21 基因的分子生物学

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Outline

21.1 遗传物质是DNA(或RNA)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

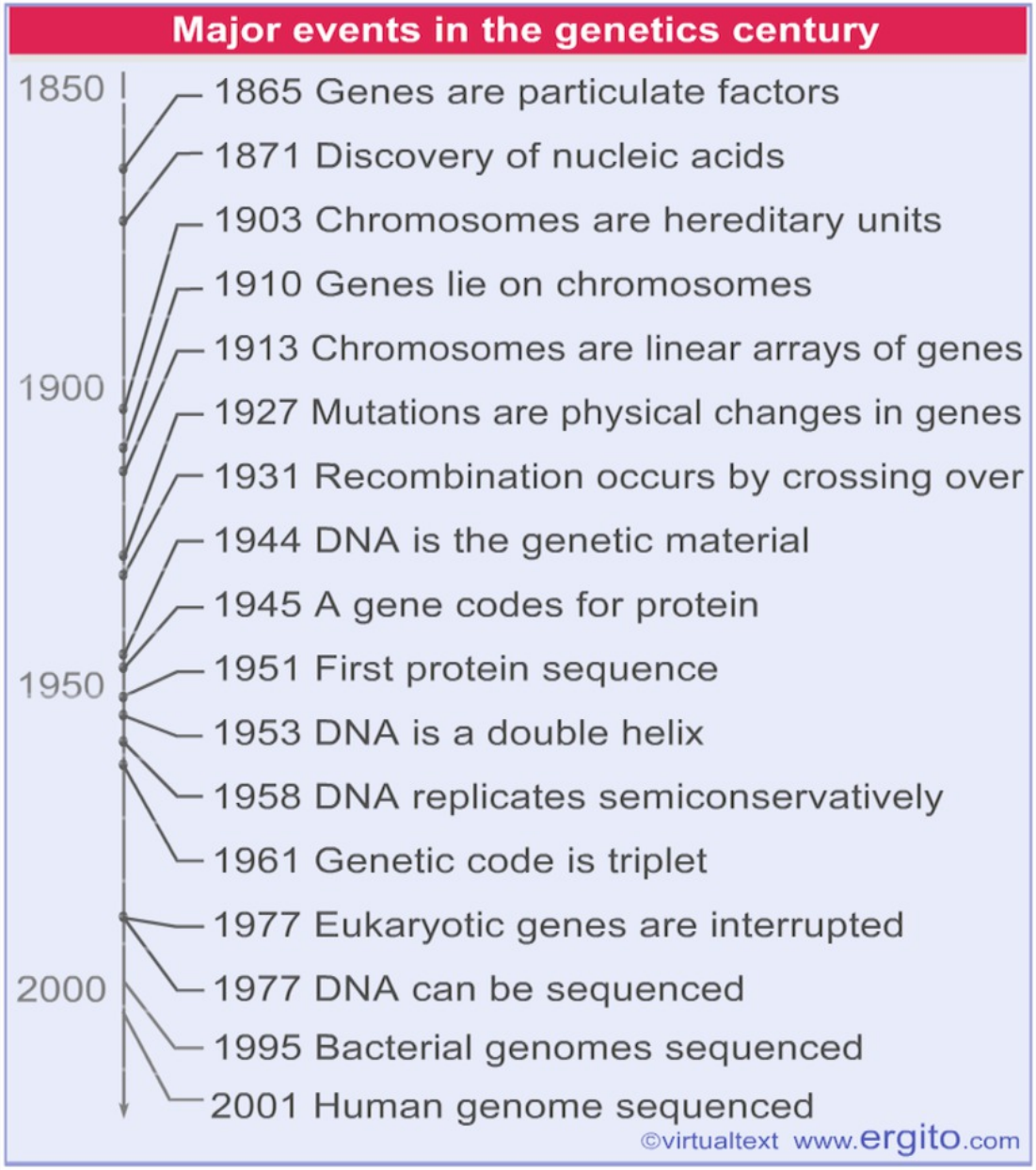


Figure 1. 遗传学世纪的大事件

21.1 遗传物质是DNA(或RNA)的证明

21.1.1 肺炎链球菌转化实验

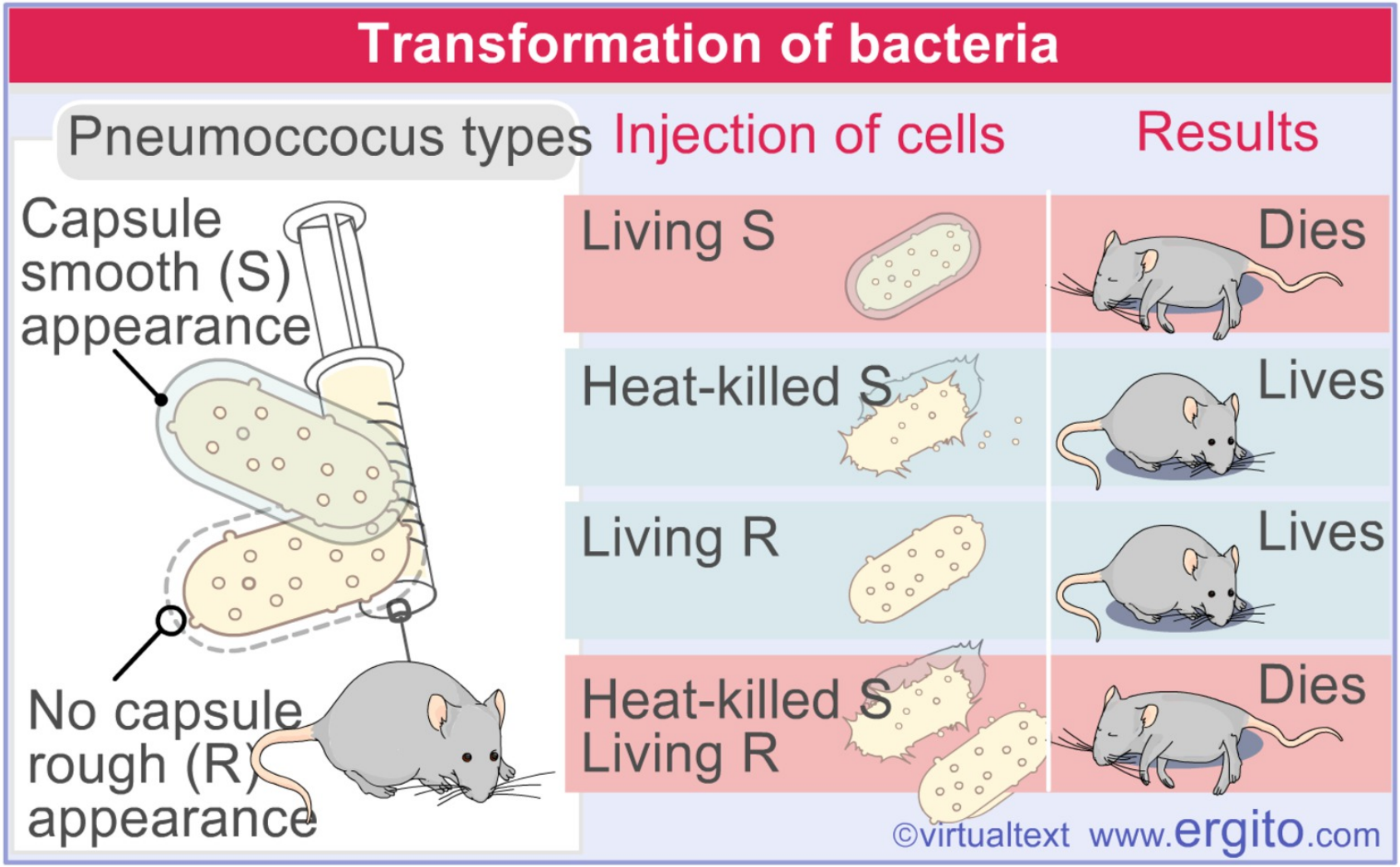


Figure 2

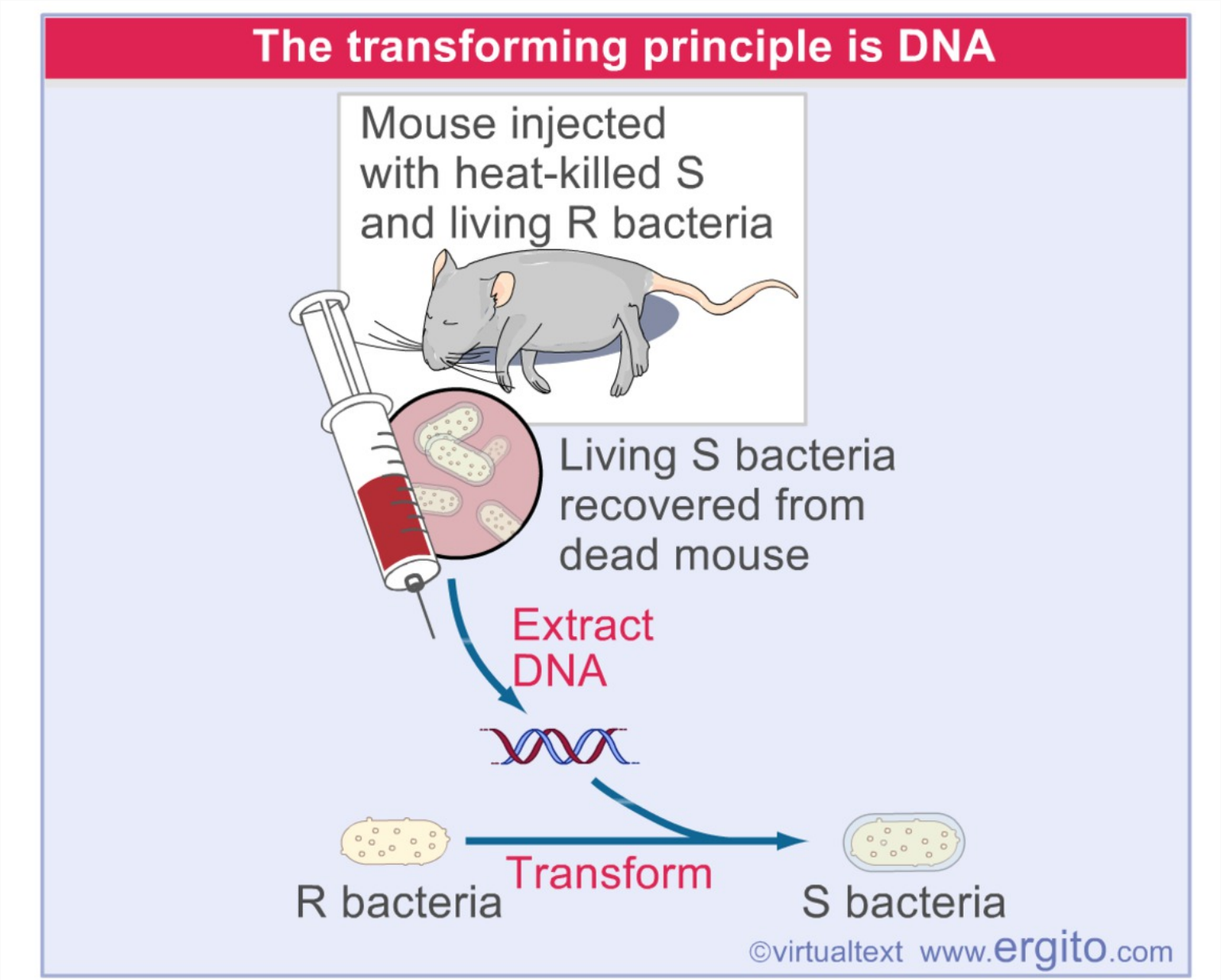


Figure 3. 转化因子是DNA

21.1.2 T2噬菌体感染实验

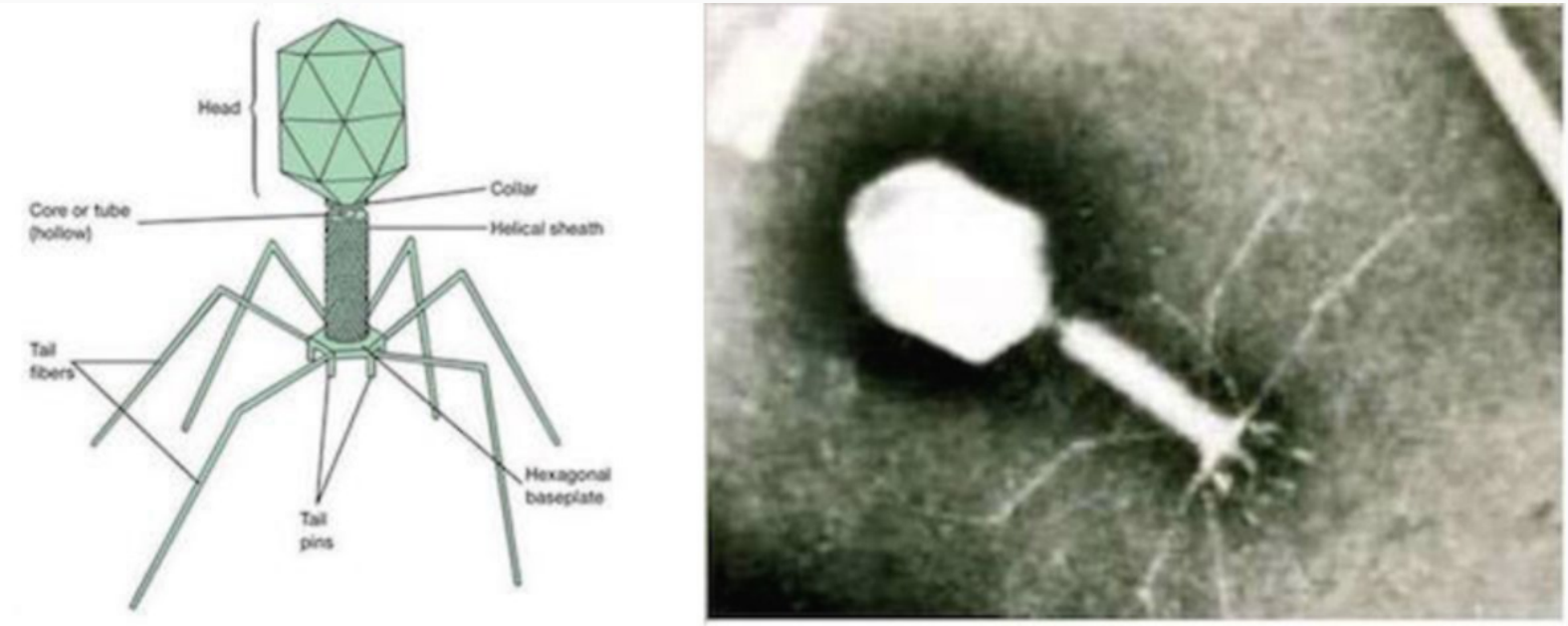


Figure 4. T2噬菌体. 左: 结构示意图; 右: 透射电镜照片.

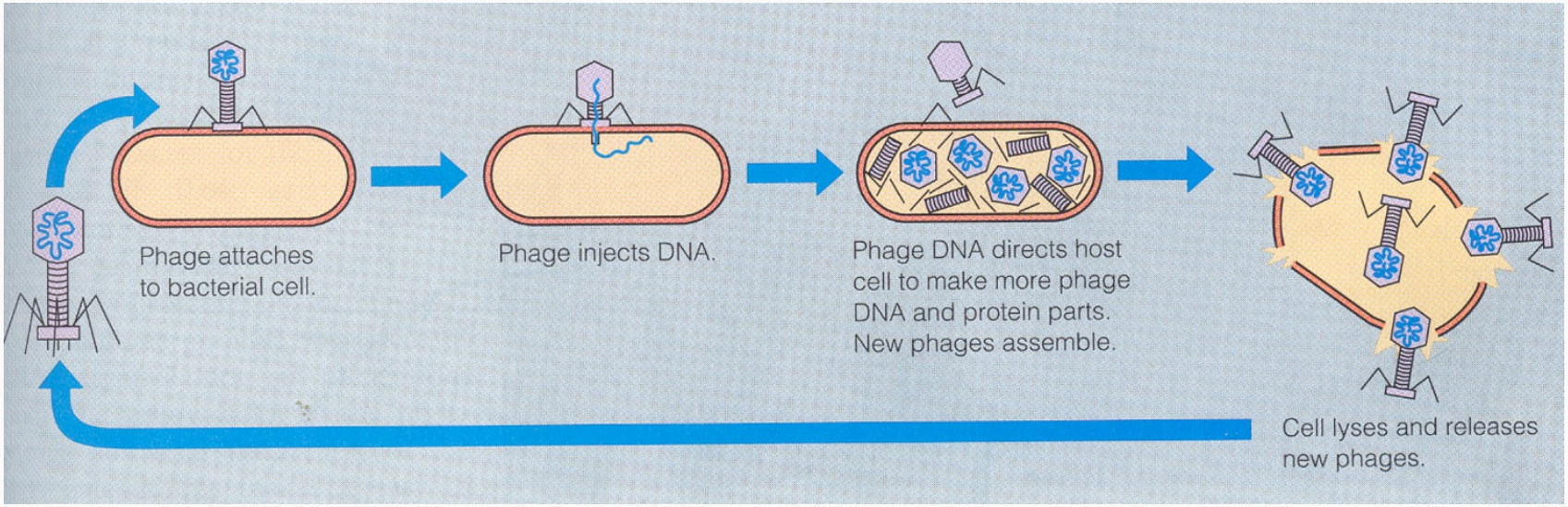


Figure 5. 噬菌体繁殖

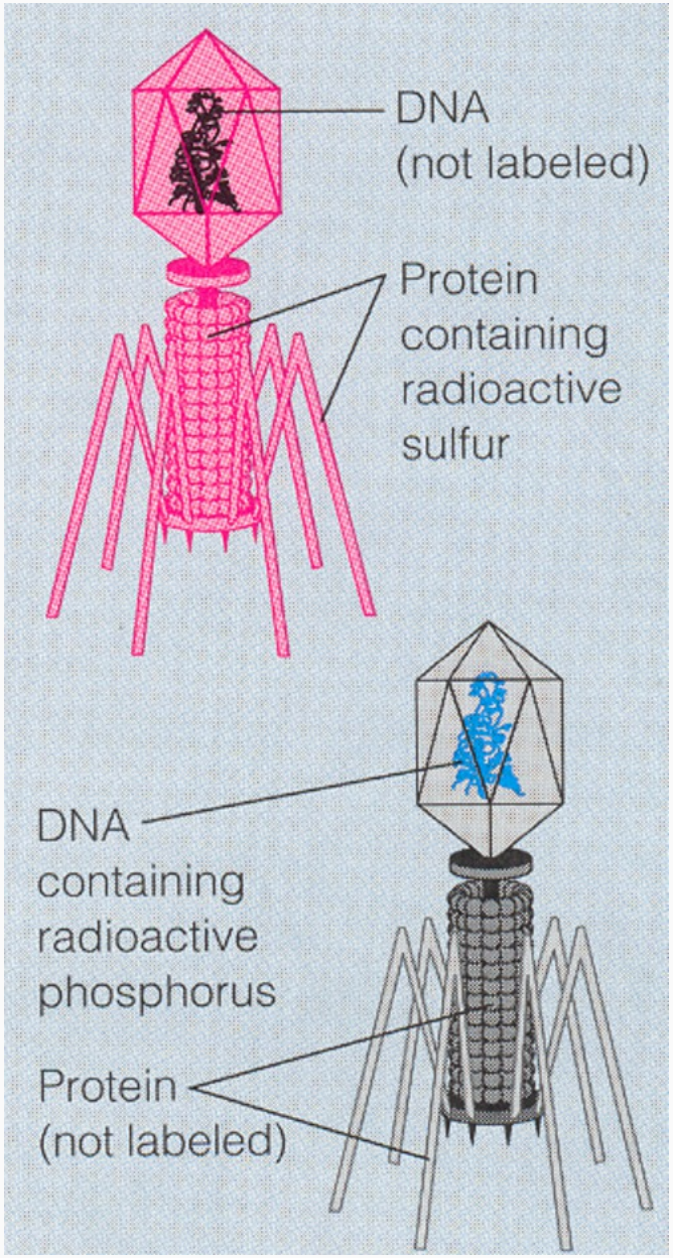


Figure 6. 放射性标记T2噬菌体

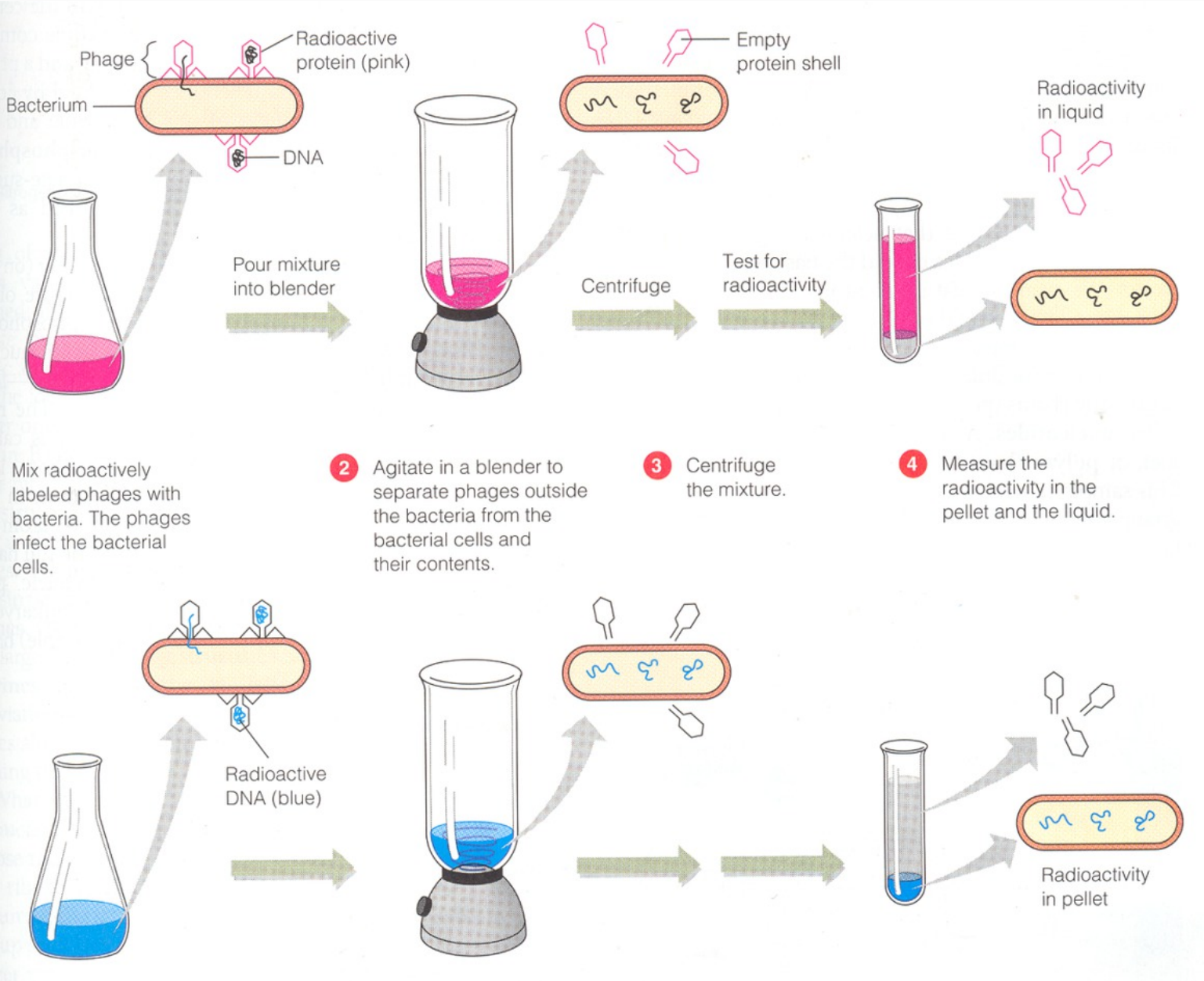


Figure 7. 赫尔希–蔡斯关于T2噬菌体的感染实验

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

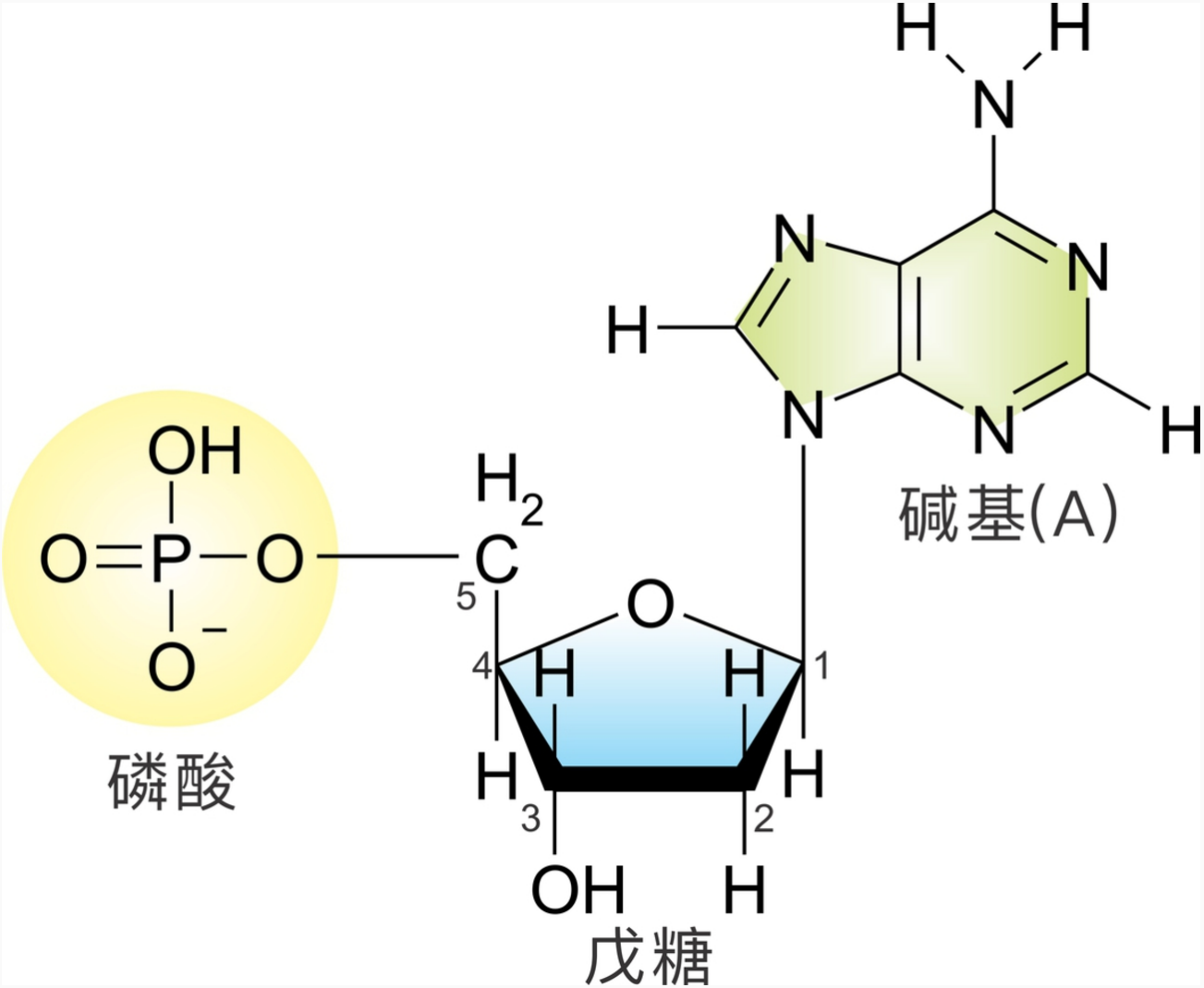


Figure 8. 核苷酸

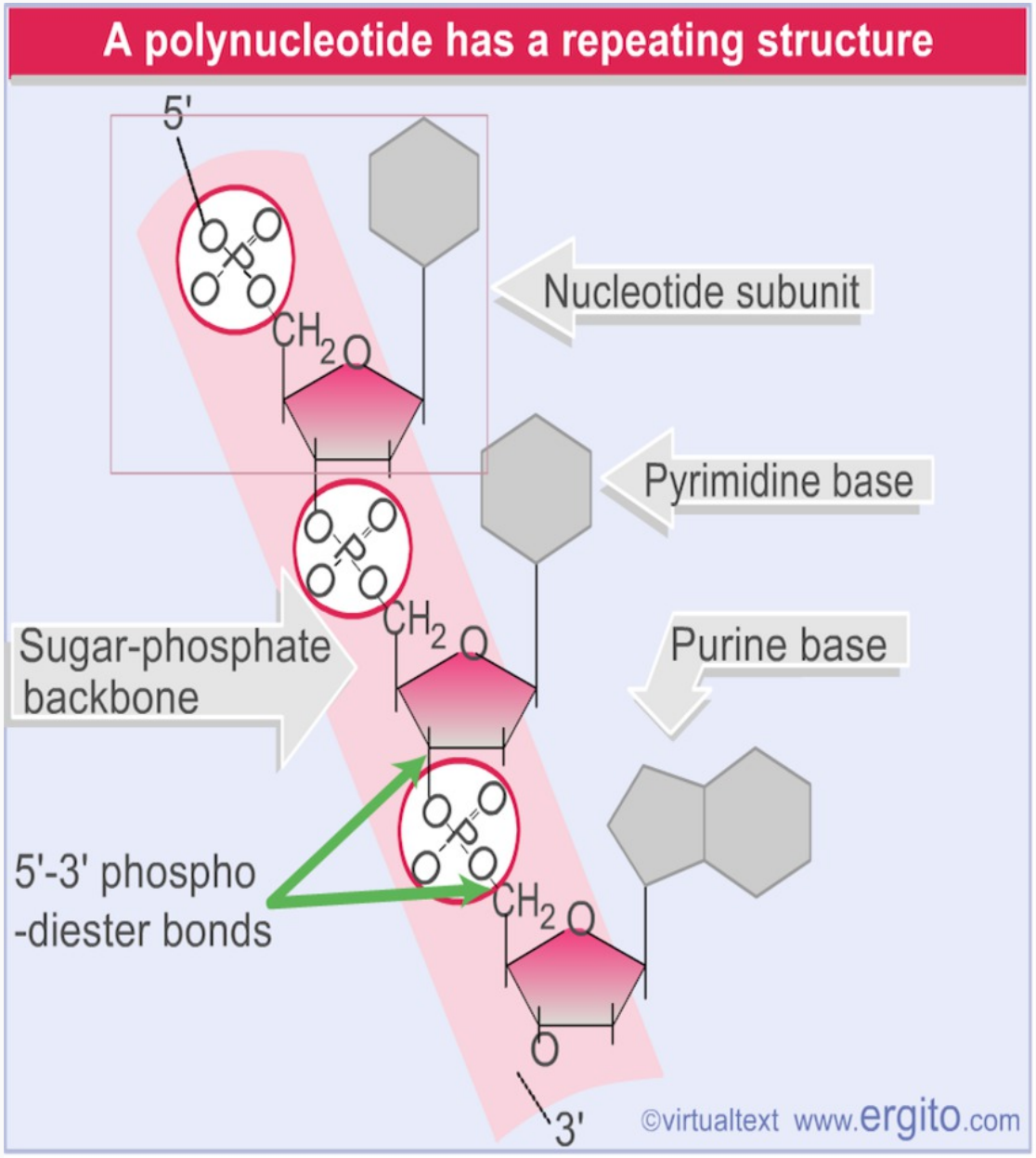


Figure 9. 多核苷酸中的重复结构

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.

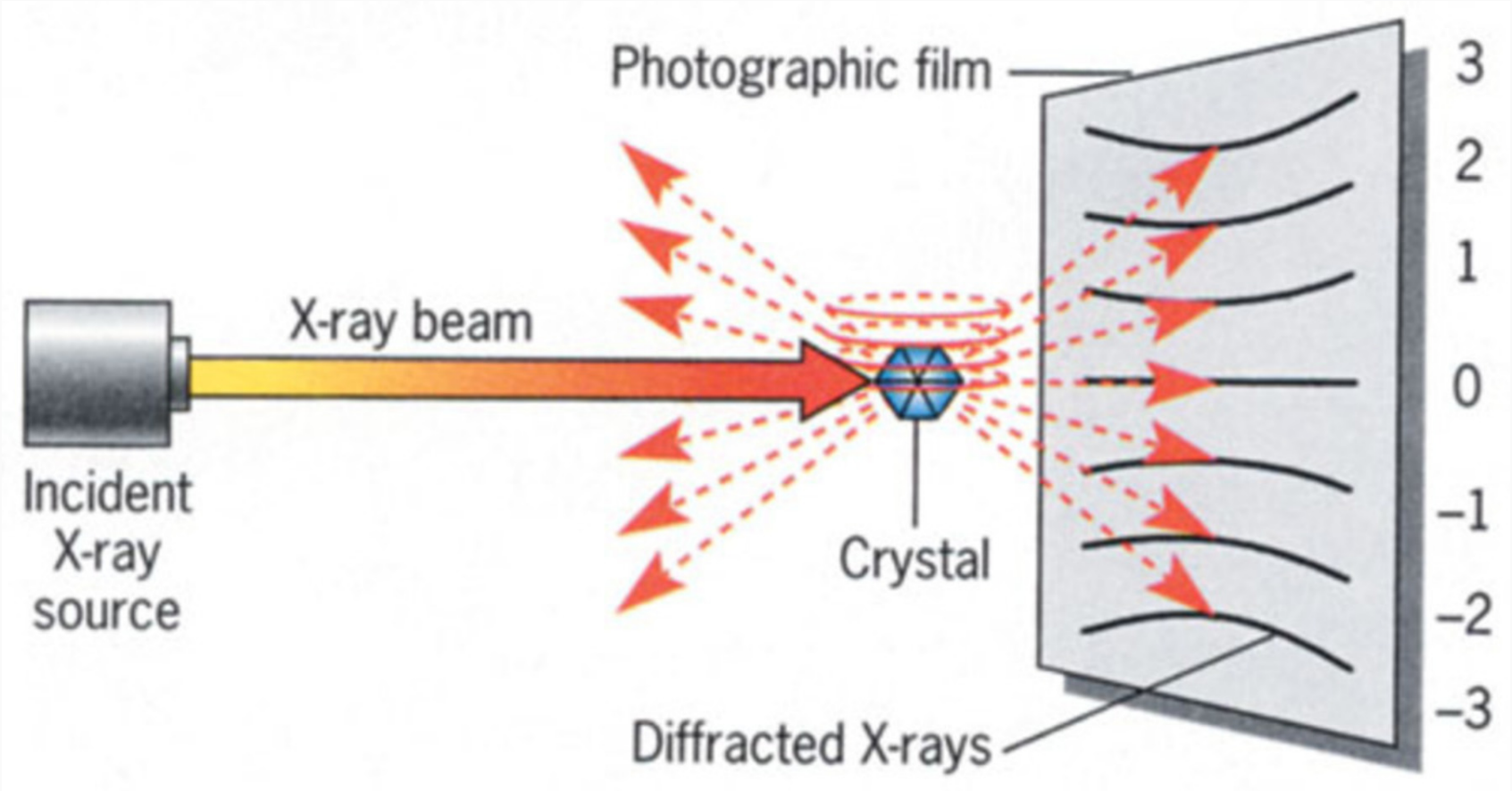


Figure 10. X-射线衍射实验

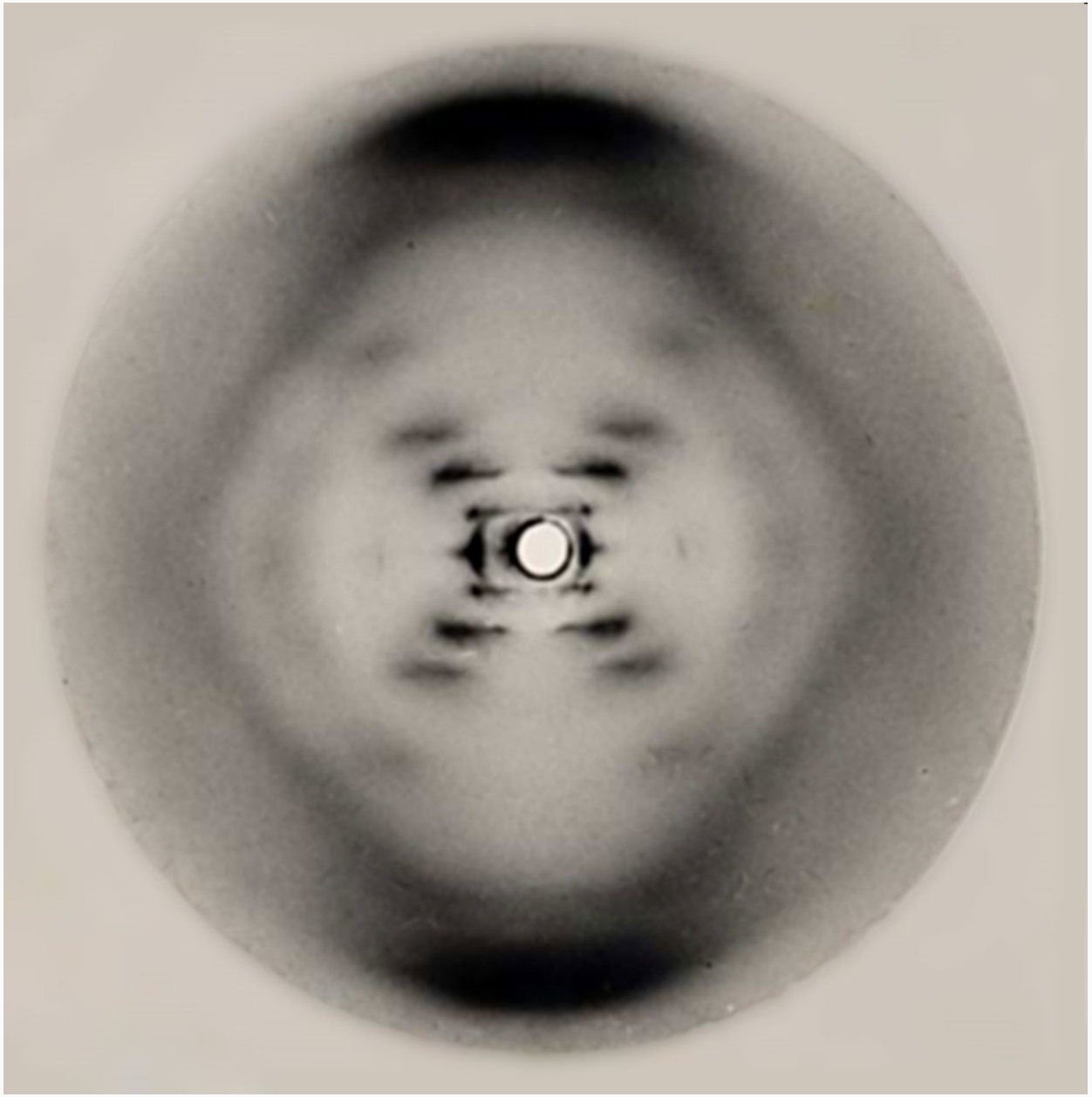


Figure 11. DNA晶体的X-射线衍射照片

(a) Rosalind Franklin

(b) Maurice Wilkins

Figure 12. 研究DNA晶体的科学家

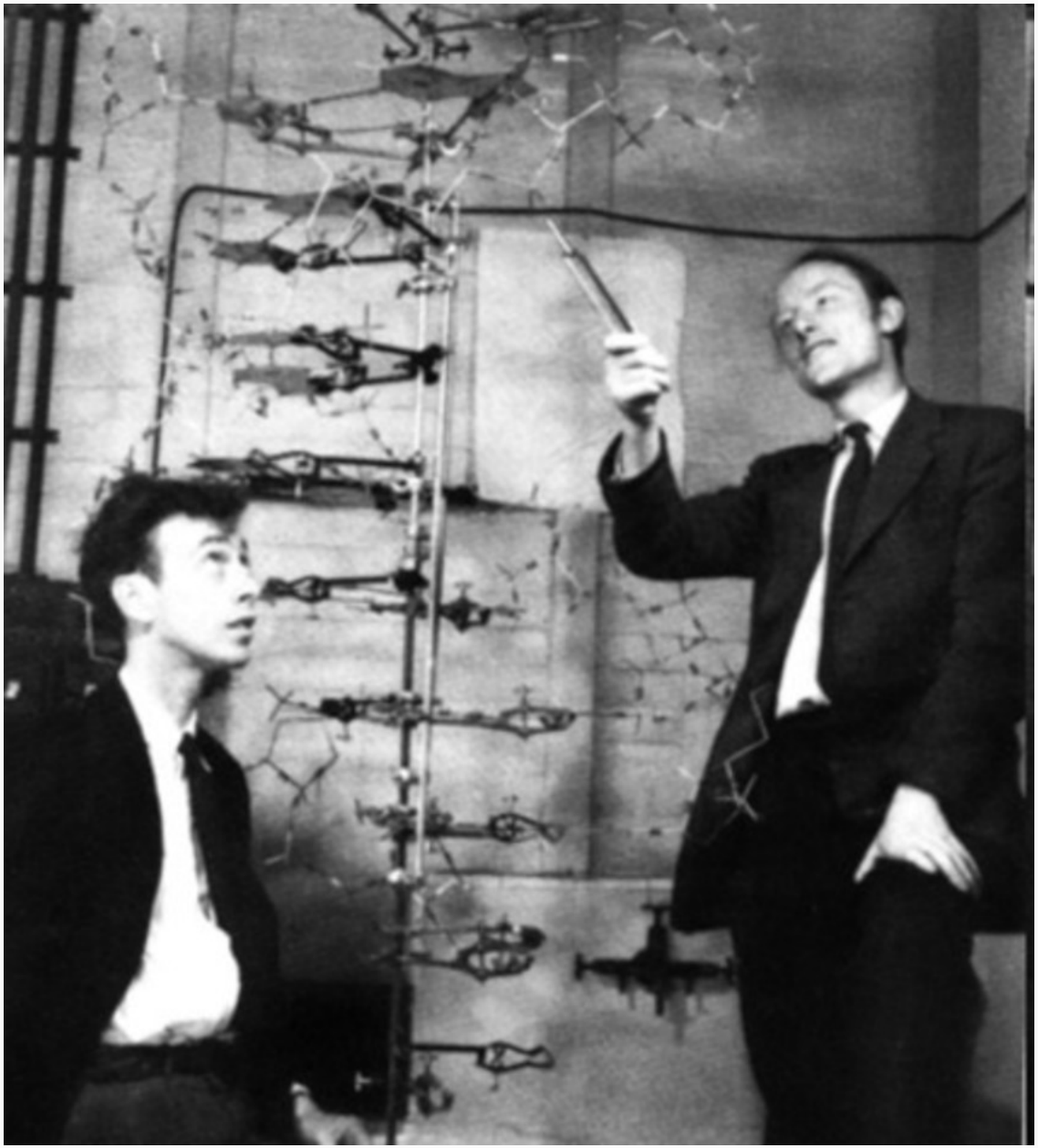


Figure 13. Watson和Crick

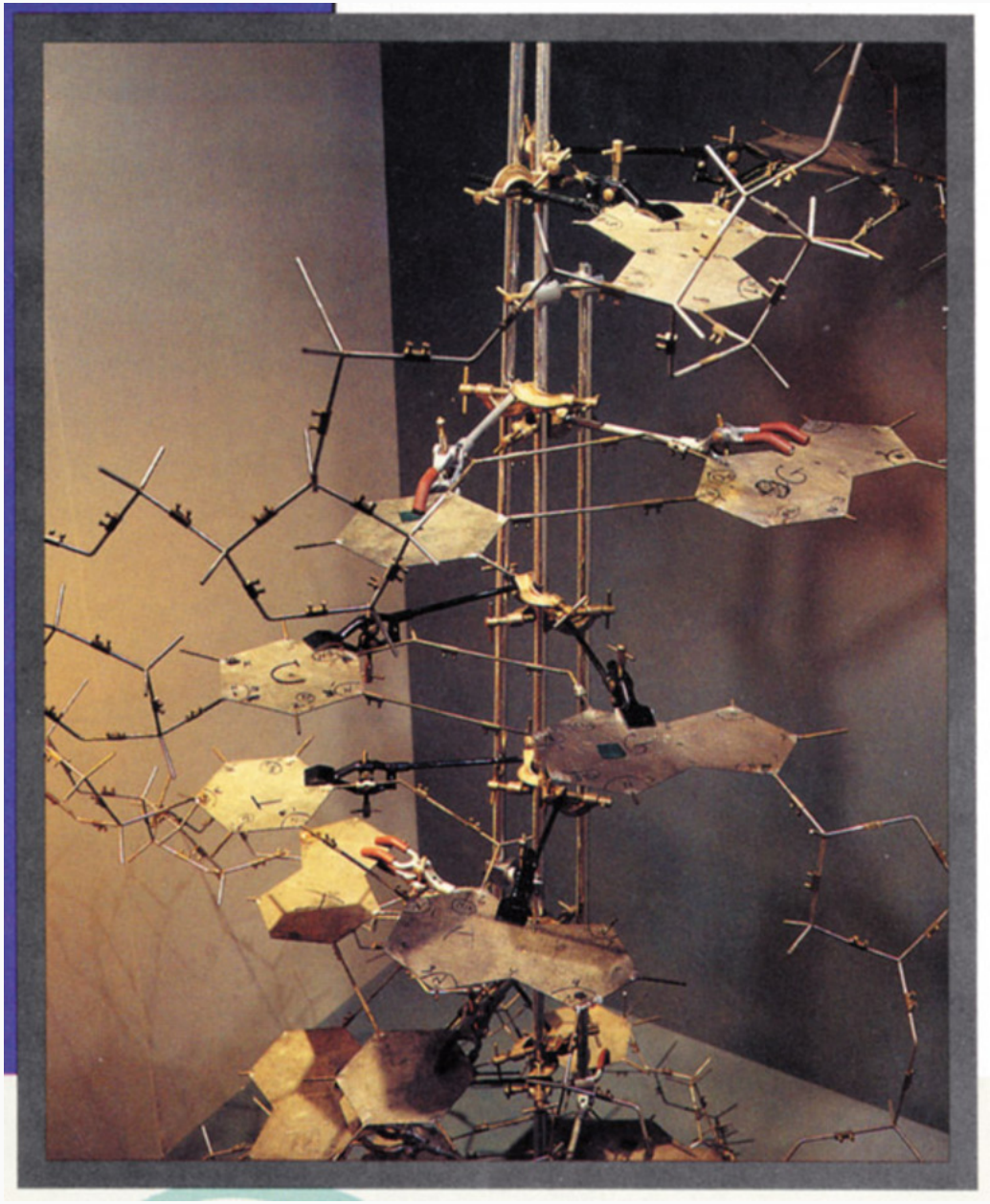


Figure 14. Model of DNA built by James Watson and Francis Crick at Cambridge University

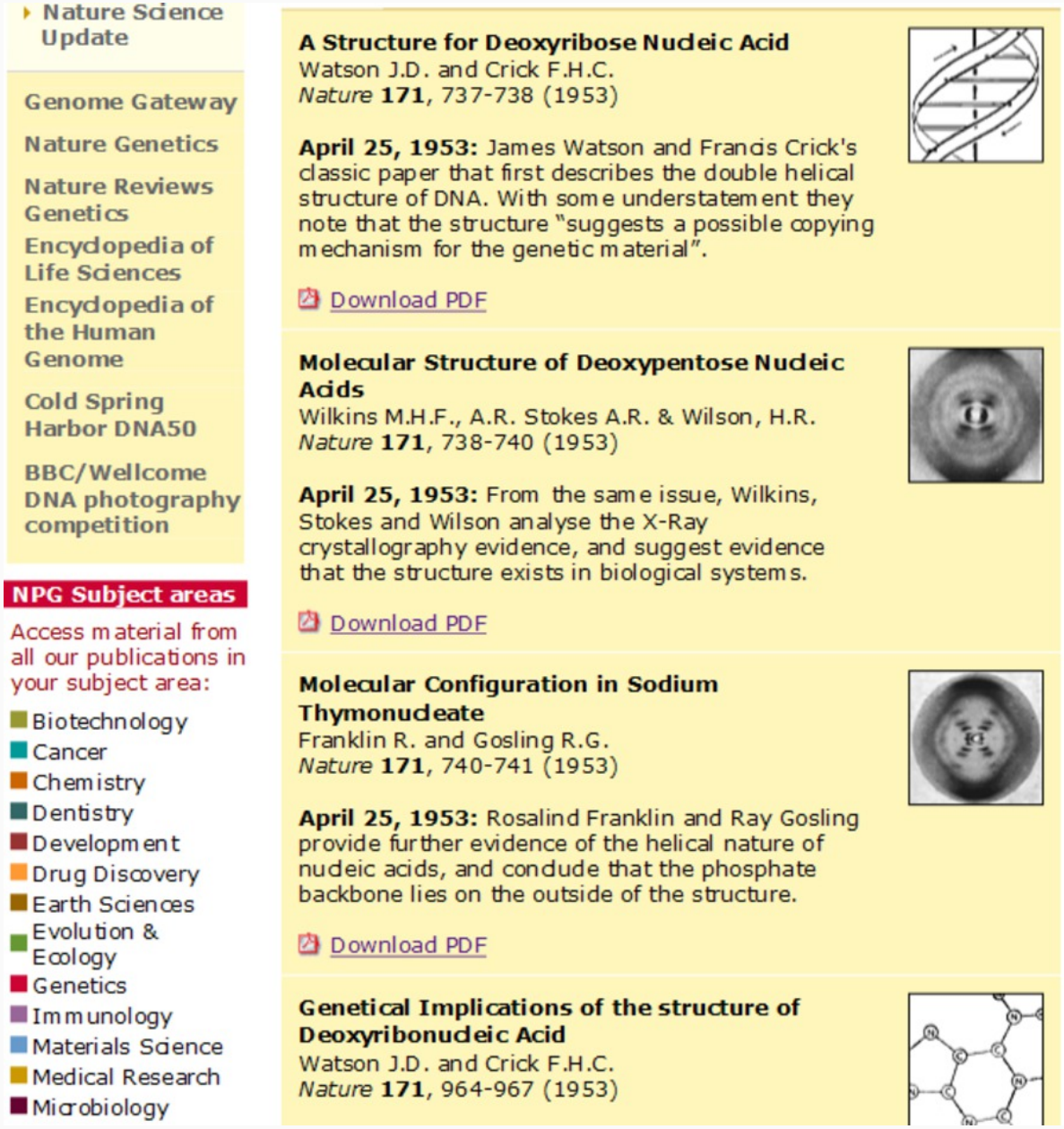


Figure 15. http://www.nature.com/nature/dna50/archive.html

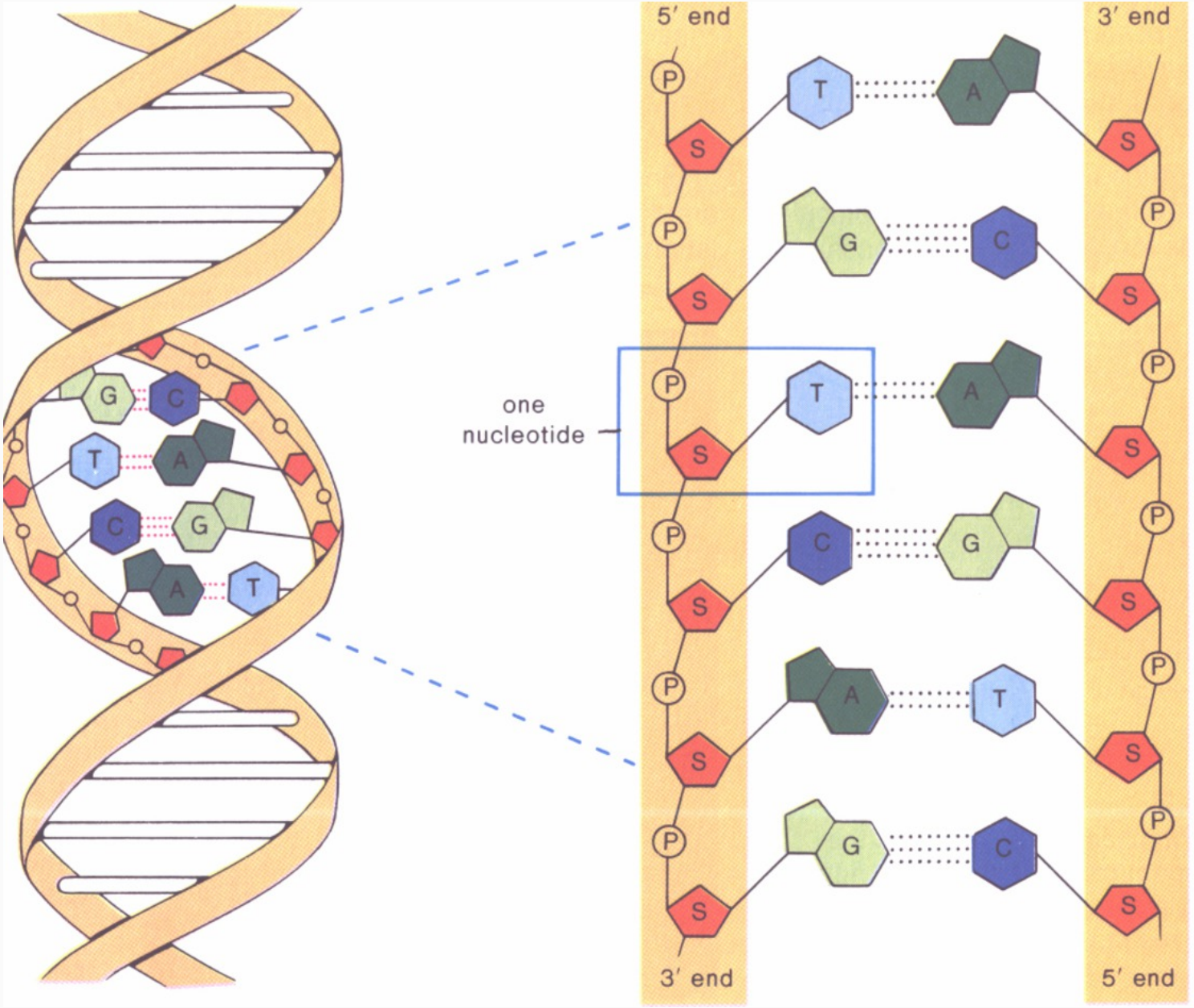


Figure 16. DNA双螺旋结构

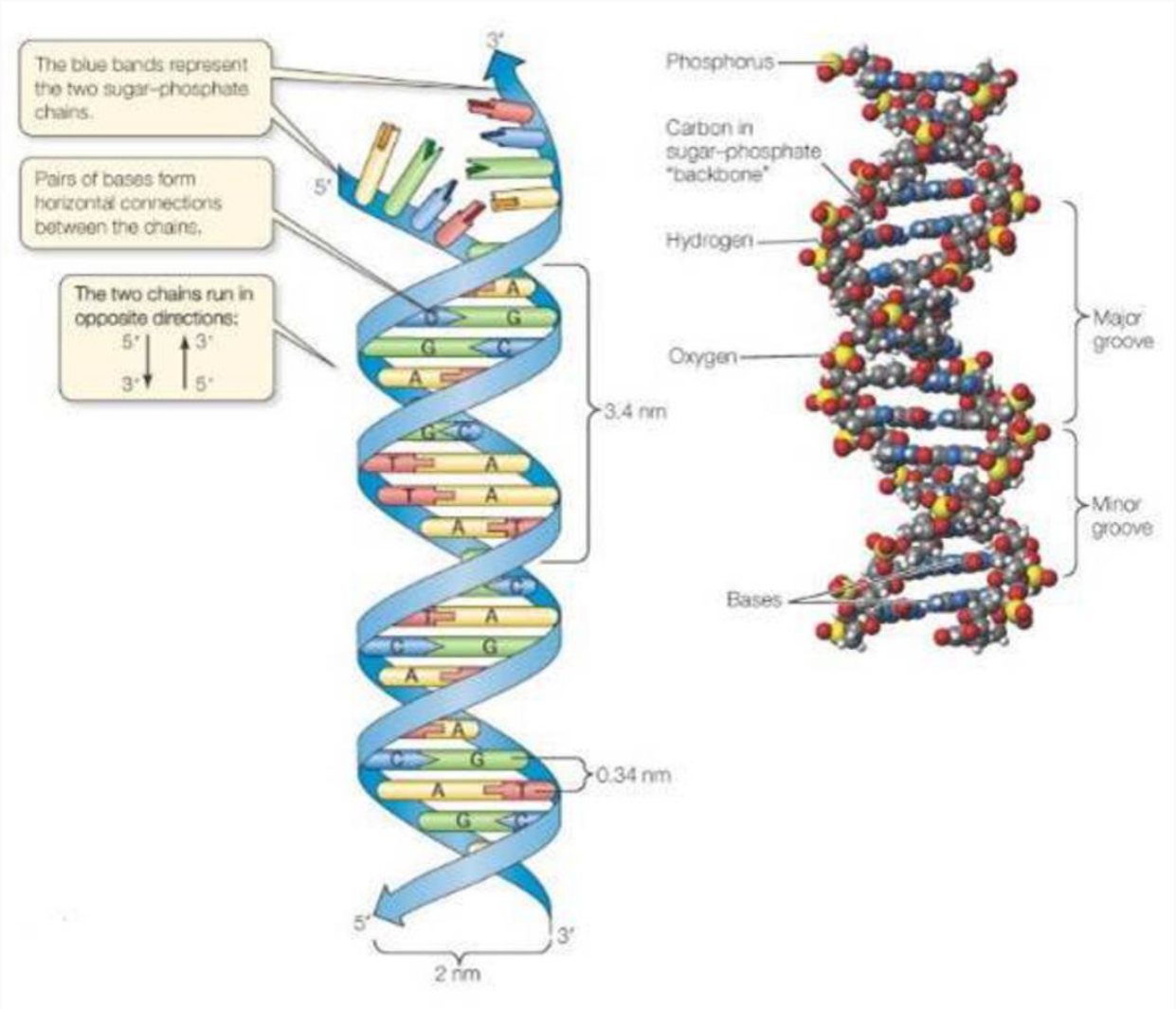


Figure 17. DNA双螺旋结构2

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.

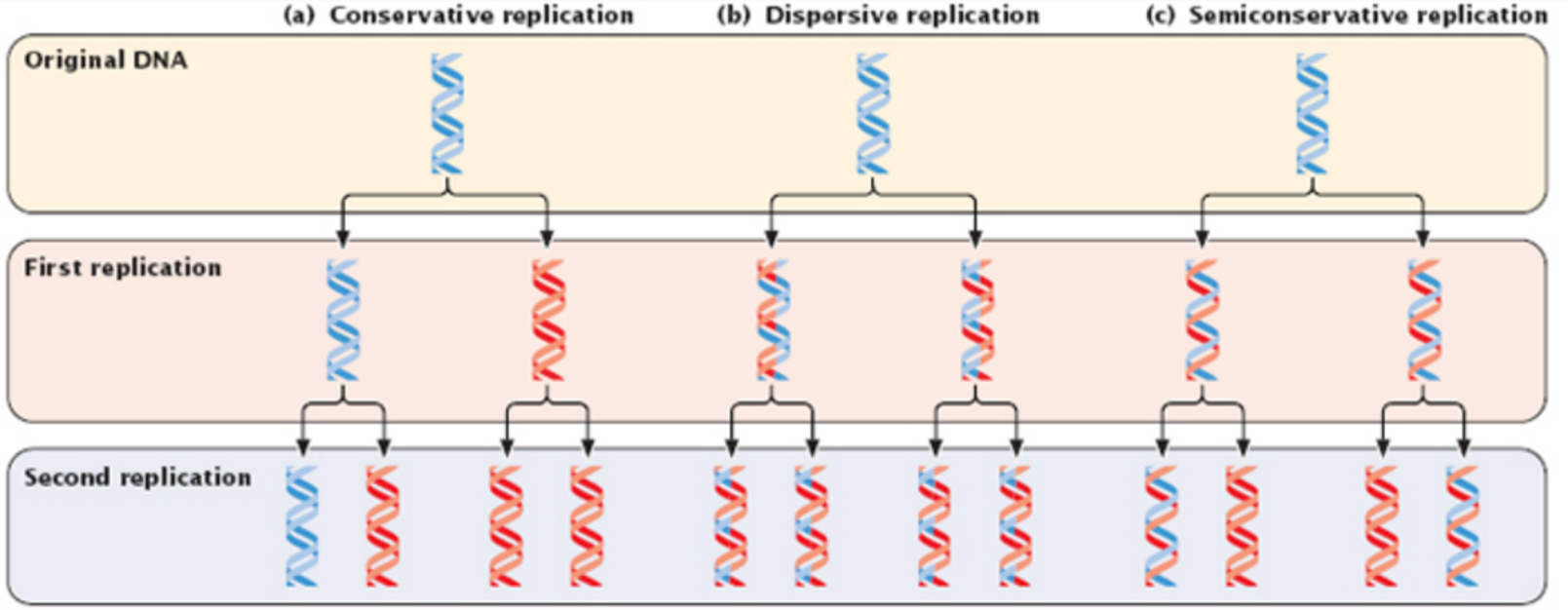


Figure 18. Three alternate schemes of replication

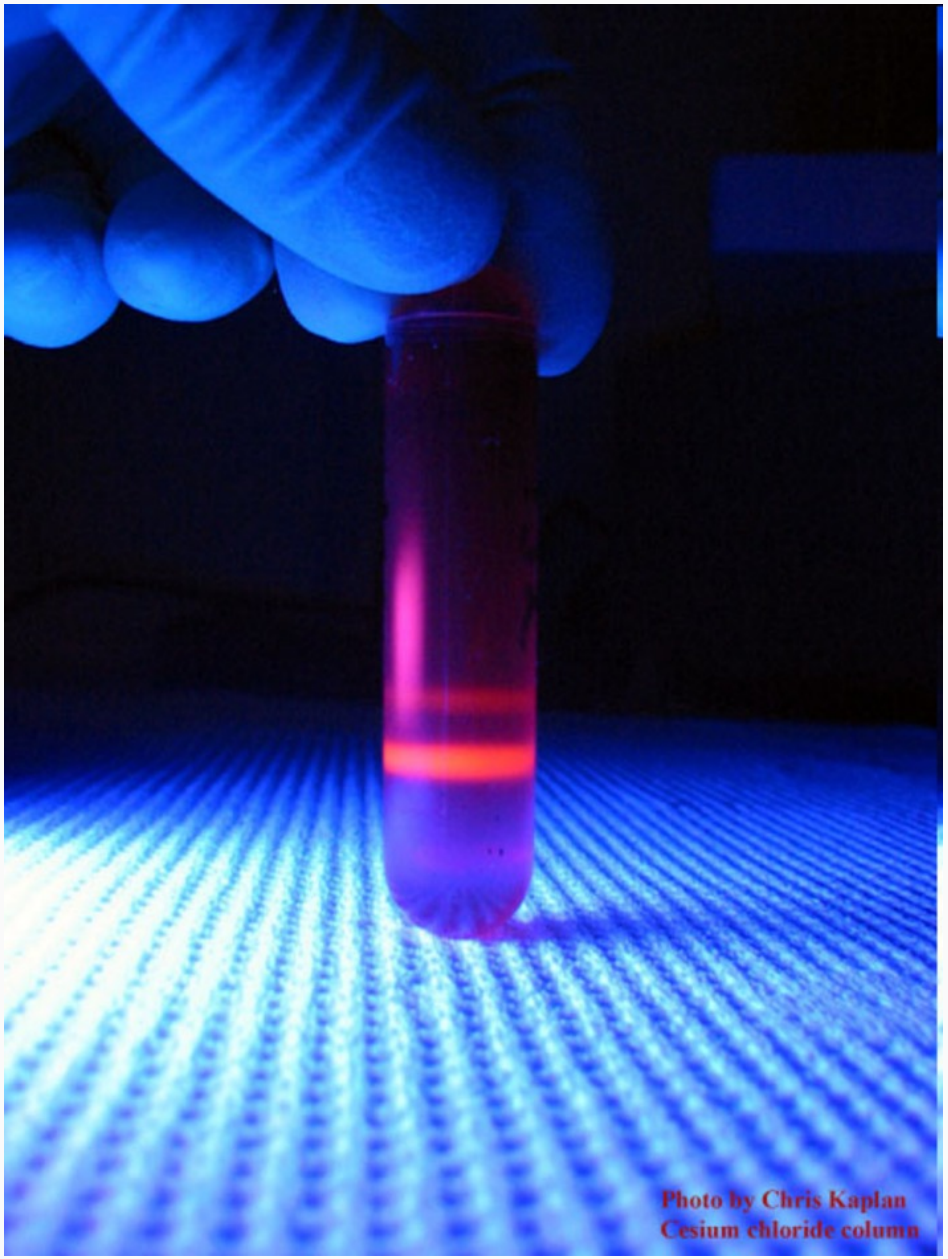


Figure 19. DNA密度梯度离心(CsCl, 氯化铯)

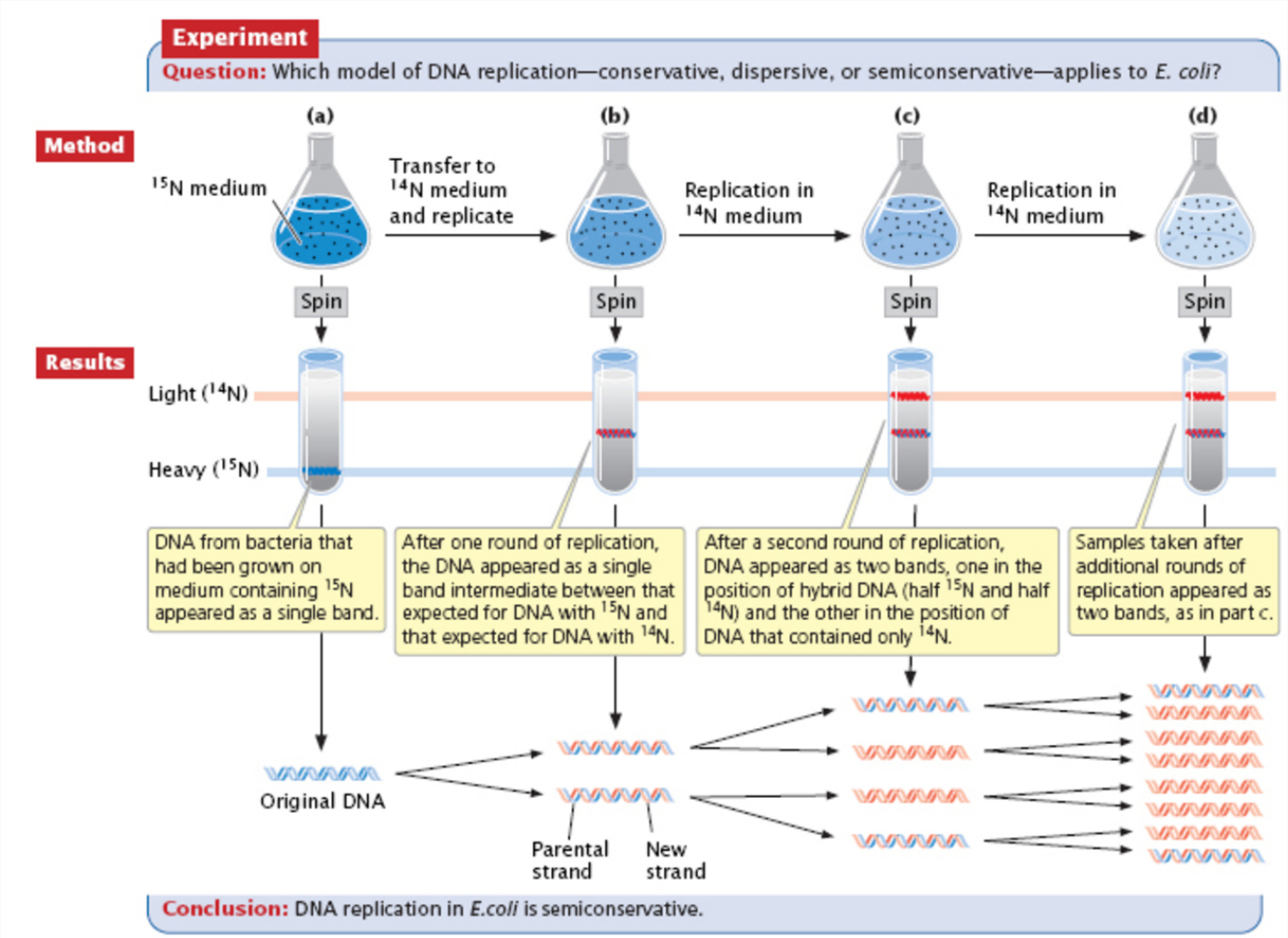


Figure 20. 大肠杆菌中的DNA复制[1]

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

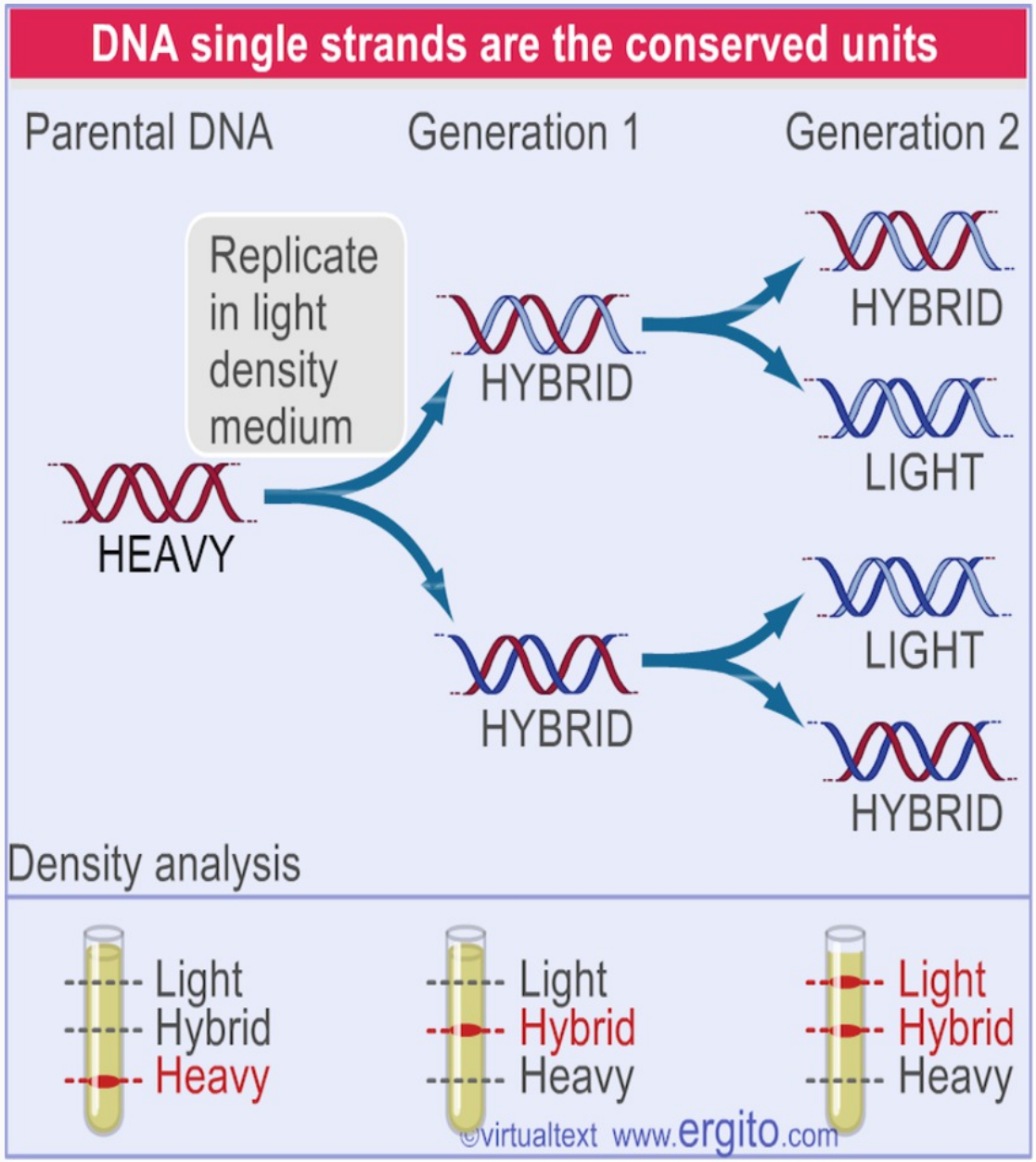


Figure 21. DNA单链是保留的单元

Figure 22. DNA半保留复制

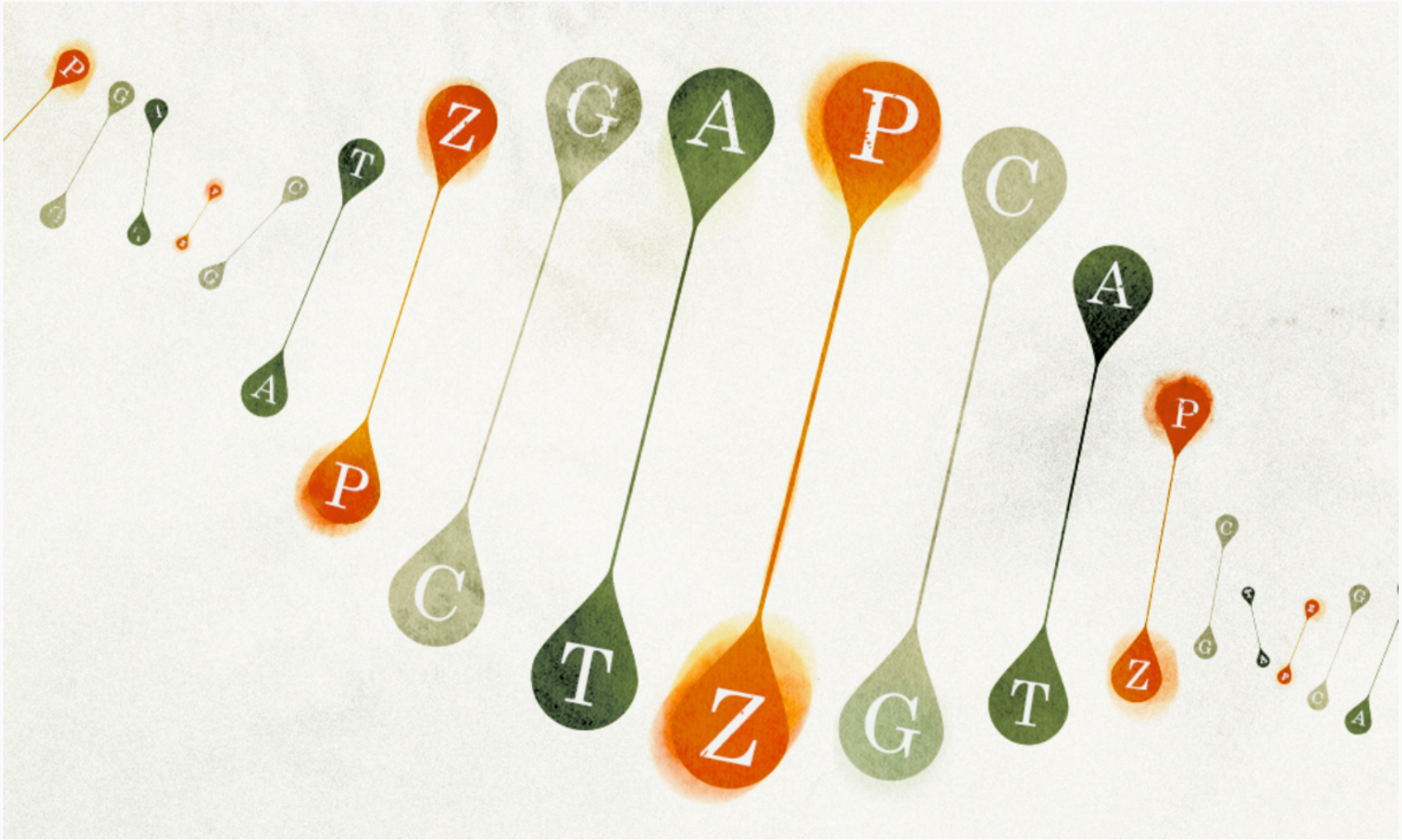


Figure 23. 合成的核苷酸P和Z

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.

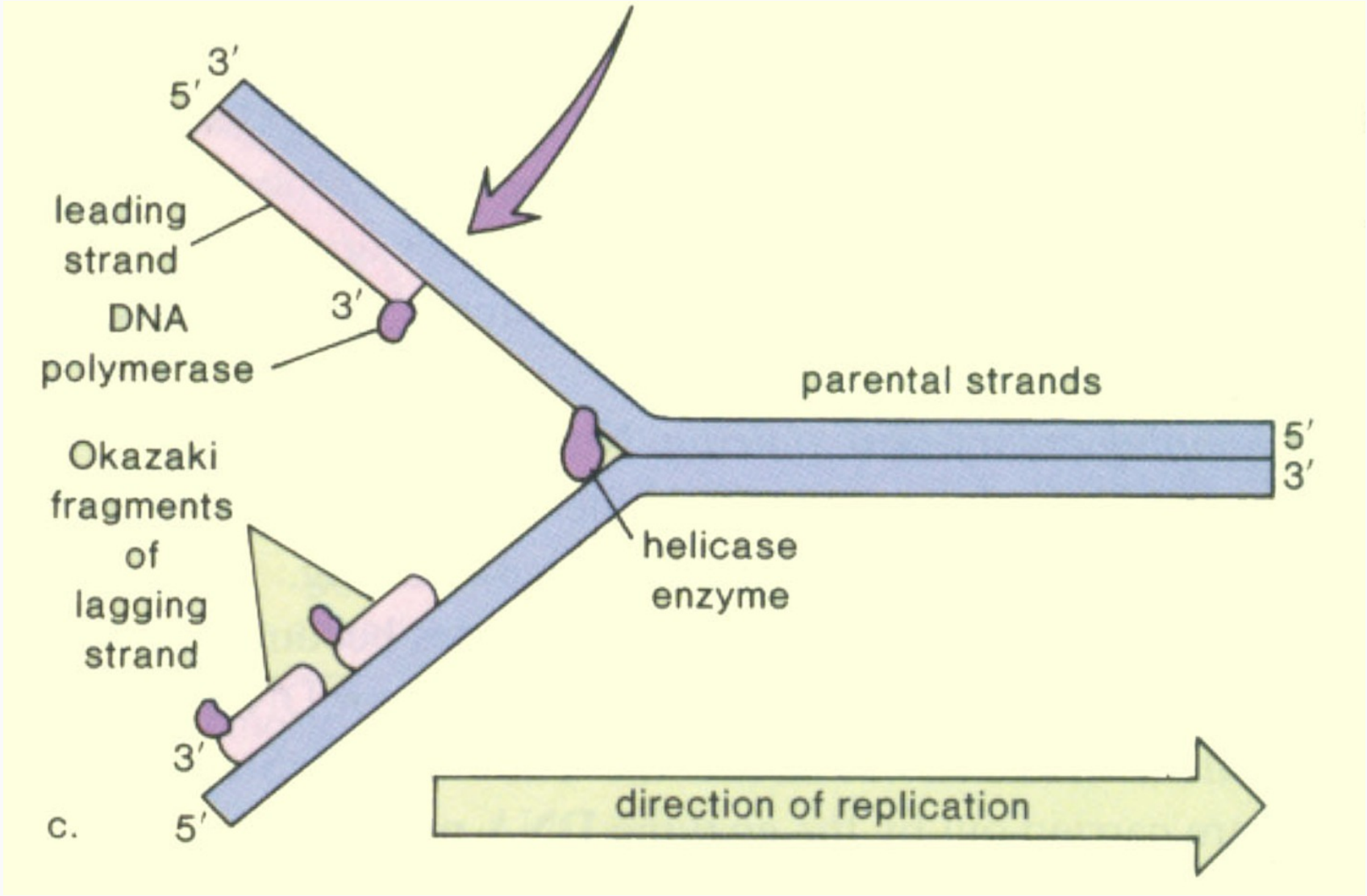


Figure 24. 复制叉

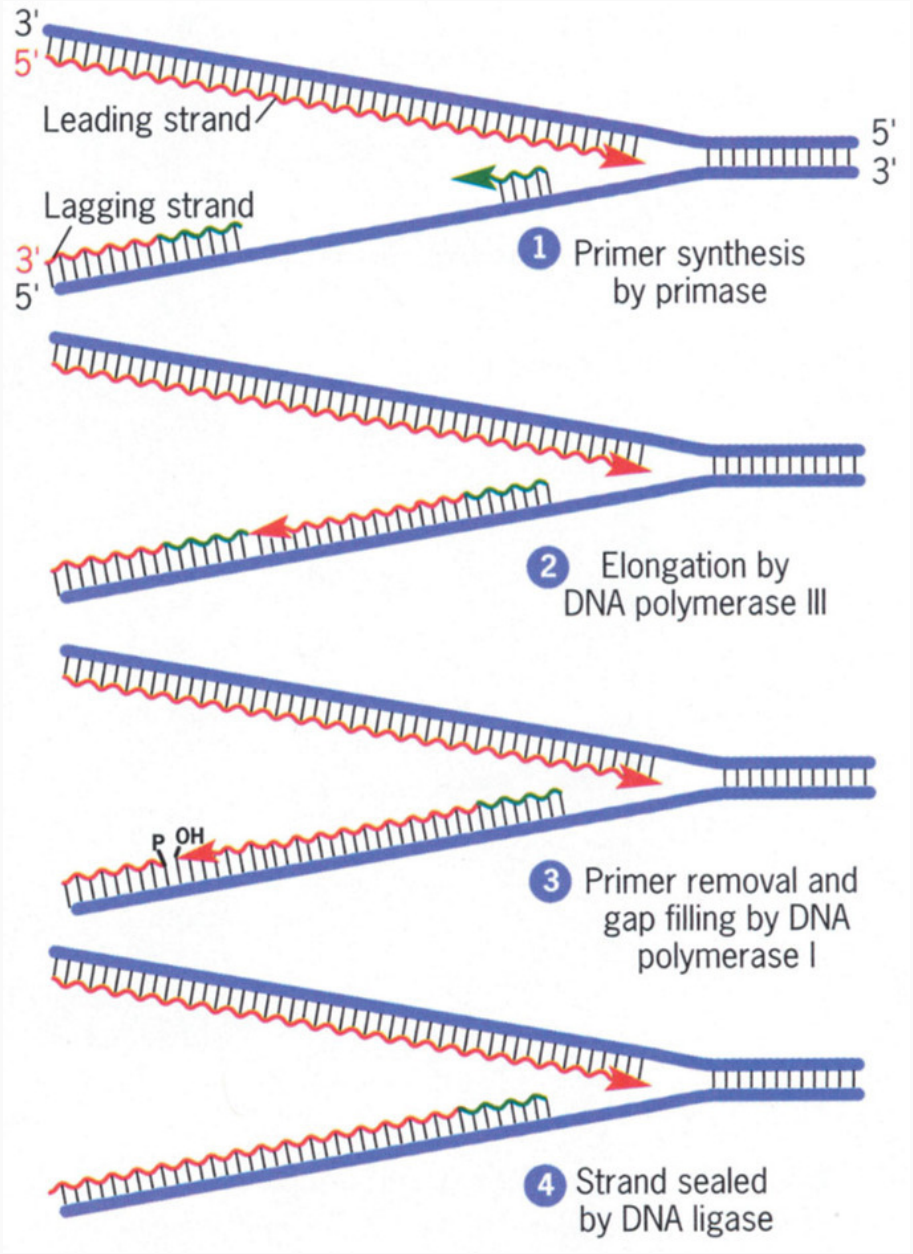


Figure 25. RNA引物的去除

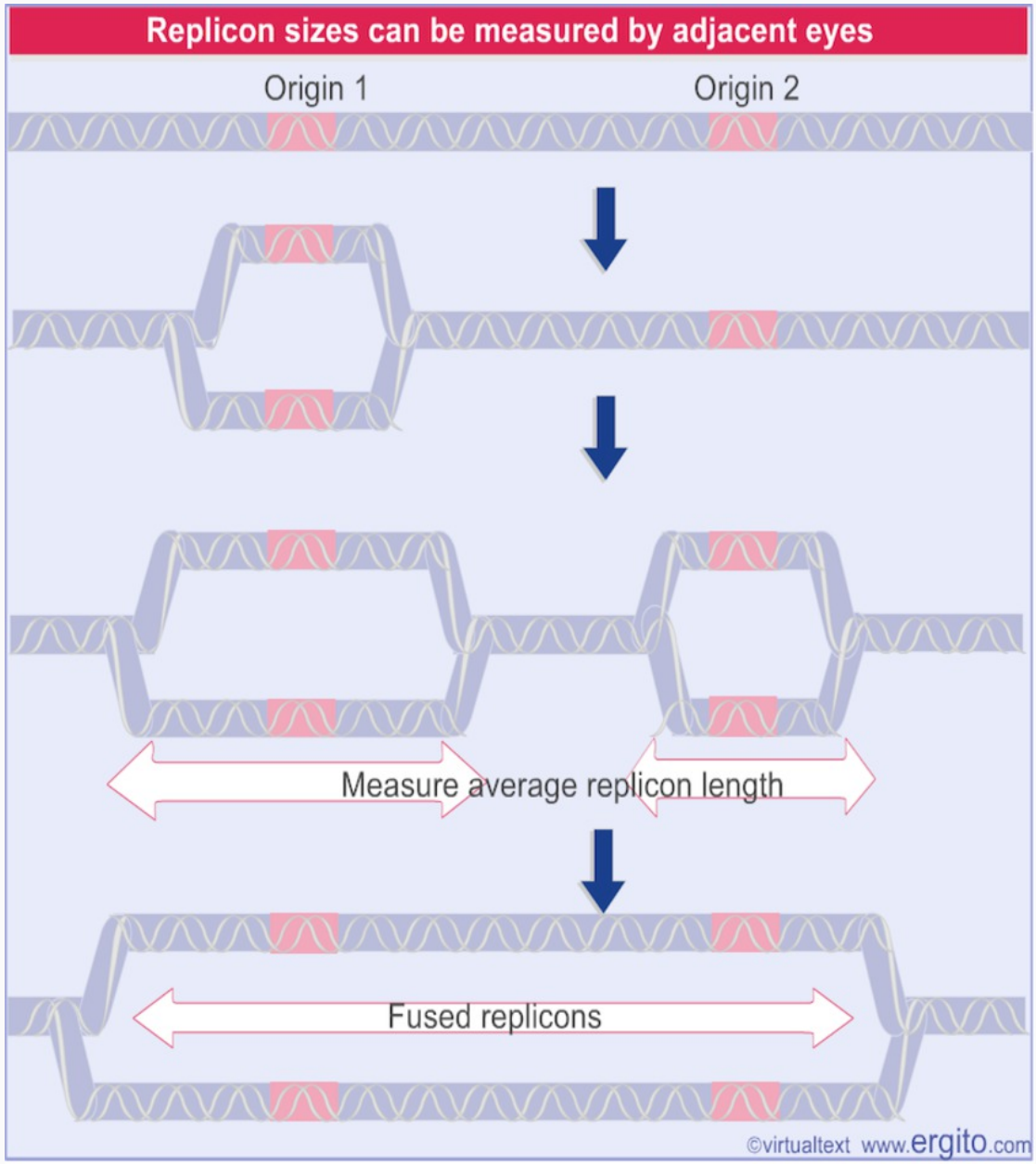


Figure 26. 真核生物的复制起始位点

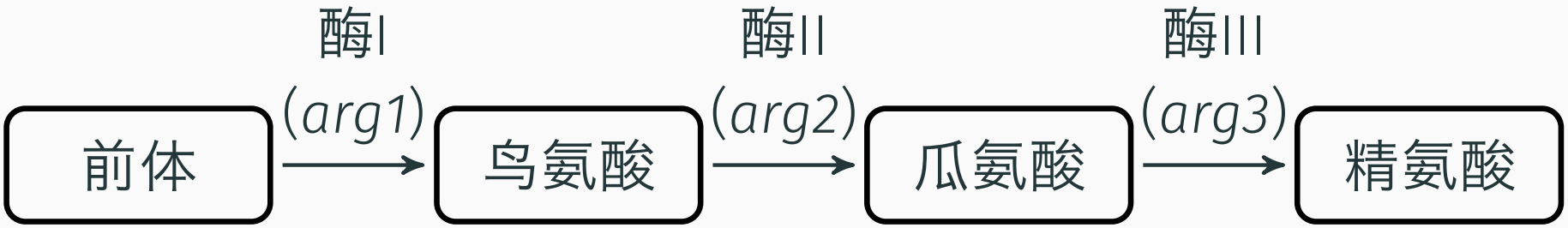
21.3 遗传信息流是从DNA到RNA到蛋白质

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)
     - ...

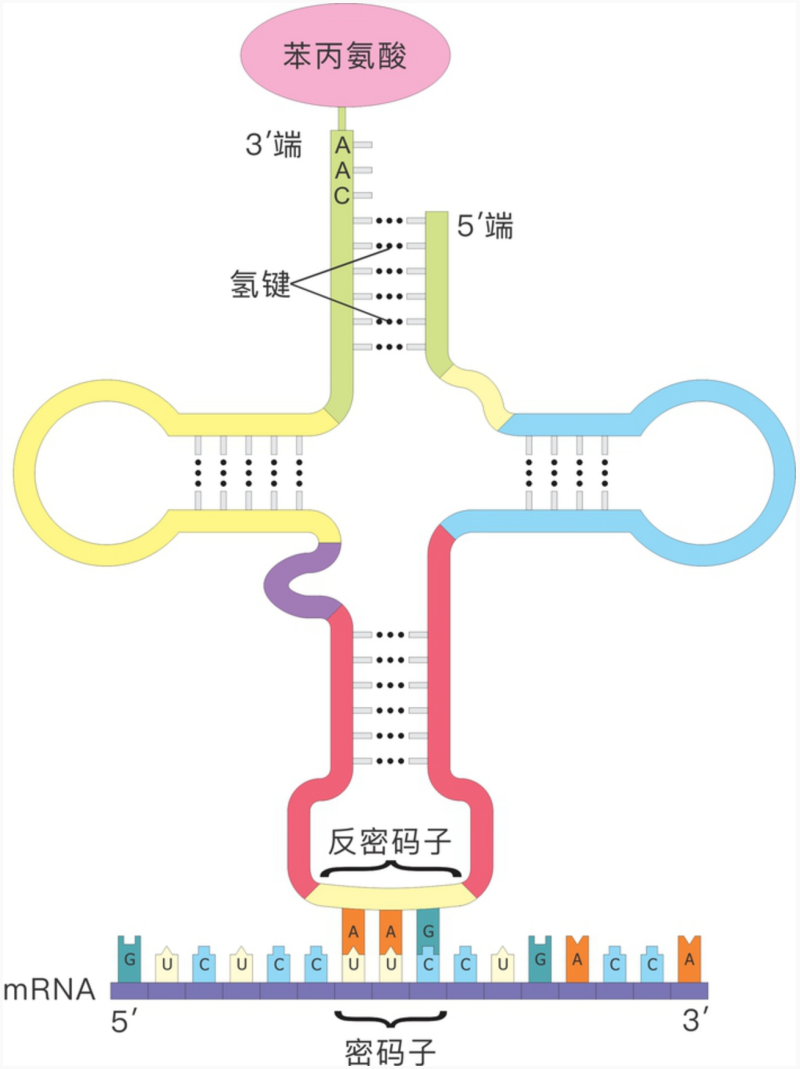


Figure 27. tRNA结构

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.

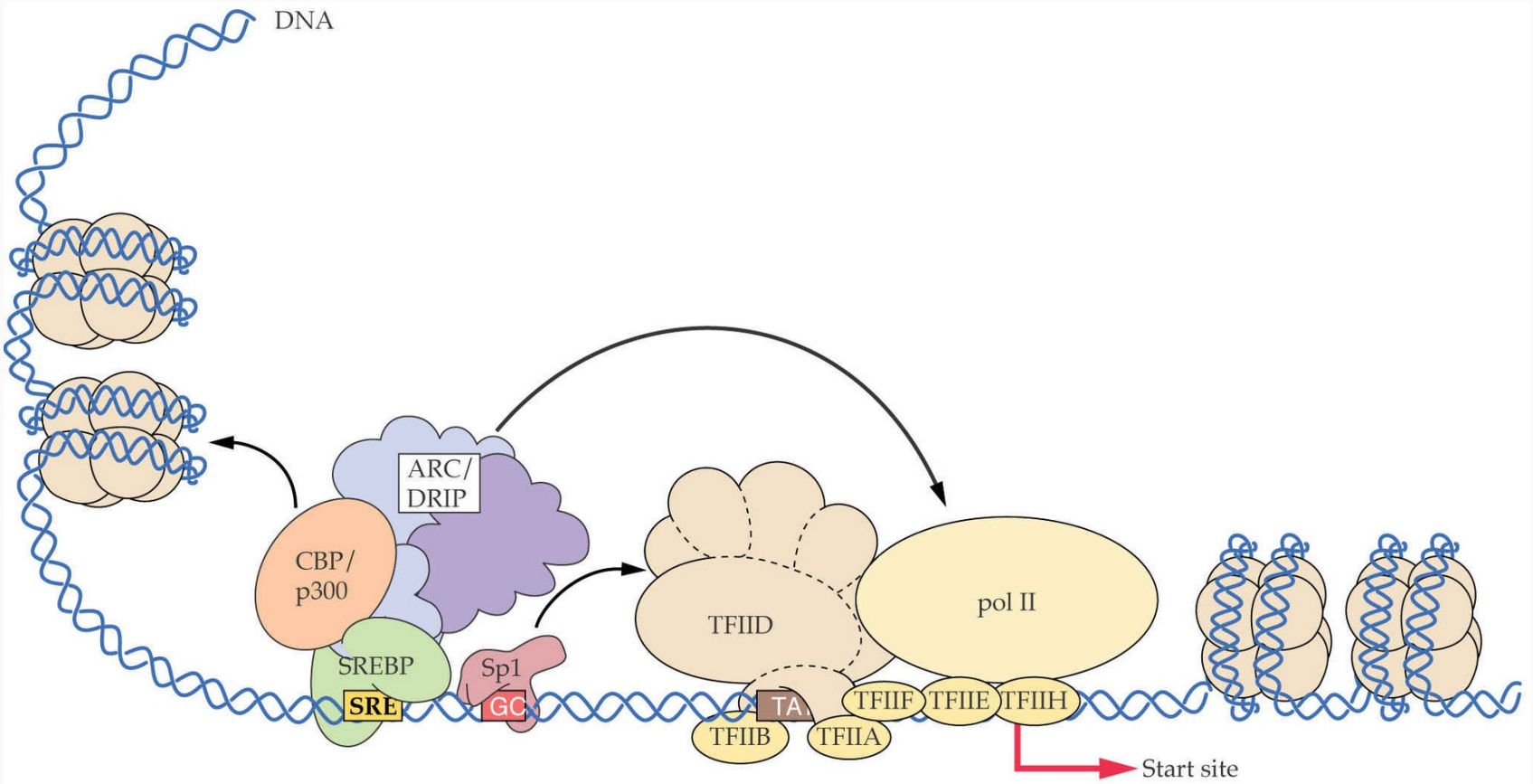


Figure 28. 基因转录起始

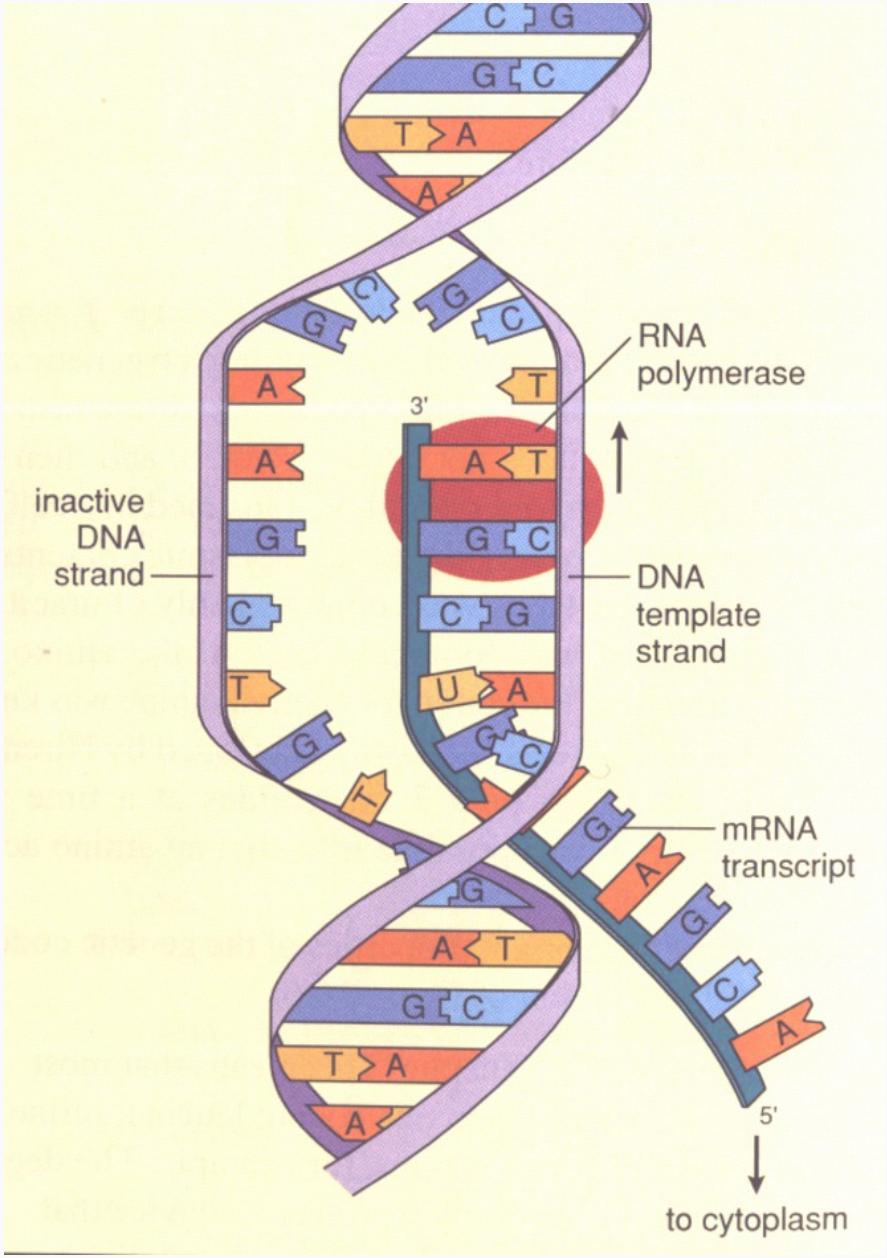

RNA
polymerase
3'
inactive
DNA
strand
DNA
template
strand
mRNA
transcript
5'
to cytoplasm

Figure 29. 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

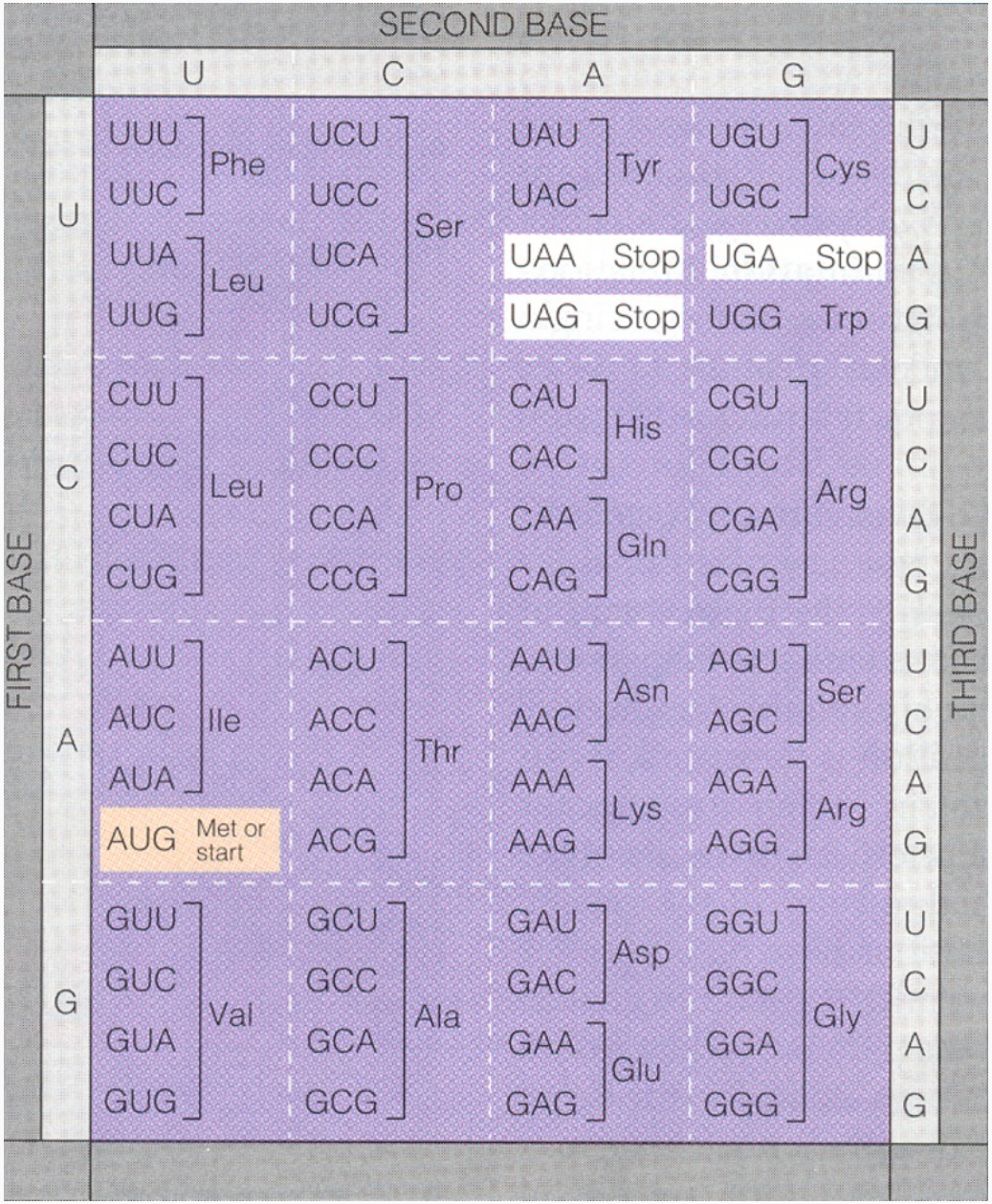


Figure 30. 遗传密码表

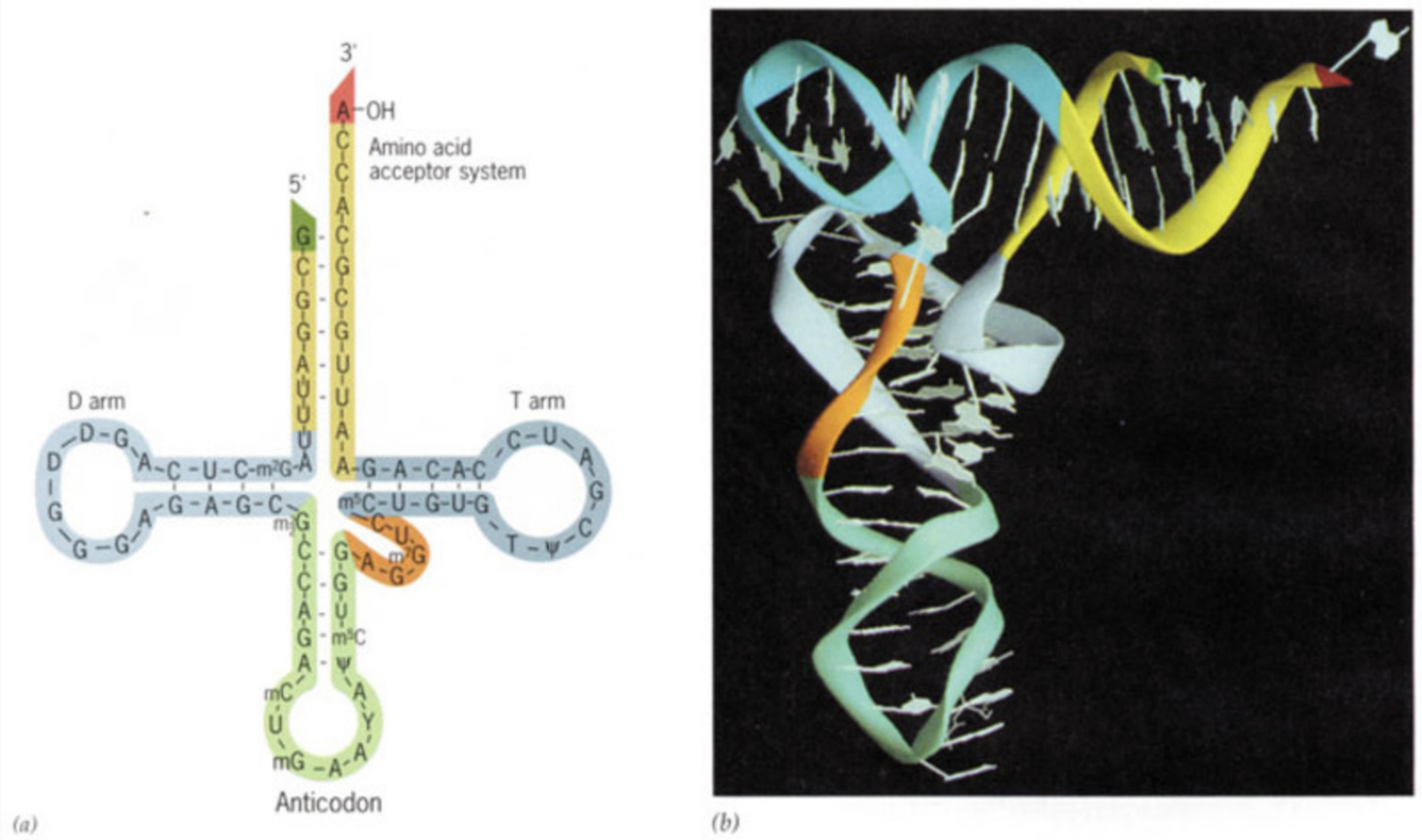


Figure 31. tRNA三级结构

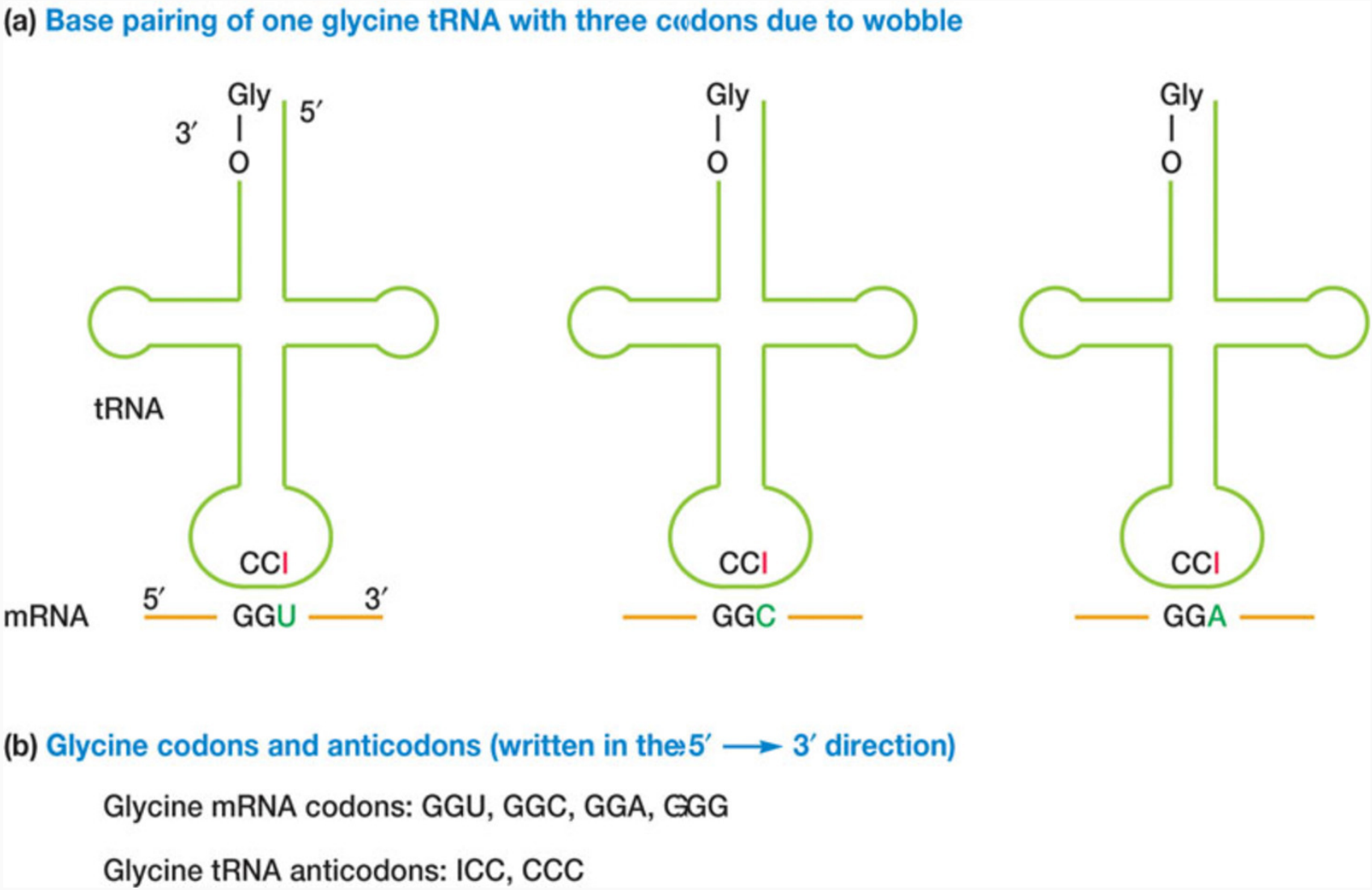


Figure 32. 摆动(Wobble)

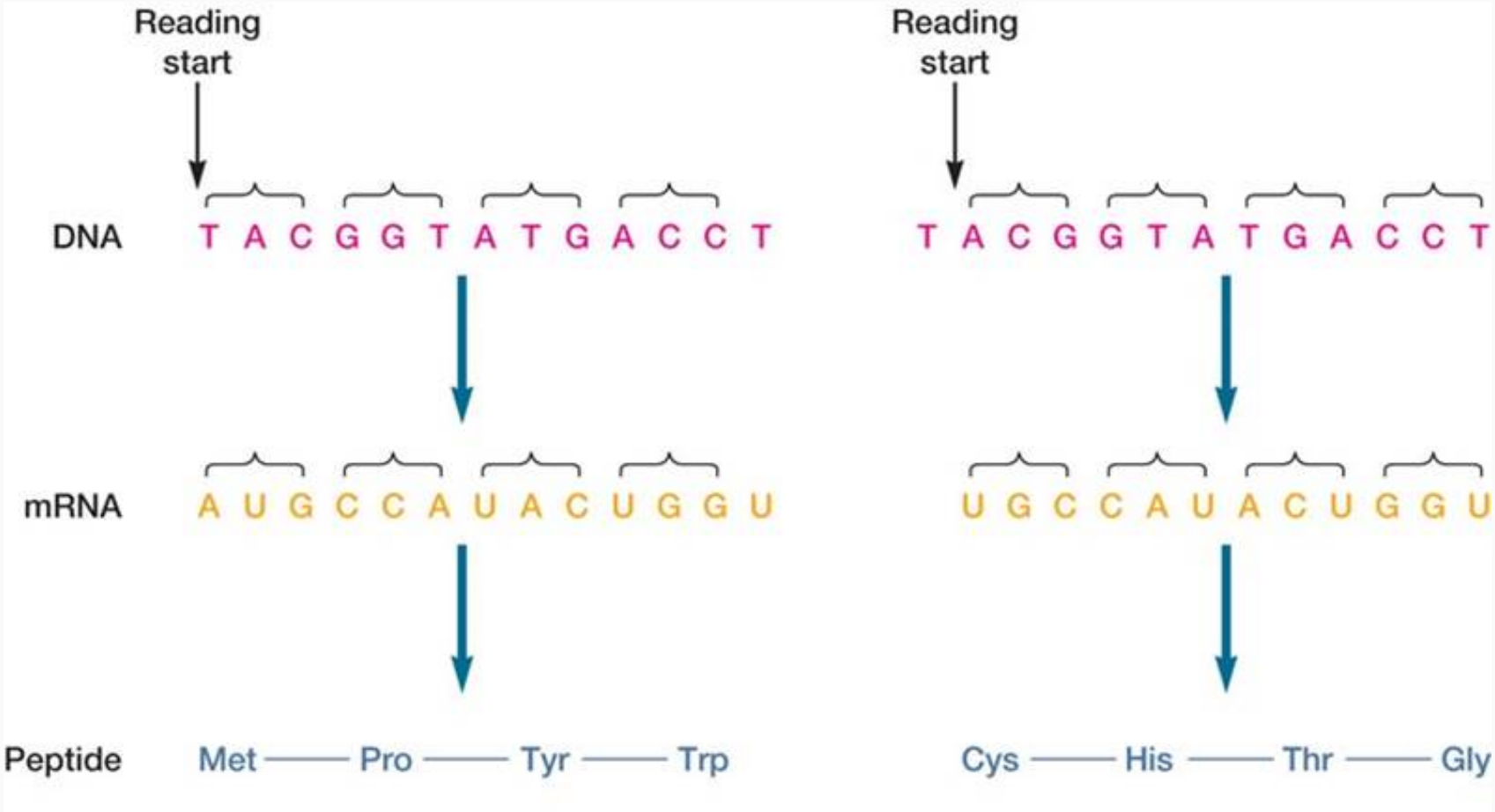


Figure 33. 阅读框及其重要性

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

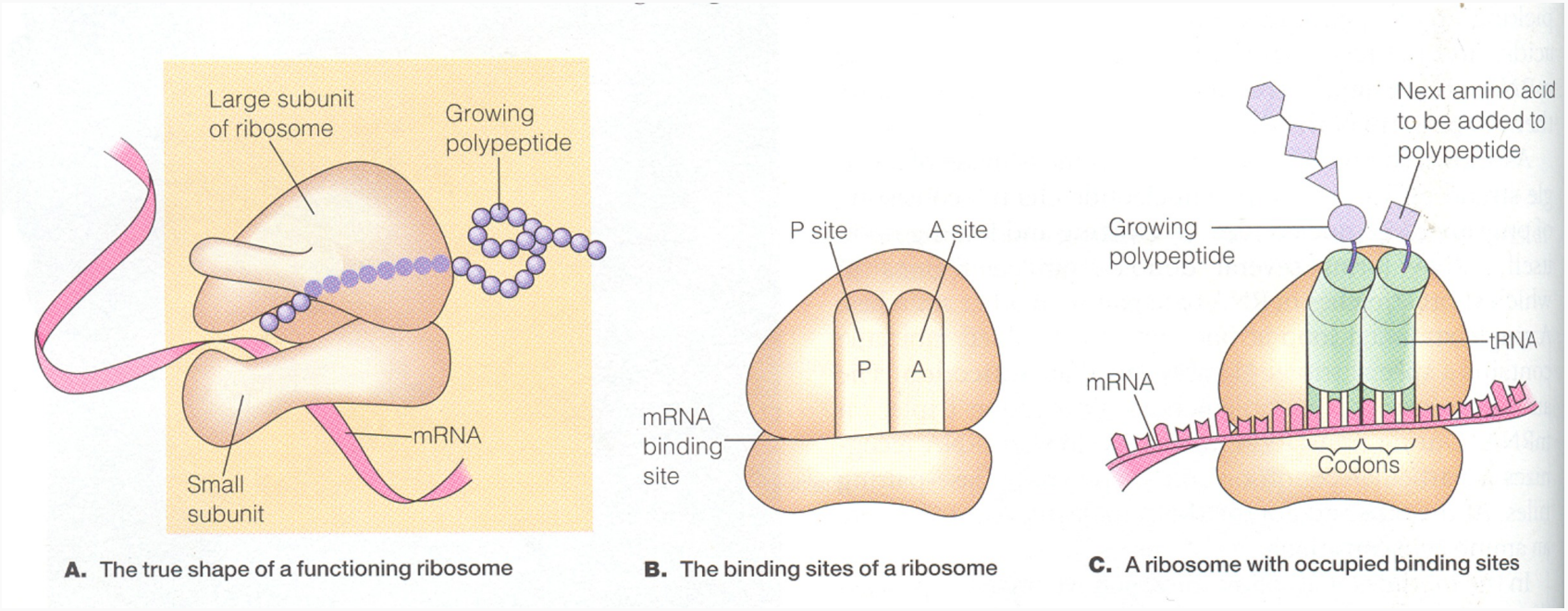


Figure 34. 核糖体

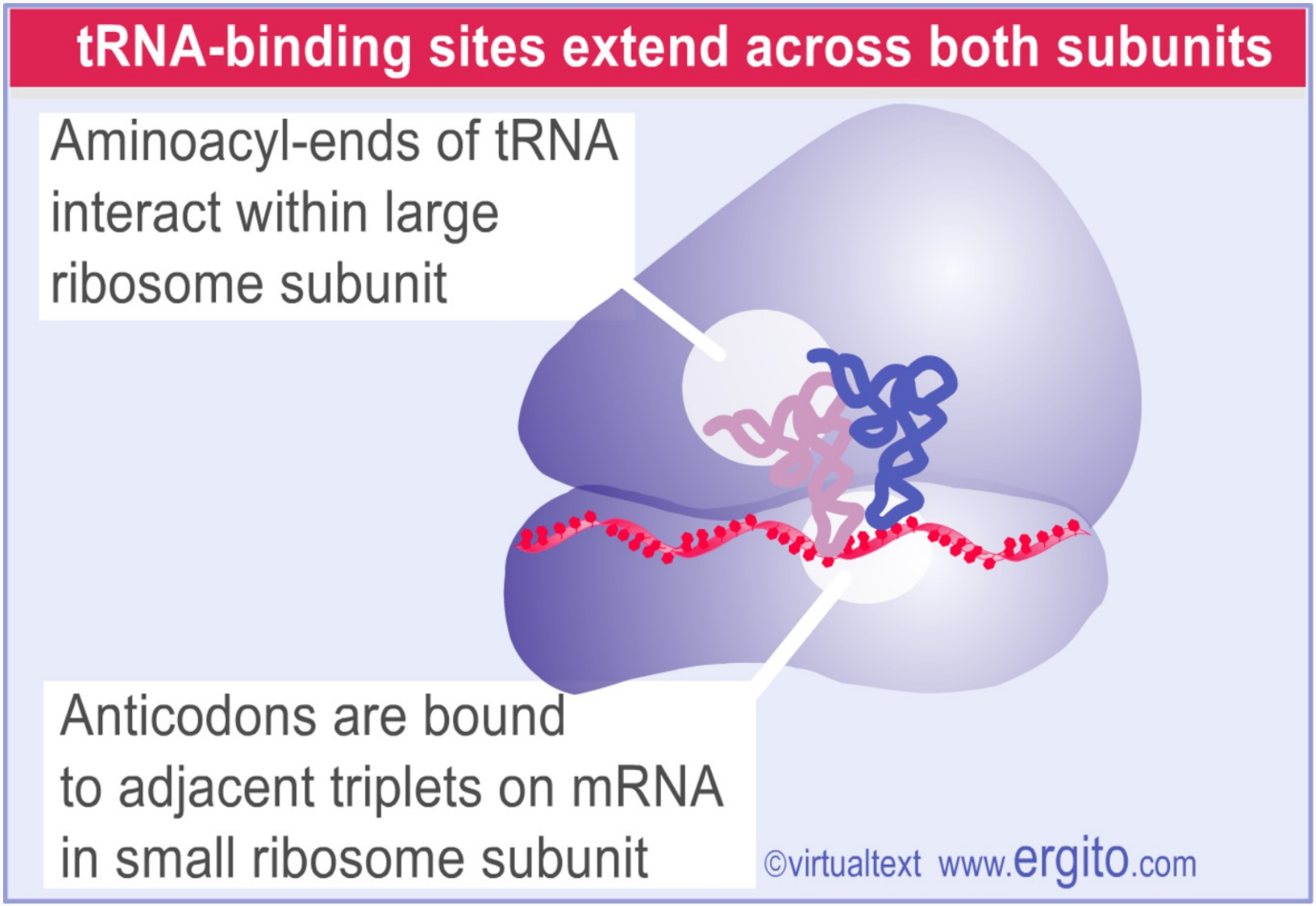


Figure 35. 核糖体中的tRNA结合位点

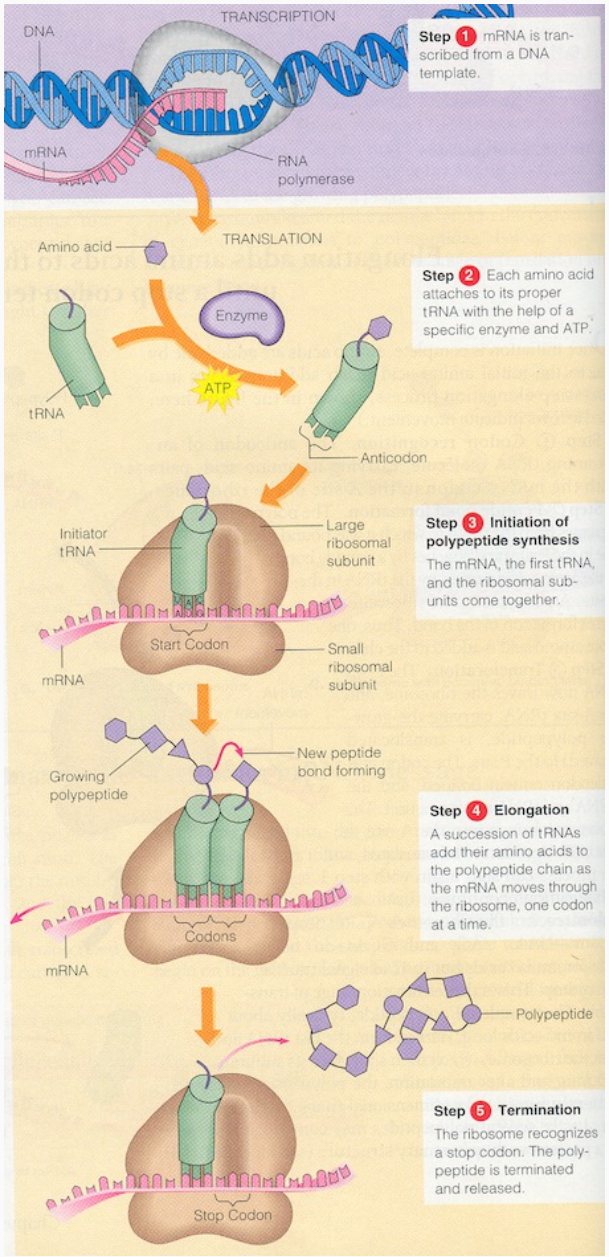


Figure 36. 转录和翻译

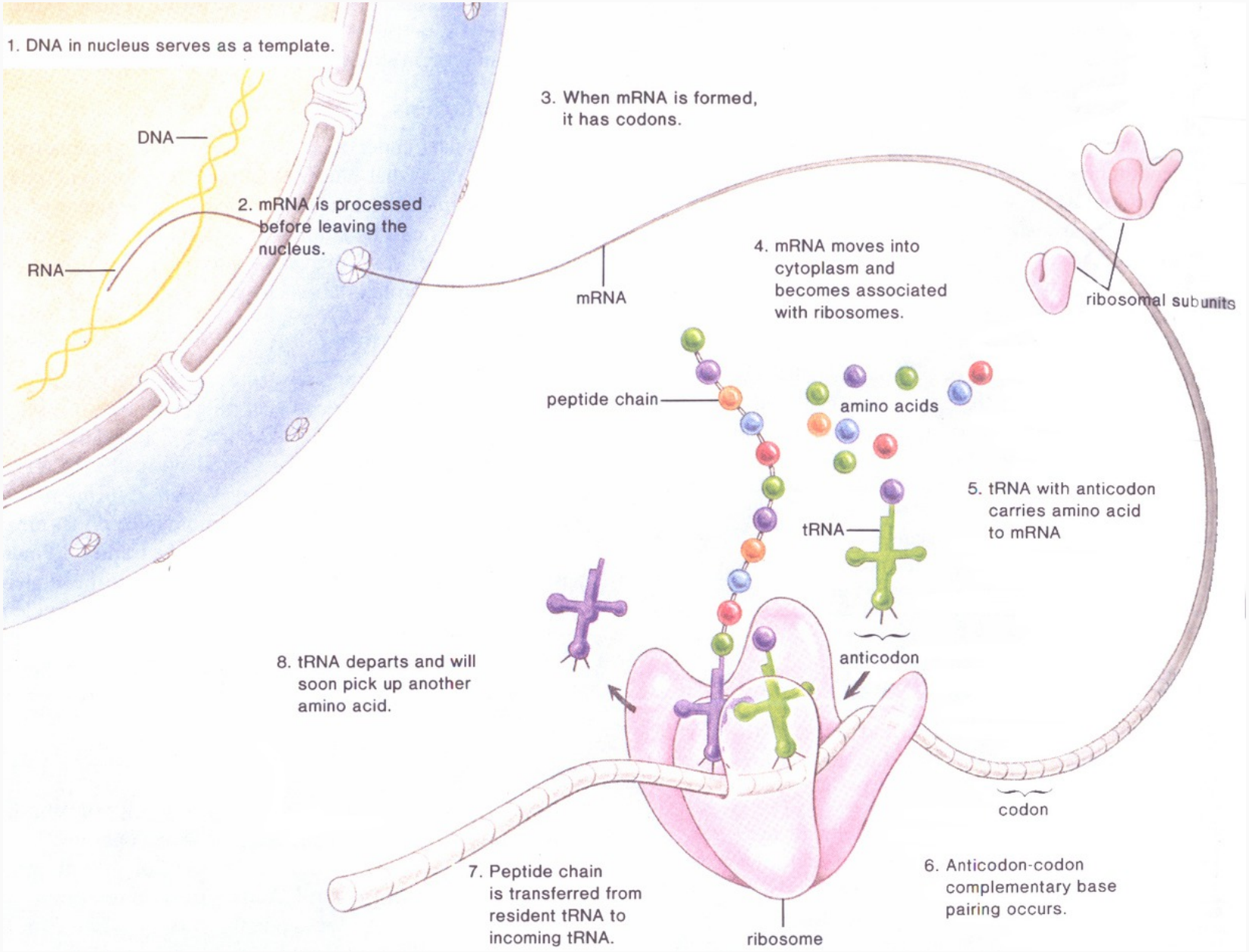
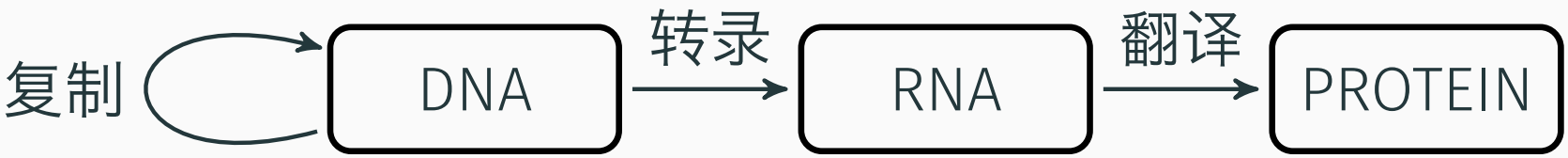
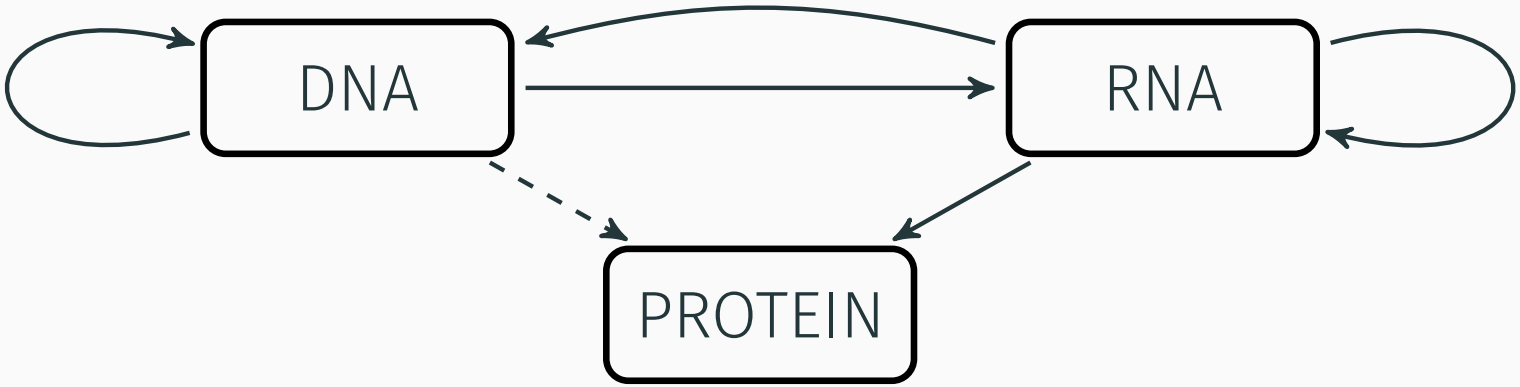


Figure 37. 转录和翻译2

21.3.4 中心法则

1. 遗传信息从DNA到RNA到蛋白质




DNA
RNA
PROTEIN

2. 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)

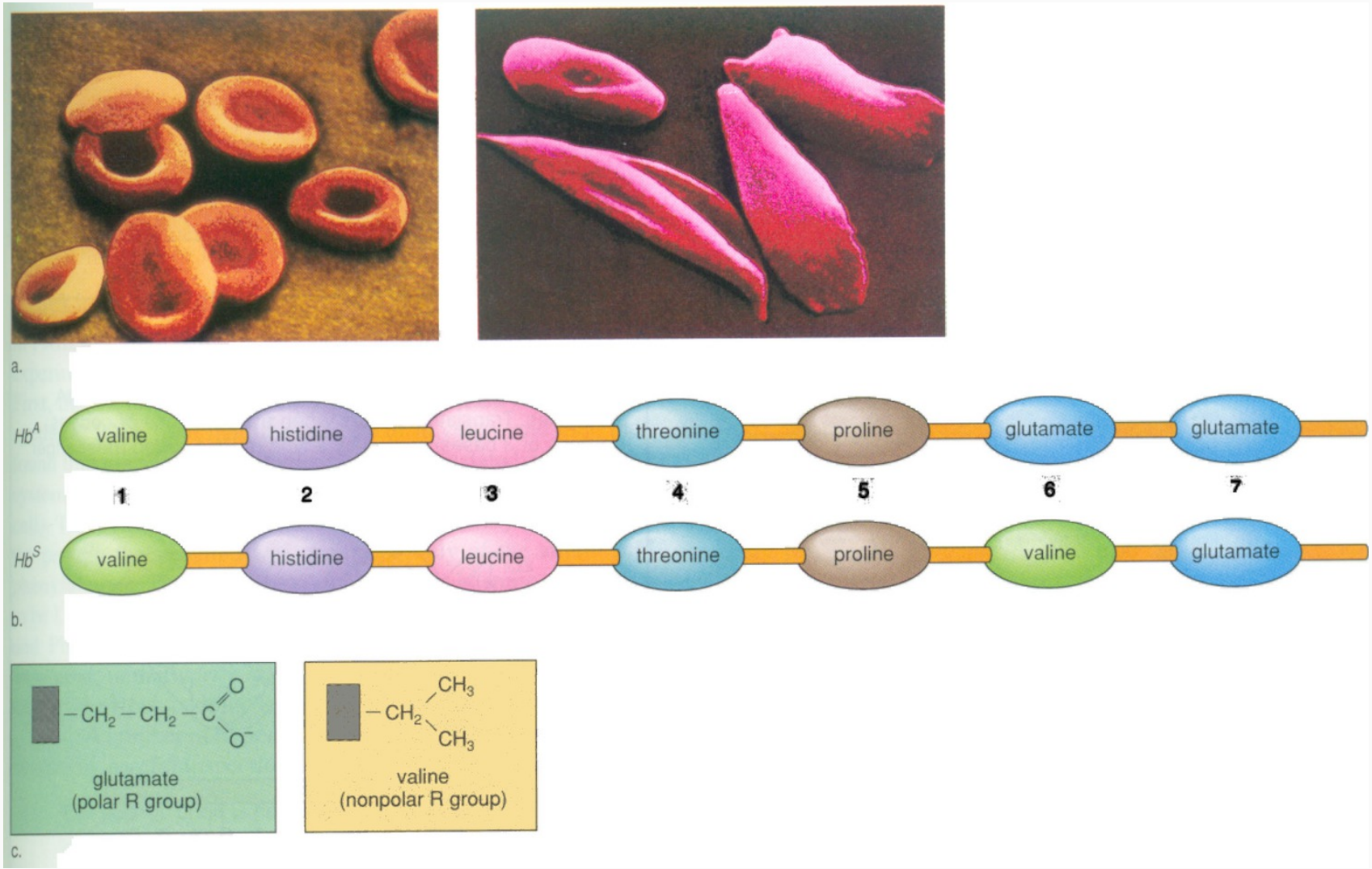


Figure 38. 镰刀形贫血症

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

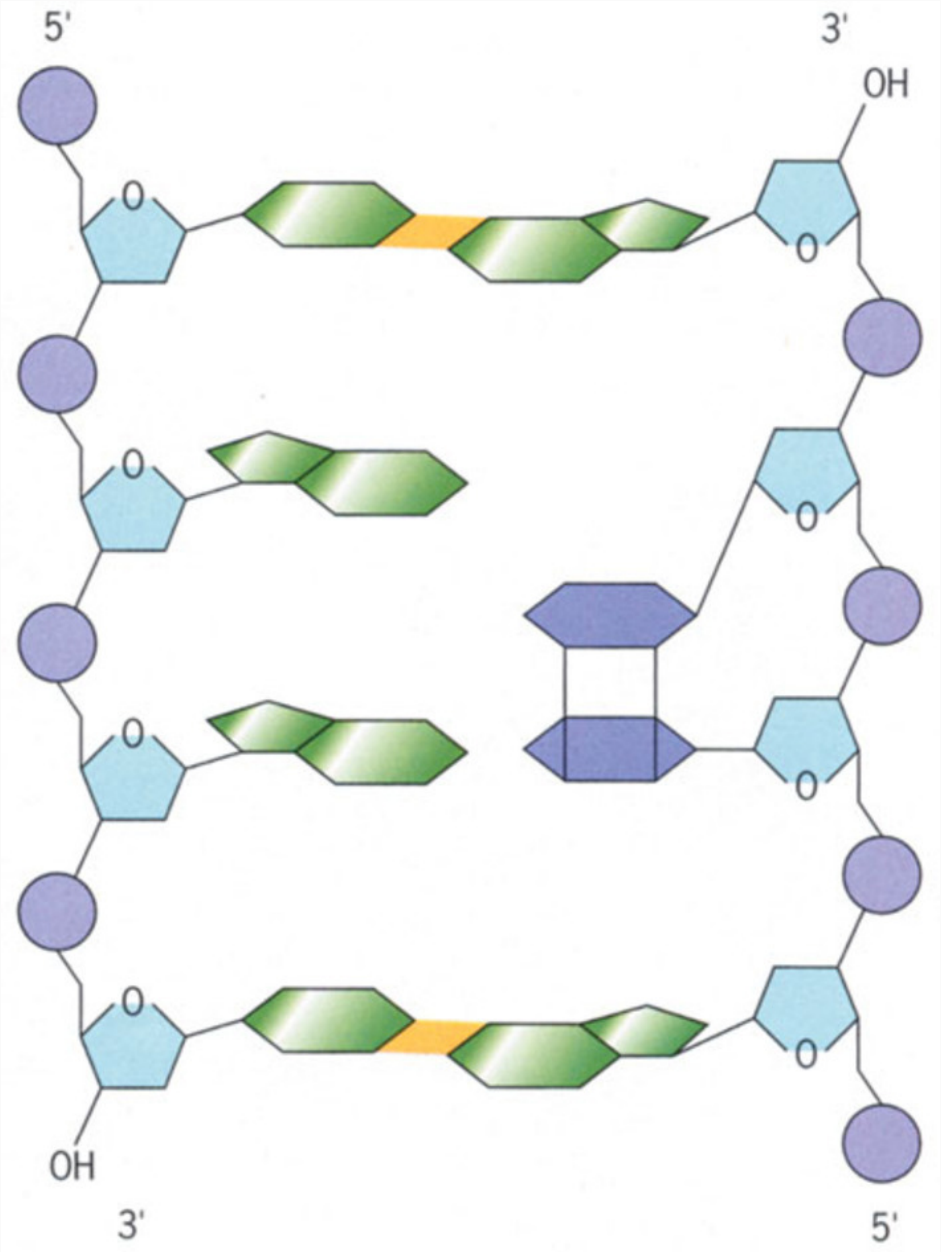


Figure 39. TT二聚体