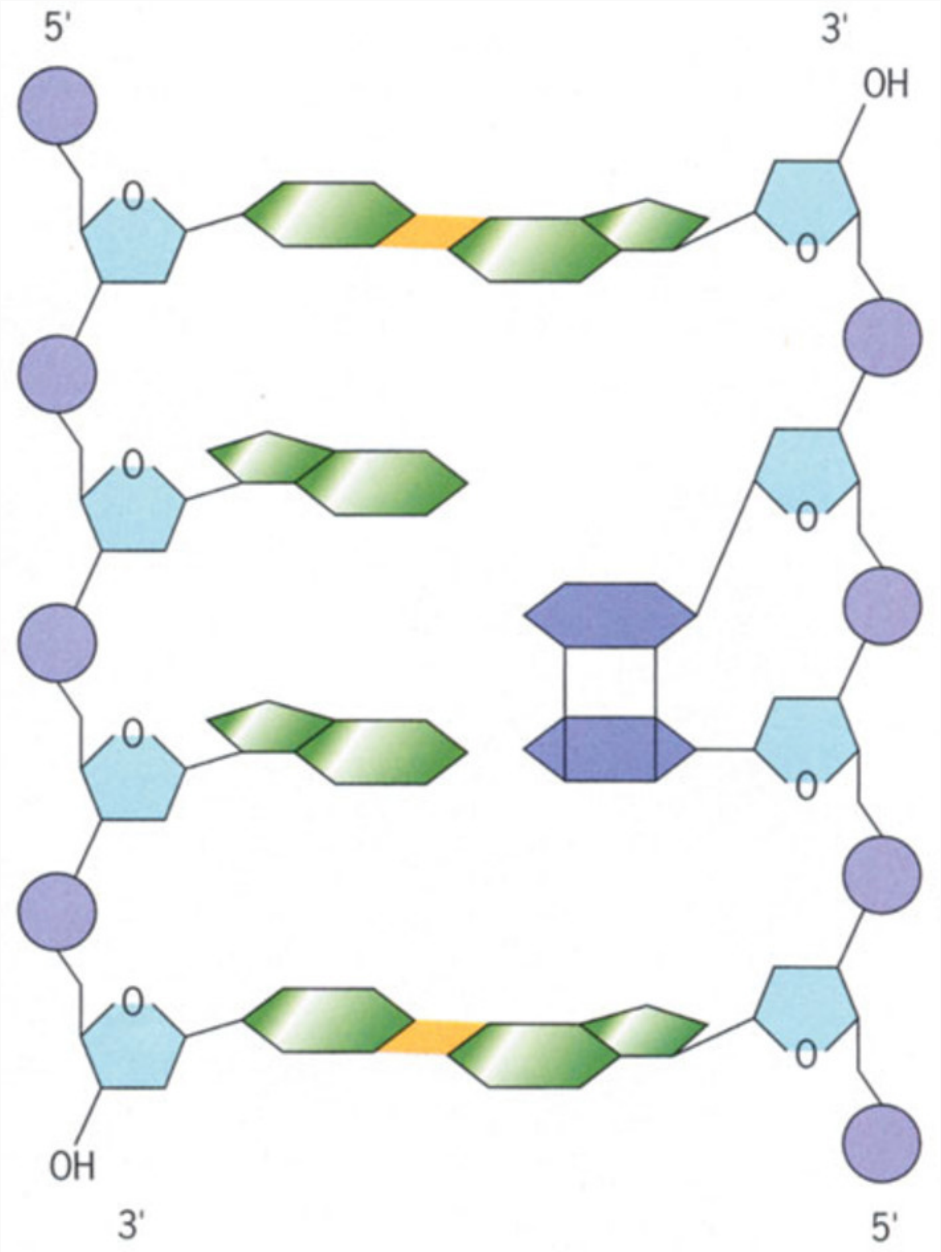


Figure 38. TT 二聚体