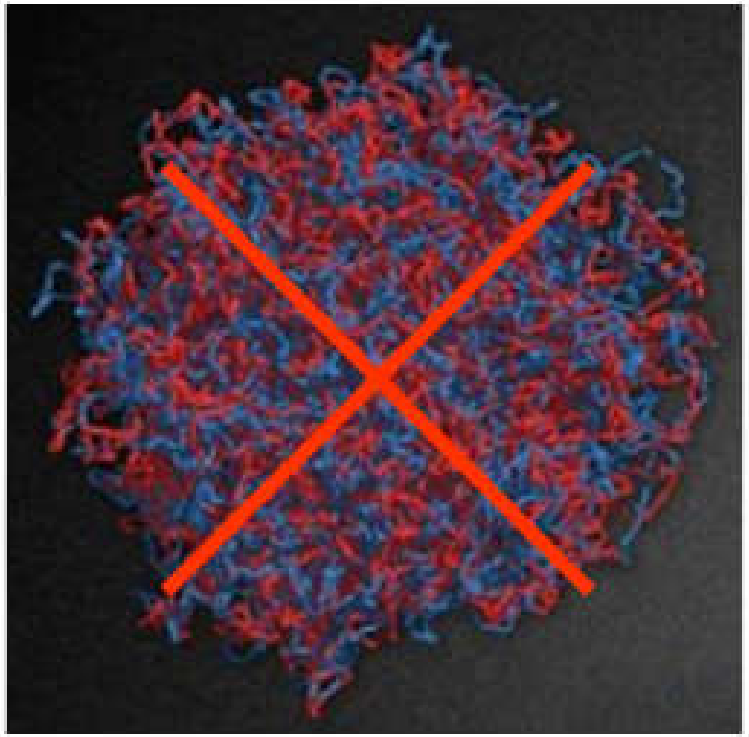
Part Ⅰ Gene structure and function

Chapter 1 Prokaryotic and eukaryotic chromosome structure

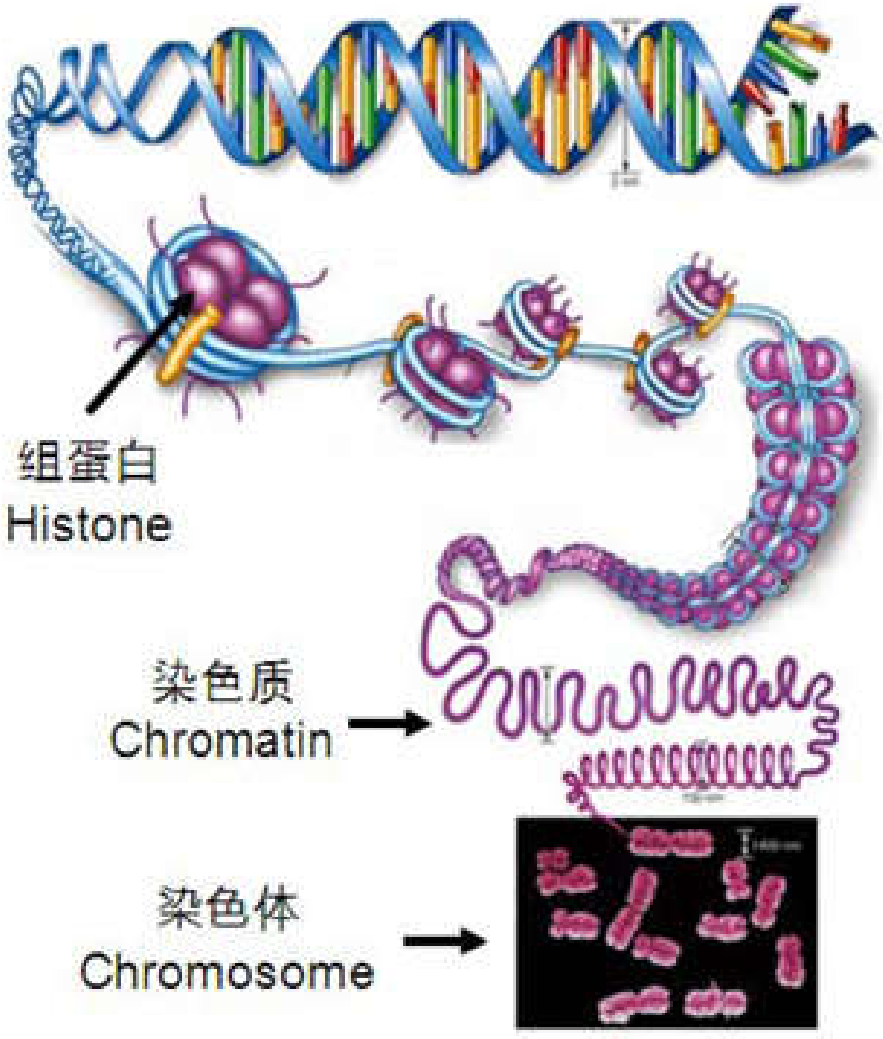
DNA is highly compacted in all types of genomes				
Compartment	Shape	Dimensions	Type of Nucleic Acid	Length
TMV	filament	0.008 x 0.3 μm	One single-stranded RNA	2 μm = 6.4 kb
Phage fd	filament	0.006 x 0.85 μm	One single-stranded DNA	2 μm = 6.0 kb
Adenovirus	icosahedron	0.07 μm diameter	One double-stranded DNA	11 μm = 35.0 kb
Phage T4	icosahedron	0.065 x 0.10 μm	One double-stranded DNA	55 μm = 170.0 kb
E. coli	cylinder	1.7 x 0.65 μm	One double-stranded DNA	1.3 mm = 4.2×10^3 kb
Mitochondrion (human)	oblate spheroid	3.0 x 0.5 μm	~10 identical double-stranded DNAs	50 μm = 16.0 kb
Nucleus (human)	spheroid	6 μm diameter	46 chromosomes of double-stranded DNA	1.8 m = 6×10^6 kb

DNA分子怎么折叠压缩？

随意压缩？



蛋白质辅助下有序压缩



What are chromosomes?

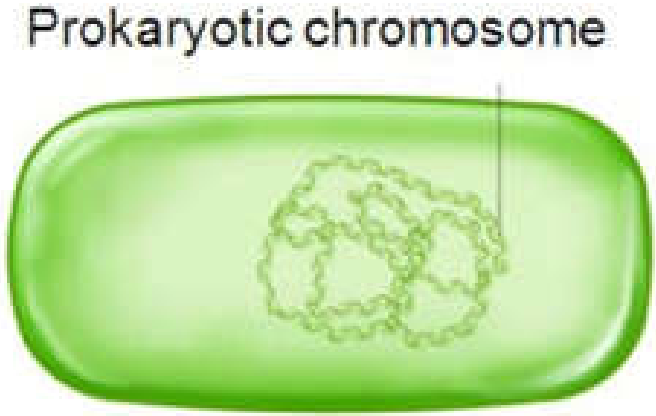
Chromosomes are the physical carriers of genetic information, consisting of DNA and associated proteins.

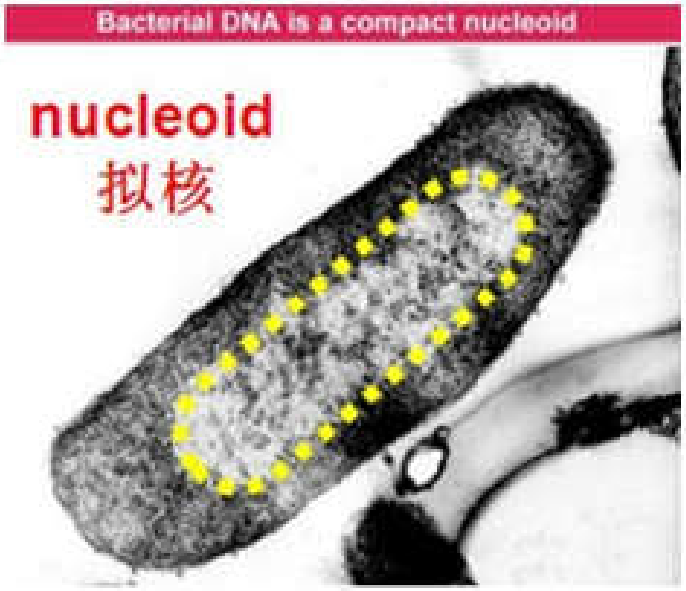
染色体是遗传信息的物理载体，由DNA和相关蛋白组成。

1. Prokaryotic chromosome structure

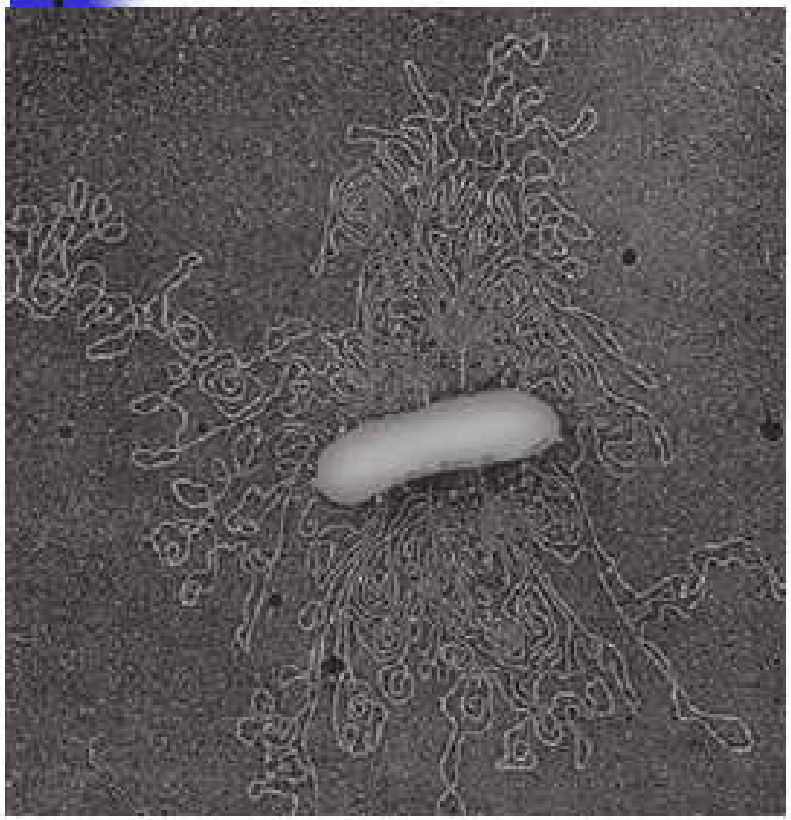
1.1 The *E.coli* chromosome

- A **single closed-circular** double-stranded DNA (**dsDNA**) molecule
- Associated proteins
- **Nucleoid** (拟核)



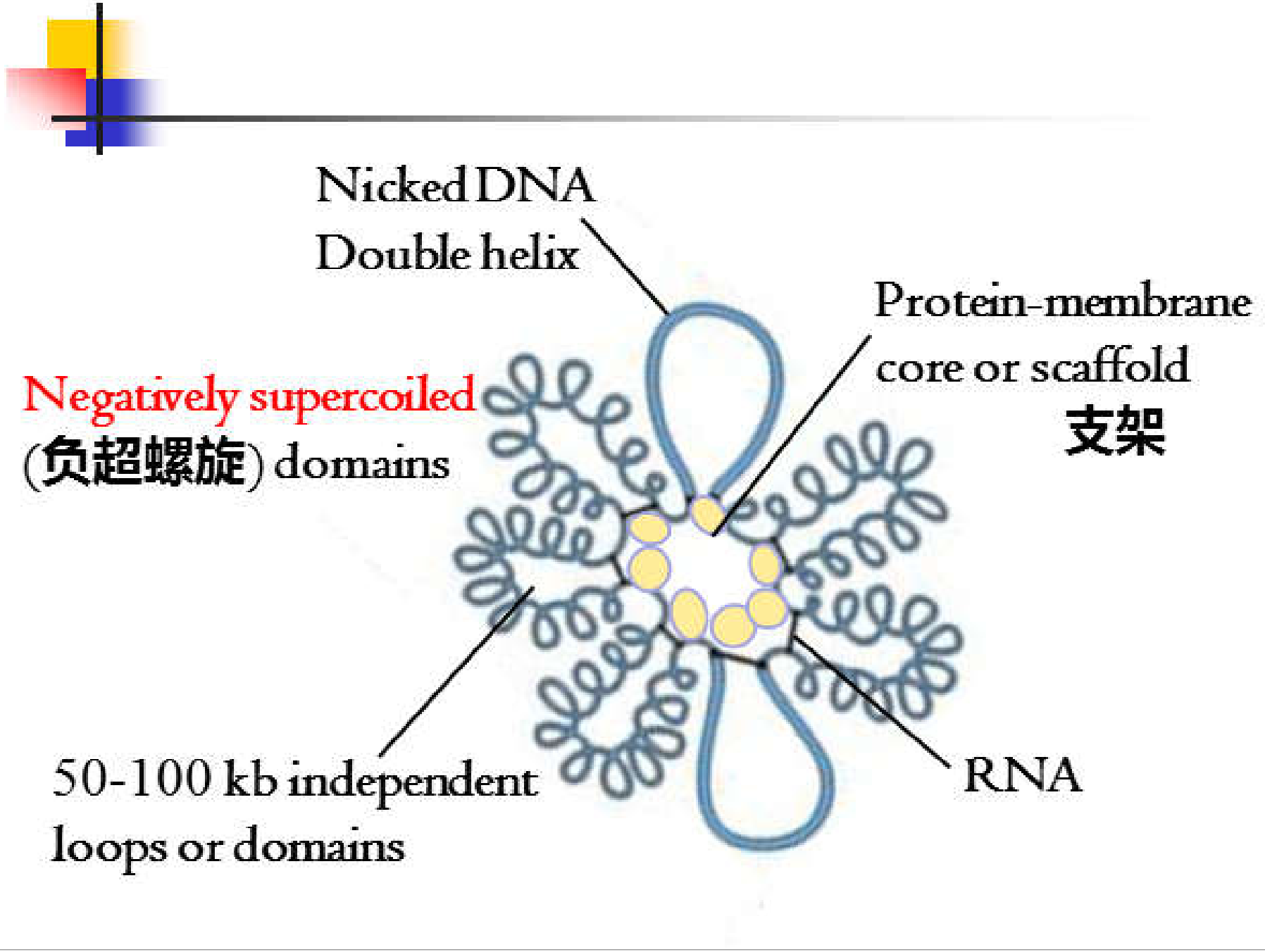


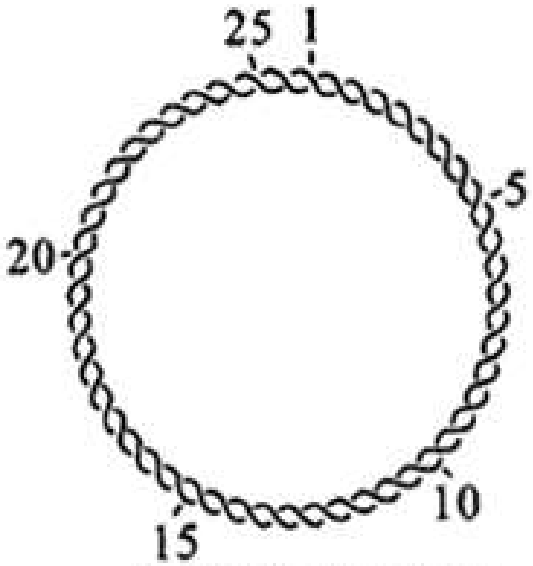
1.2 The *E.coli* DNA



E.coli 细胞裂解后，细菌拟核以带环的纤维形式被释放出来，并与细胞膜的碎片相附着。

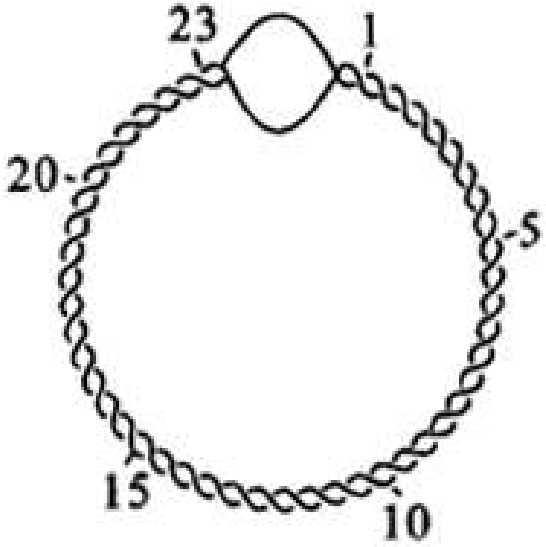
- The DNA consists of 50-100 domains or loops.
- The ends of loops are constrained by binding to a structure which probably consists of proteins attached to part of the cell membrane.
- The loops are about 50-100 kb in size.


Nicked DNA
Double helix
Protein-membrane
core or scaffold
支架
Negatively supercoiled
(负超螺旋) domains
50-100 kb independent
loops or domains
RNA



$L=25, T=25, W=0$

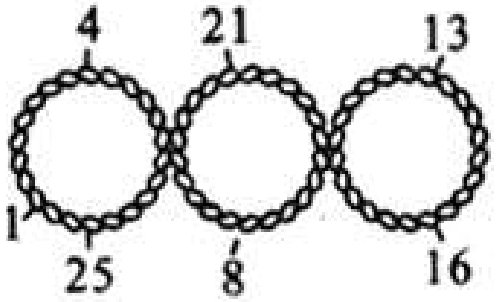
松弛环状



$L=23, T=23, W=0$

解链环状

$$L=T+W$$



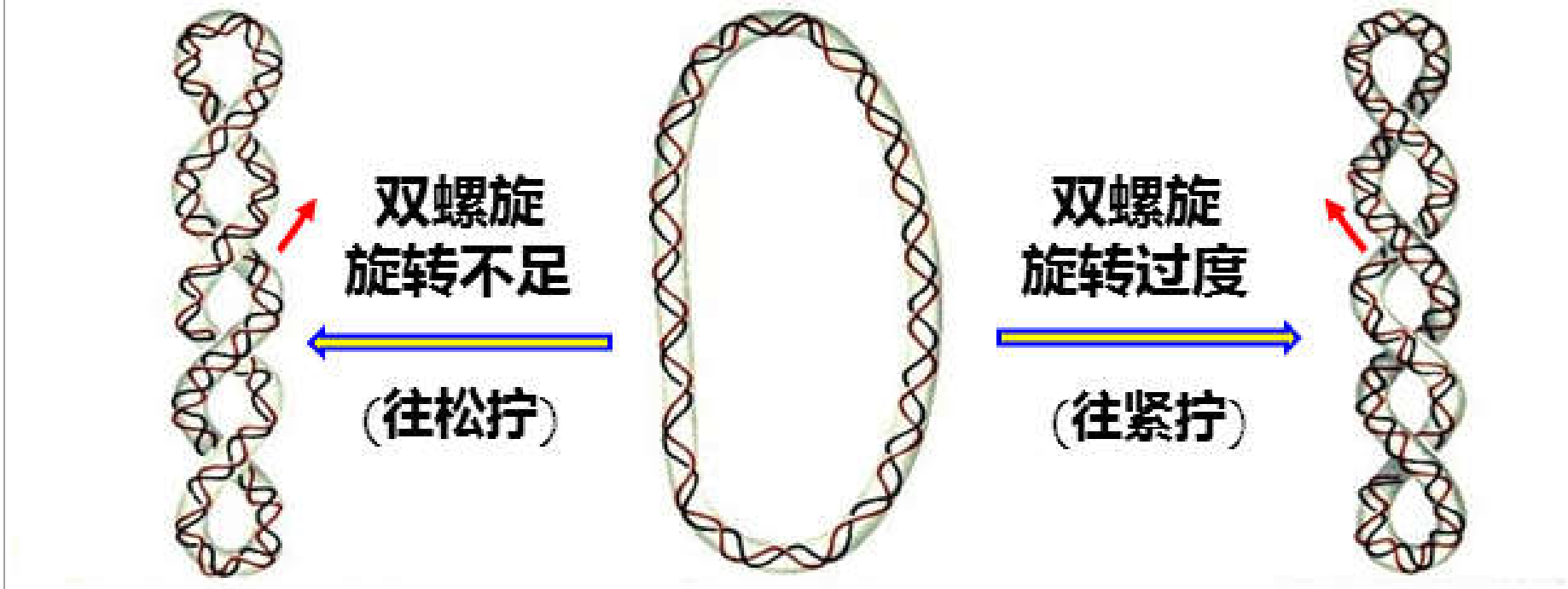
$L=23, T=25, W=-2$

负超螺旋

扭转数（twist number）：在双螺旋DNA中，一条链绕另一条链缠绕的次数。以“T”表示。定义右手螺旋为正，左手螺旋为负。

超螺旋数或缠绕数（writhing number）：正超螺旋与负超螺旋。以“W”表示。环状DNA正超螺旋为左手螺旋，负超螺旋为右手螺旋。

连环数（linking number）：扭转数与超螺旋数之和。以“L”



Negatively supercoiled DNA have a tendency to unwind partially.

1.3 DNA-binding proteins in *E.coli*

1.3.1 HU

- A small basic (positively charged) dimeric protein
- Binds DNA nonspecifically
- Histone-like protein
- Compacts DNA, which is essential for the packaging of the DNA into the nucleoid.
- Stabilizes and constrains the supercoiling of the chromosome.
- Participates in the initiation of DNA replication

1.3.2 H-NS (H1)

- A monomeric neutral protein
- Binds DNA nonspecifically, but has a preference for regions of DNA which are intrinsically bent.
- Histone-like protein
- Compacts DNA, which is essential for the packaging of the DNA into the nucleoid.
- Stabilizes and constrains the supercoiling of the chromosome.
- Participates in the regulation of gene expression

1.3.3 Integration host factor (IHF)

整合宿主因子

- A homolog of HU
- Binds to specific DNA sequences and bends DNA
- Participates in site-specific recombination (位点特异性重组)

Other proteins: RNA polymerase…

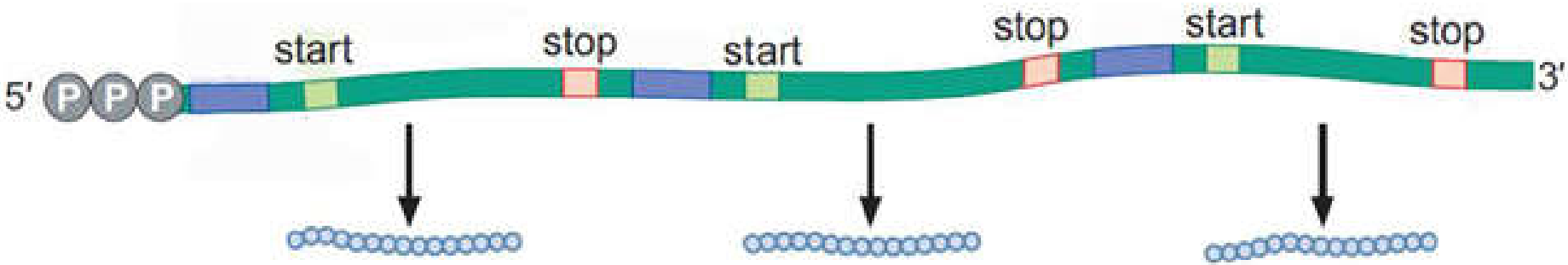
1.4 Characteristics of prokaryotic genome

1.4.1 Chromosome DNA

(1) Usually consists of only **one circular dsDNA** molecule

(2) Has **operon** (操纵子)

Polycistronic (多顺反子) mRNA - mRNA that includes coding regions representing more than one gene.



(3) Less non-coding sequences

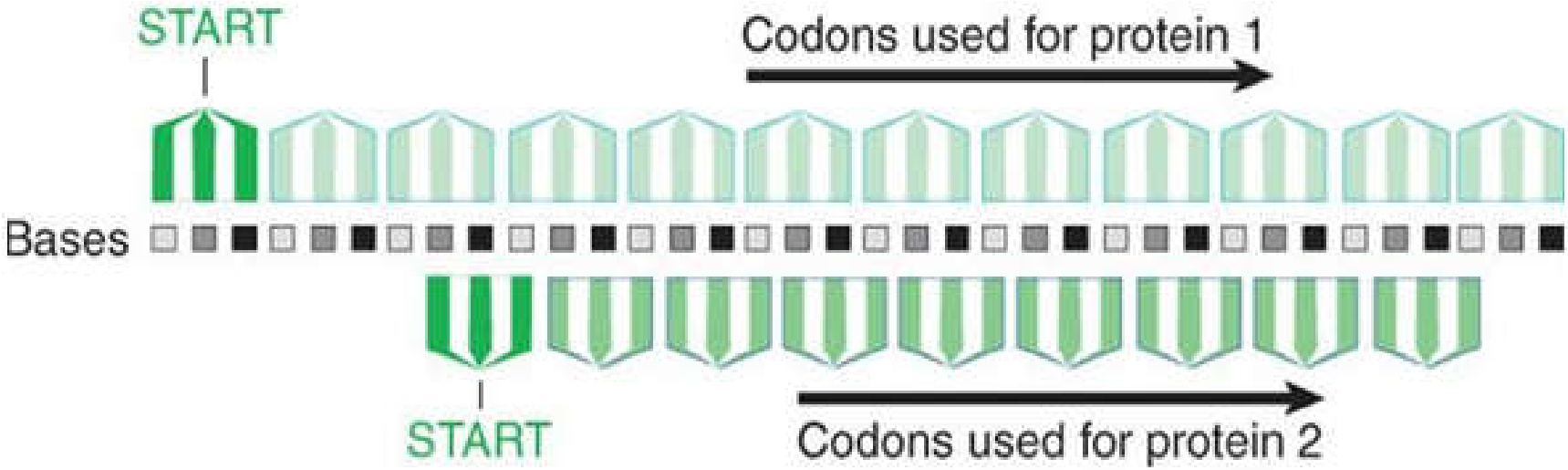
(4) Each protein is encoded by a single-copy gene (unique sequence).

(5) Non-interrupted gene

Interrupted gene
断裂基因

(6) Coding sequences are less overlapped (重叠) than viral DNA.

Overlapping gene (**重叠基因**): A gene in which part or all of the sequence is found within part of the sequence of another gene.



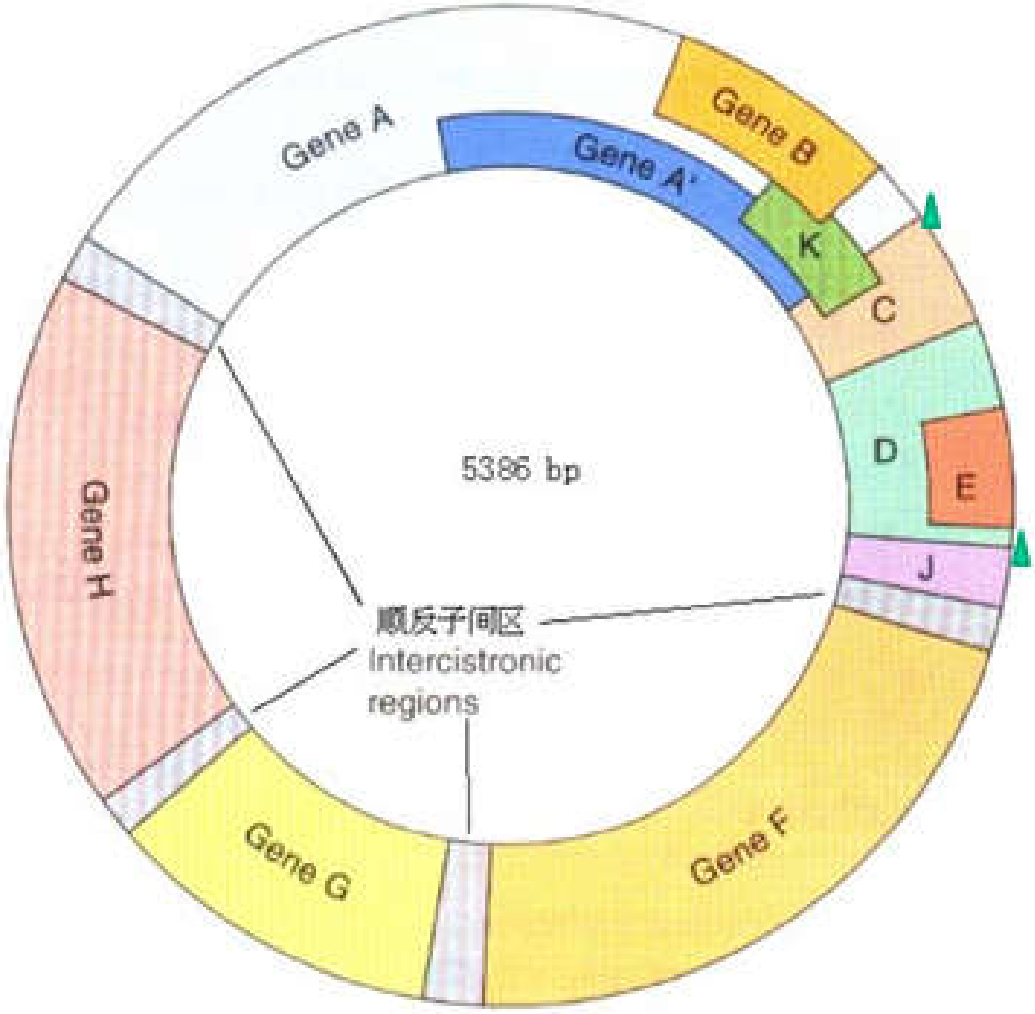
重叠基因由于阅读框的不同或起始终止早晚的不同，能够编码2种（或以上）不同的多肽链。

最早完成全基因组测序的生物

噬菌体φX174的重叠基因

- 完全重叠
- 部分重叠
- 重叠一个碱基

病毒、线粒体和质粒DNA有基因重叠现象，细胞染色体DNA少见。这种结构能够**使较小的基因组能够携带较多的遗传信息。**



1.4.2 Plasmid DNA

A **plasmid** is a small DNA molecule within a cell that is physically separated from a chromosomal DNA.

- Most of the plasmids are **circular supercoiled dsDNA** molecules.
- Not essential to the survival of the host cell under normal circumstances
- Certain genes in the plasmid facilitate the survival of the host cell.
- Can be used as a **genetic engineering vector**