



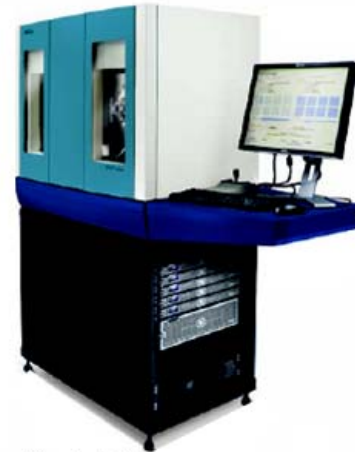
Applied Biosystems
ABI 3730XL
1 Mb / day



Roche / 454
Genome Sequencer FLX
100 Mb / run



Illumina / Solexa
Genetic Analyzer
2000 Mb / run



Applied Biosystems
SOLiD
3000 Mb / run

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NasdaqGS - NasdaqGS Real Time Price. Currency in USD

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342.68 +19.95 (+6.18%)

At close: November 7 4:00PM EST

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Summary

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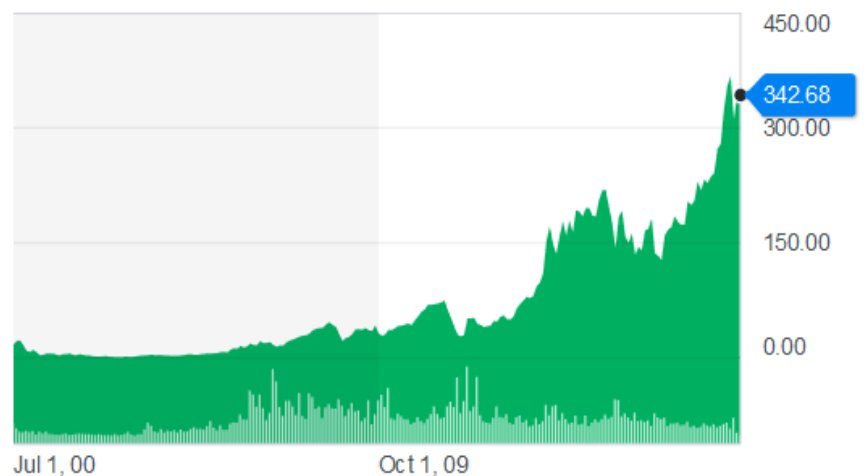
[Options](#)

[Holders](#)

[Sustainability](#)

Previous Close	322.73	Market Cap	50.374B
Open	325.00	Beta (3Y Monthly)	2.04
Bid	304.93 x 800	PE Ratio (TTM)	77.92
Ask	350.00 x 800	EPS (TTM)	4.40
Day's Range	318.38 - 343.04	Earnings Date	Jan 28, 2019 - Feb 1, 2019
52 Week Range	203.83 - 372.61	Forward Dividend & Yield	N/A (N/A)
Volume	1,273,158	Ex-Dividend Date	N/A
Avg. Volume	1,019,553	1y Target Est	359.75

1D 5D 1M 6M YTD 1Y 5Y **Max**  [Full screen](#)



Trade prices are not sourced from all markets

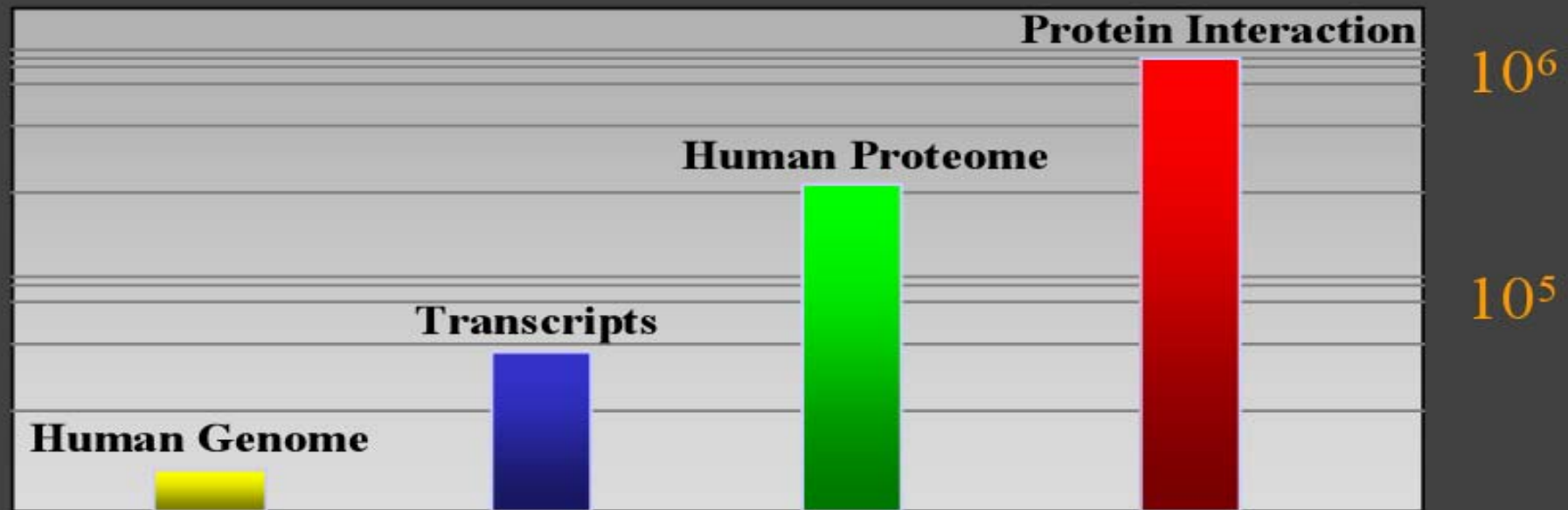
Genome: 30.000 genes

↓

Transcriptome: 40-100.000 mRNAs

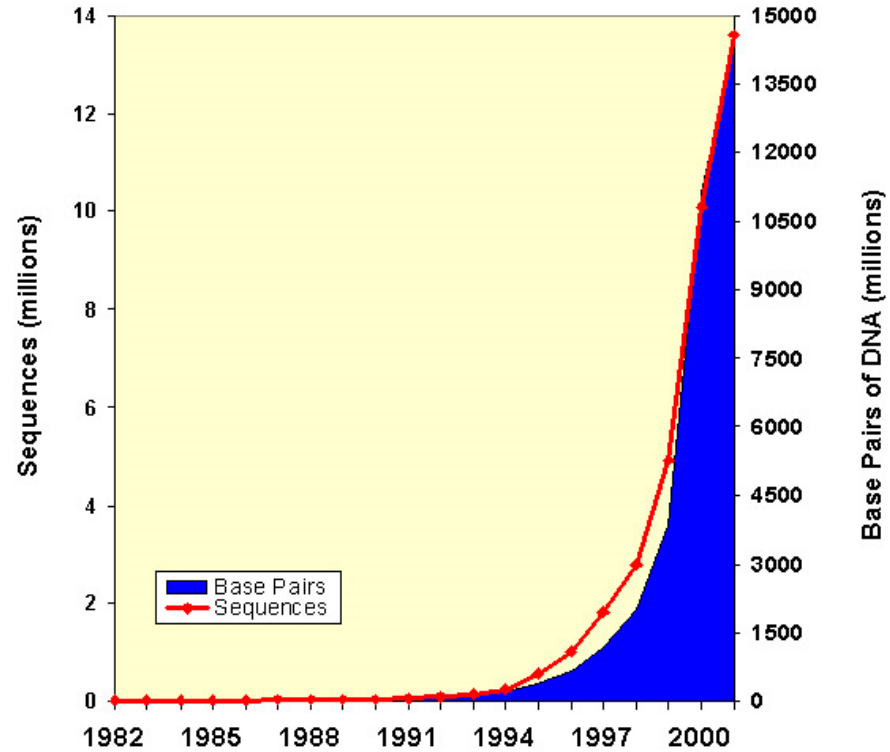
↓

Proteome: 100-400.000 proteins
>1.000.000 interactions



Genome sequencing

GenBank 1982 Los Alamos Sequence Database



Walter Goad

Frederick Sanger

1958 – Nobel prize – insuline structure

1975 - Dideoxy sequencing method

1977 – Φ -X174 (5,368 bp) sequence

1980 – second Nobel prize

λ phage sequence

shotgun method (48,502 bp)



Genome sequencing

- **1986** Leroy Hood:
automatic sequencing machine
- **1986** Human Genome Initiative



Leroy Hood



Genome sequencing

- **1995** John Craig Venter
first bacterial genome



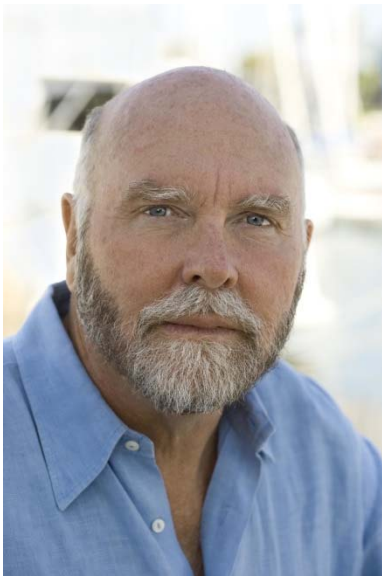
John Craig Venter

Craig Venter

Global Ocean Sampling Expedition

Synthetic genomics

Human Longevity Inc



<http://www.youtube.com/watch?v=J0rDFbrhjtI>

2010 Human super genome reference

2010 Human super genome reference





Learn how your DNA may affect your health.

Our genes are a part of who we are, so naturally they impact our health. By knowing more about your DNA, you may be able to take steps towards living a healthier life.

Keep in mind that many conditions and traits are influenced by multiple factors. Our reports are intended for informational purposes only and do not diagnose disease or illness.

- **Plan for the future.**

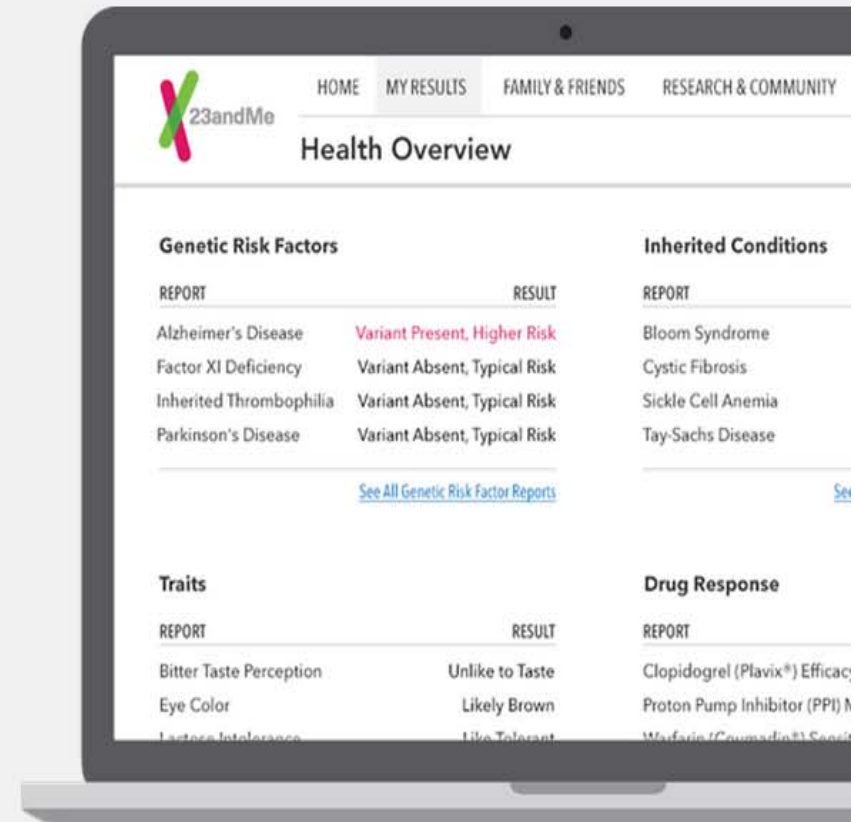
Learn if you are a carrier for certain inherited conditions, so you and your family can be prepared.

- **Stay one step ahead.**

Find out if you have certain genetic risk factors, so you can make better lifestyle choices and appropriately monitor your health.

- **Engage in your health care.**

Understand how your DNA may affect your health and response to





MATERNAL LINE: H1

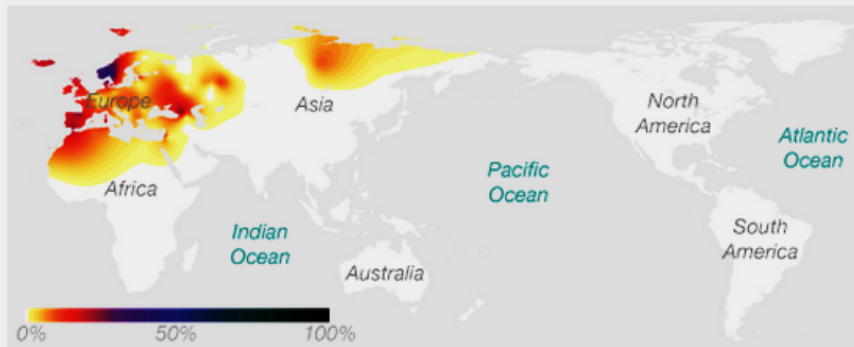
Overview

History

Haplogroup Tree

Community

Locations of haplogroup H1 before the widespread migrations of the past few hundred years.



Haplogroup H1 is widespread in Europe, especially the western part of the continent. It originated about 13,000 years ago, not long after the Ice Age ended.

Maternal haplogroups are families of mitochondrial DNA types that all trace back to a single mutation at a specific place and time. By looking at the geographic distribution of mtDNA types, we learn how our ancient female ancestors migrated throughout the world.

Haplogroup: H1, a subgroup of H

Age: 13,000 years

Region: Europe, Near East, Central Asia, Northwestern Africa

Example Populations: Spanish, Berbers, Lebanese

Highlight: H1 appears to have been common in Doggerland, an ancient land now flooded by the North Sea.

PATERNAL LINE: I1*

Overview

History

Haplogroup Tree

Community

I1* is a subgroup of I1

Locations of haplogroup I1 before the widespread migrations of the past few hundred years.



Haplogroup I1 can be found at levels of 10% and higher in many parts of Europe, due to its expansion with men who migrated northward after the end of the Ice Age about 12,000 years ago. It reaches its highest levels in Denmark and the southern parts of Sweden and Norway.

Paternal haplogroups are families of Y chromosomes that all trace back to a single mutation at a specific place and time. By looking at the geographic distribution of these related lineages, we learn how our ancient male ancestors migrated throughout the world.

Haplogroup: I1, a subgroup of I

Age: 28,000 years

Region: Northern Europe

Example Populations: Finns, Norwegians, Swedes

Highlight: Haplogroup I1 reaches highest frequencies in Scandinavia.

Haplogroups of You and Your Connections

I1*

Roman Hobza

Haplogroups of Example Profiles

SHOW RESULTS FOR Roman Hobza ▾[SEE NEW AND RECENTLY UPDATED REPORTS »](#)

These reports provide information about your possible risk for developing certain health conditions based on genetics. Environmental and lifestyle factors also often play a large role in your risk for developing these conditions.

Elevated Risk ?

NAME	CONFIDENCE	YOUR RISK	AVG. RISK	COMPARED TO AVERAGE
Venous Thromboembolism	★★★★★	41.8%	12.3%	3.39x 
Gout	★★★★★	35.7%	22.8%	1.57x 
Melanoma	★★★★★	4.0%	2.9%	1.38x 
Restless Legs Syndrome	★★★★★	2.5%	2.0%	1.25x 
Exfoliation Glaucoma	★★★★★	2.2%	0.7%	2.90x 
Esophageal Squamous Cell Carcinoma (ESCC)	★★★★★	0.43%	0.36%	1.21x 
Stomach Cancer (Gastric Cardia Adenocarcinoma)	★★★★★	0.28%	0.23%	1.22x 
Primary Biliary Cirrhosis	★★★★★	0.11%	0.08%	1.43x 
Scleroderma (Limited Cutaneous Type)	★★★★★	0.08%	0.07%	1.24x 

Show information for assuming ethnicity and an age range of



Roman Hobza 41.8 out of 100

men of European ethnicity who share Roman Hobza's genotype will develop Venous Thromboembolism between the ages of 0 and 79.



Average 12.3 out of 100

men of European ethnicity will develop Venous Thromboembolism between the ages of 0 and 79.

What does the Odds Calculator show me?

Use the ethnicity and age range selectors above to see the estimated incidence of Venous Thromboembolism due to genetics for men with **Roman Hobza's** genotype. The 23andMe Odds Calculator assumes that a person is free of the condition at the lower age in the range. You can use the name selector above to see the estimated incidence of Venous Thromboembolism for the genotypes of other people in your account.

The 23andMe Odds Calculator only takes into account effects of markers with known associations that are also on our genotyping chip. Keep in mind that aside from genetics, environment and lifestyle may also contribute to one's risk for Venous Thromboembolism.

55 %
Attributable to
Genetics



Understanding Your Results

The heritability of venous thromboembolism is estimated to be 55%. This means that genetics (including unknown factors and known ones such as the SNPs we describe here) and environment play nearly equal roles in this condition. There are a number of environmental factors of various strengths that contribute to venous thromboembolism. Strong risk factors include hip or leg fractures, hip or knee replacement, major surgery or trauma, and spinal cord injury or surgery. Moderate risk factors include arthroscopic knee surgery, having central venous lines, congestive heart or respiratory failure, hormone replacement or oral contraceptive use, cancer, pregnancy, paralytic stroke, previous venous thromboembolism, and thrombophilia. Weak risk factors include bed rest for more than three days, immobility due to sitting (such as a long car or plane trip), specific types of chemotherapy, increasing age, laparoscopic surgery, obesity, and varicose veins. ([sources](#))

What You Can Do

Assuming the ethnicity setting above is correct, your test results indicate you are at increased risk for venous thromboembolism based on genetics. Note that family history and non-genetic factors can also influence your risk for venous thromboembolism. Below are some steps you can take to reduce your risk.

Gene or region: F5
SNP: rs6025

	SNP used	Genotype	Adjusted Odds Ratio*
Roman Hobza	rs6025	CT	European: 4.69

* Odds ratios are reported for all available ethnicities.

Factor V is the last clotting factor in the pathway before the activation step that turns prothrombin into thrombin. Clotting is usually kept from spiraling out of control by a feedback loop, similar to the way a thermostat operates. Once enough thrombin has been activated, it binds to a protein called "protein C." Protein C then inactivates factor V, thus cutting off activation of prothrombin into thrombin.

The SNP in the F5 gene causes a change in the protein sequence of factor V that prevents protein C from inactivating it. Since this version of factor V can still participate in the activation of thrombin, a situation results in which thrombin can be turned on but cannot be turned off. Once the clotting cascade is set off (whether appropriately or not), the riskier version of the SNP makes it more difficult to shut it off.

The riskiness of the T version of this SNP is further increased for women who also take hormonal birth control.

(The riskier version of this gene is also sometimes called Factor V Leiden, after the city in the Netherlands where this SNP and its effects on factor V's role in clotting were first discovered.)

The studies whose data we report as applicable to those of "European" ancestry confirmed the association between this SNP and VTE in samples from the Netherlands, Sweden, the United Kingdom, Brazil, Italy, and France.

African and Asian populations appear to have only one version of the SNP, meaning that association studies are very difficult to perform.

Citations

[Rosendaal et al. \(1995\)](#). "High risk of thrombosis in patients homozygous for factor V Leiden (activated protein C resistance)." *Blood* 85(6):1504-8.

[Smith et al. \(2007\)](#). "Association of genetic variations with nonfatal venous thrombosis in postmenopausal women." *JAMA* 297(5):489-98.










[Emmerich et al. \(2001\)](#). "Combined effect of factor V Leiden and prothrombin 20210A on the risk of venous thromboembolism--pooled analysis of 8 case-control studies including 2310 cases and 3204 controls. Study Group for Pooled-Analysis in Venous Thromboembolism." *Thromb Haemost* 86(3):809-16.

[Bertina et al. \(1994\)](#). "Mutation in blood coagulation factor V associated with resistance to activated protein C." *Nature* 369(6475):64-7.

[Lane et al. \(2000\)](#). "Role of hemostatic gene polymorphisms in venous and arterial thrombotic disease." *Blood* 95(5):1517-32.

Gene or region: F2
SNP: i3002432

Decreased Risk ?

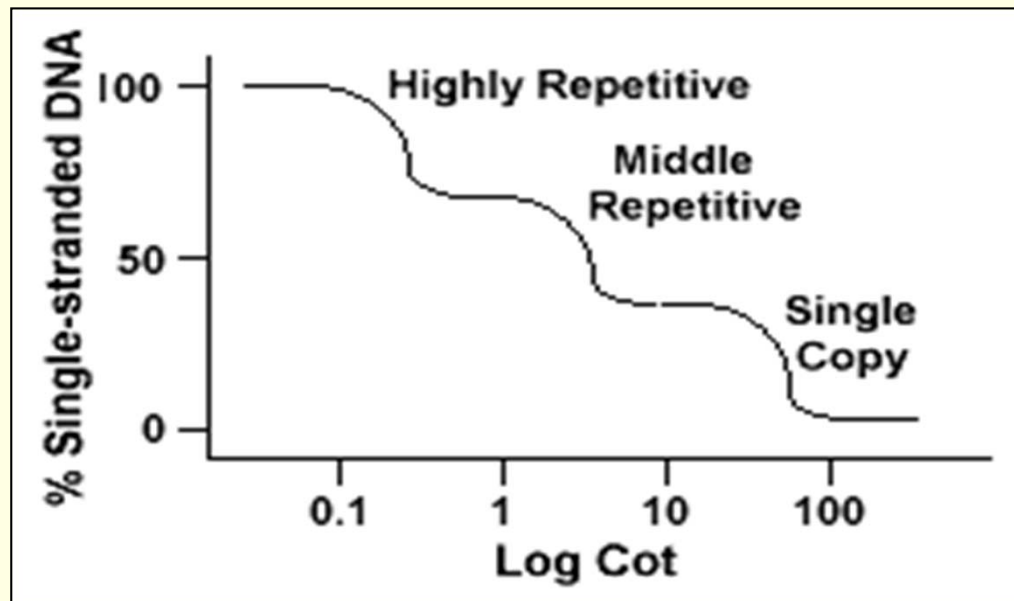
NAME	CONFIDENCE	YOUR RISK	AVG. RISK	COMPARED TO AVERAGE
Type 2 Diabetes	★★★★	17.7%	25.7%	0.69x 
Alzheimer's Disease	★★★★	4.3%	7.2%	0.60x 
Rheumatoid Arthritis	★★★★	1.6%	2.4%	0.68x 
Parkinson's Disease	★★★★	1.2%	1.6%	0.73x 
Age-related Macular Degeneration	★★★★	0.92%	6.55%	0.14x 
Crohn's Disease	★★★★	0.31%	0.53%	0.58x 
Multiple Sclerosis	★★★★	0.24%	0.34%	0.69x 
Type 1 Diabetes	★★★★	0.12%	1.02%	0.12x 
Celiac Disease	★★★★	0.05%	0.12%	0.44x 

BRCA Cancer Mutations (Selected)	★★★★	Variant Absent
Beta Thalassemia	★★★★	Variant Absent
Bloom's Syndrome	★★★★	Variant Absent
Canavan Disease	★★★★	Variant Absent
Congenital Disorder of Glycosylation Type 1a (PMM2-CDG)	★★★★	Variant Absent
Connexin 26-Related Sensorineural Hearing Loss	★★★★	Variant Absent
Cystic Fibrosis	★★★★	Variant Absent
D-Bifunctional Protein Deficiency	★★★★	Variant Absent
DPD Deficiency	★★★★	Variant Absent
Dihydrolipoamide Dehydrogenase Deficiency	★★★★	Variant Absent
Factor XI Deficiency	★★★★	Variant Absent
Familial Dysautonomia	★★★★	Variant Absent
Familial Hypercholesterolemia Type B	★★★★	Variant Absent
Familial Hyperinsulinism (ABCC8-related)	★★★★	Variant Absent
Familial Mediterranean Fever	★★★★	Variant Absent
Fanconi Anemia (FANCC-related)	★★★★	Variant Absent
G6PD Deficiency	★★★★	Variant Absent

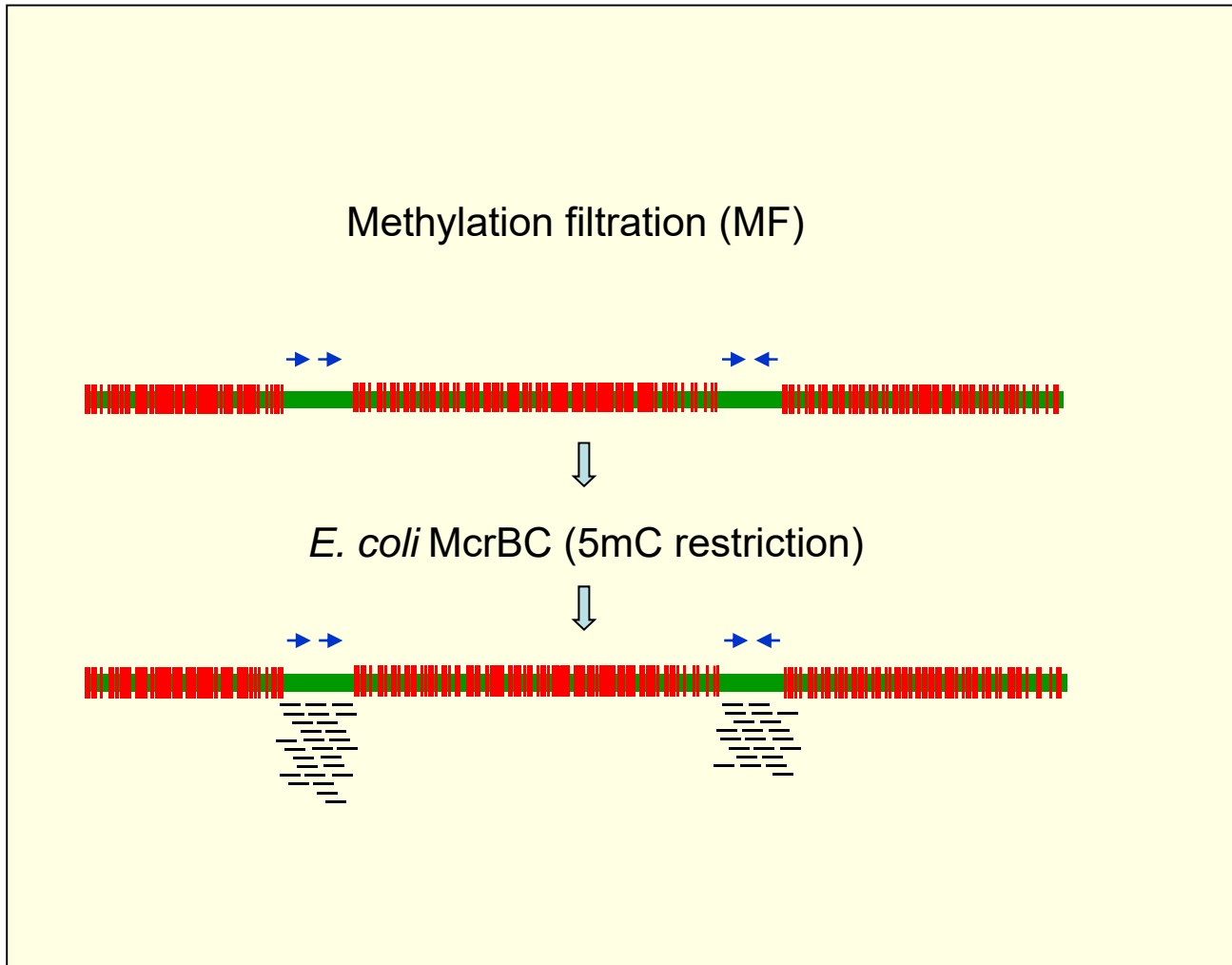
Reading Ability	***	Typical Nonword Reading Score
Response to Diet	***	See Report
Response to Exercise	***	See Report
Sex Hormone Regulation	***	See Report
Sweet Taste Preference 🍬	***	See Report
Tooth Development	***	See Report
Tuberculosis Susceptibility	***	See Report
Breast Morphology ♀ 🍬	***	Not Applicable
Menarche ♀	***	Not Applicable
Menopause ♀	***	Not Applicable
Eating Behavior	**	Greater tendency to overeat
HIV Progression	**	See Report
Hair Thickness	**	Typical, if European or African
Longevity	**	See Report
Measures of Intelligence	**	Lower Non-Verbal IQ
Memory	**	Typical Episodic Memory
Odor Detection	**	Typical Sensitivity to Sweaty Odor
Pain Sensitivity	**	Increased
Avoidance of Errors	*	See Report

Complexity reduction

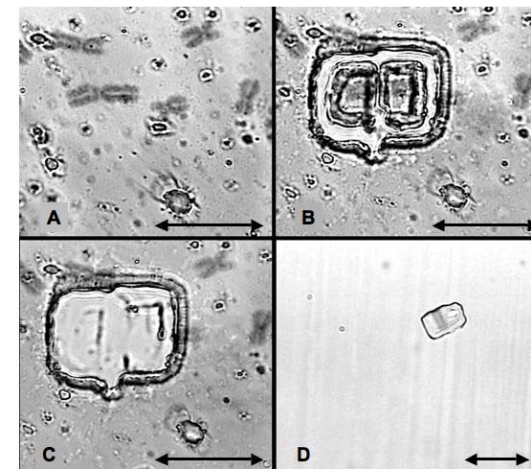
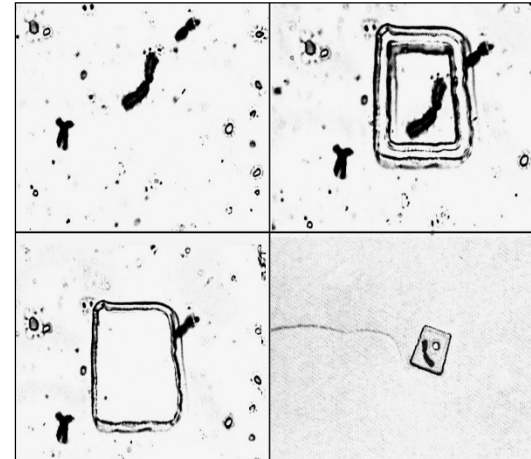
Hi-Cot selection



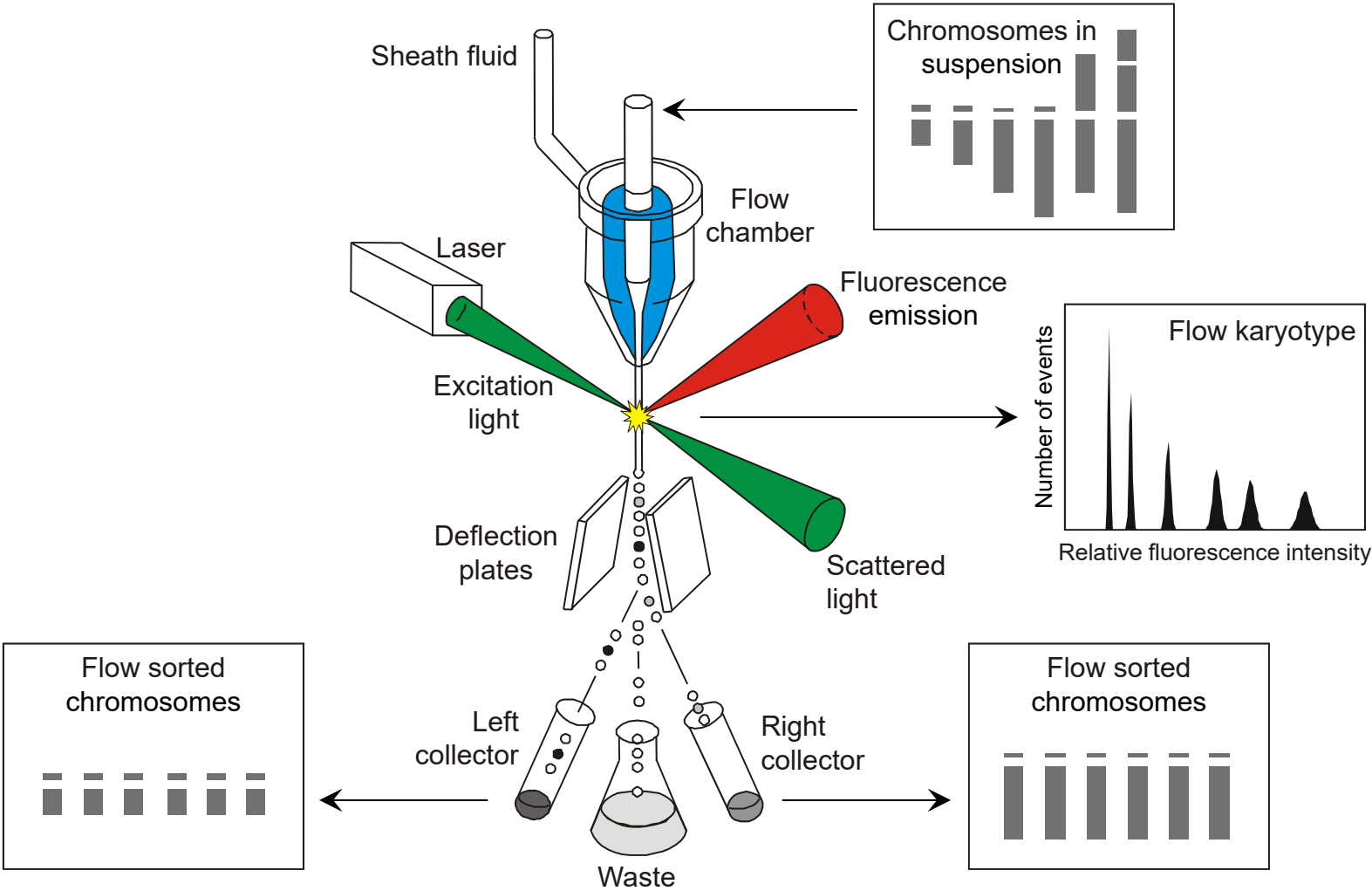
Complexity reduction



Laser microdissection

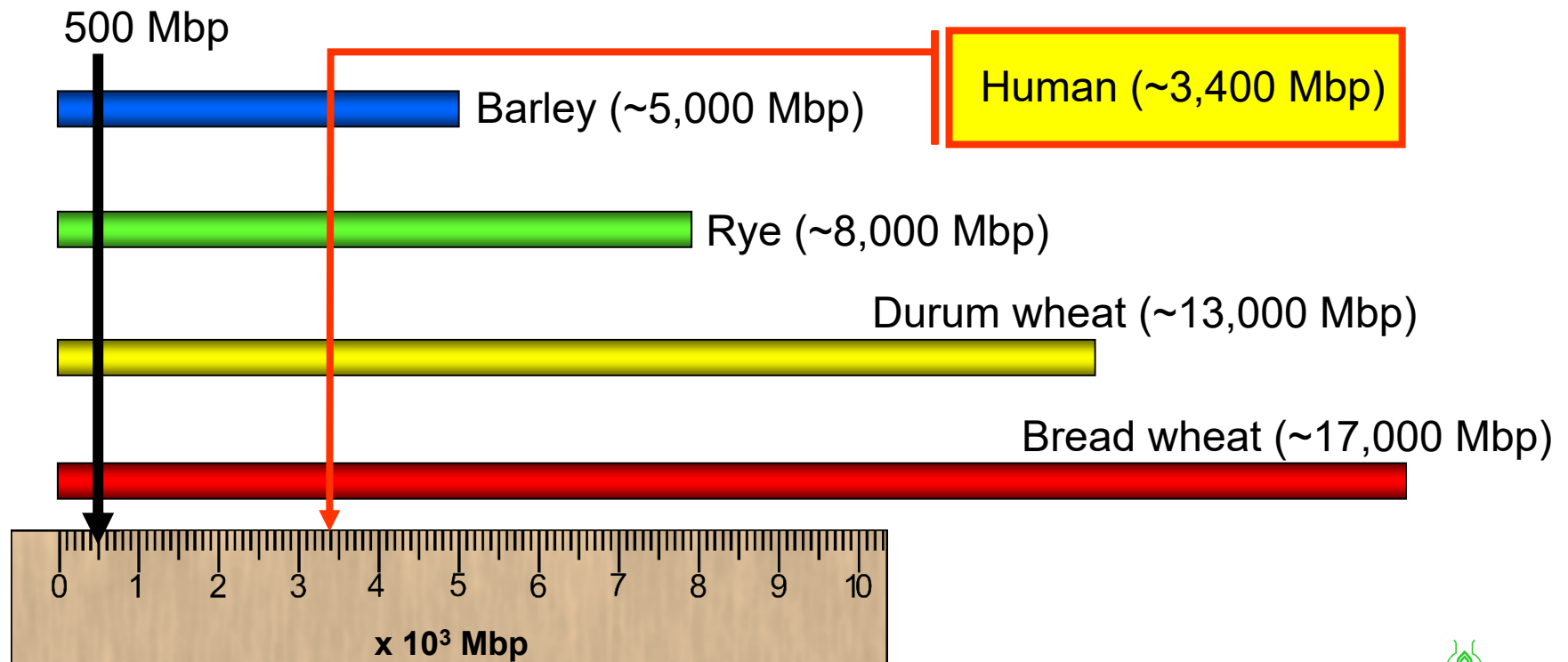


Flow sorting



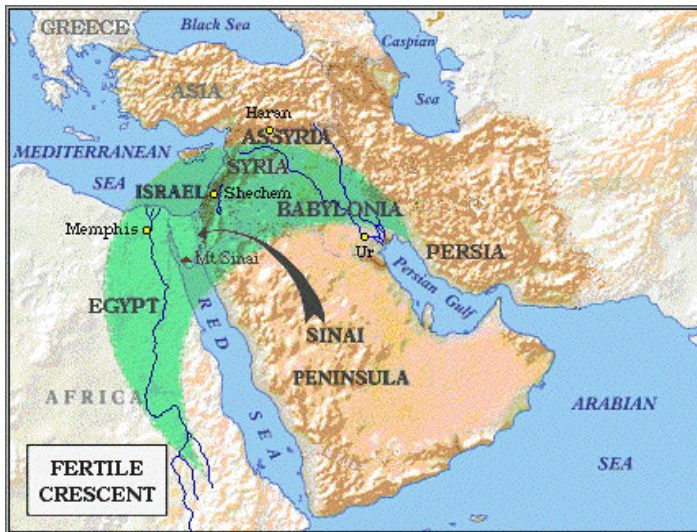
Why chromosome flow sorting ?

- Most of the genomes that will be sequenced in the near future are smaller than 500 Mbp
- But many genomes are much larger (and polyploid)!



The case of bread wheat

- Grown on more areas of land than any other crop plant
- A staple food of 40 % of the world's population
- Provides for 20 % of the calories consumed



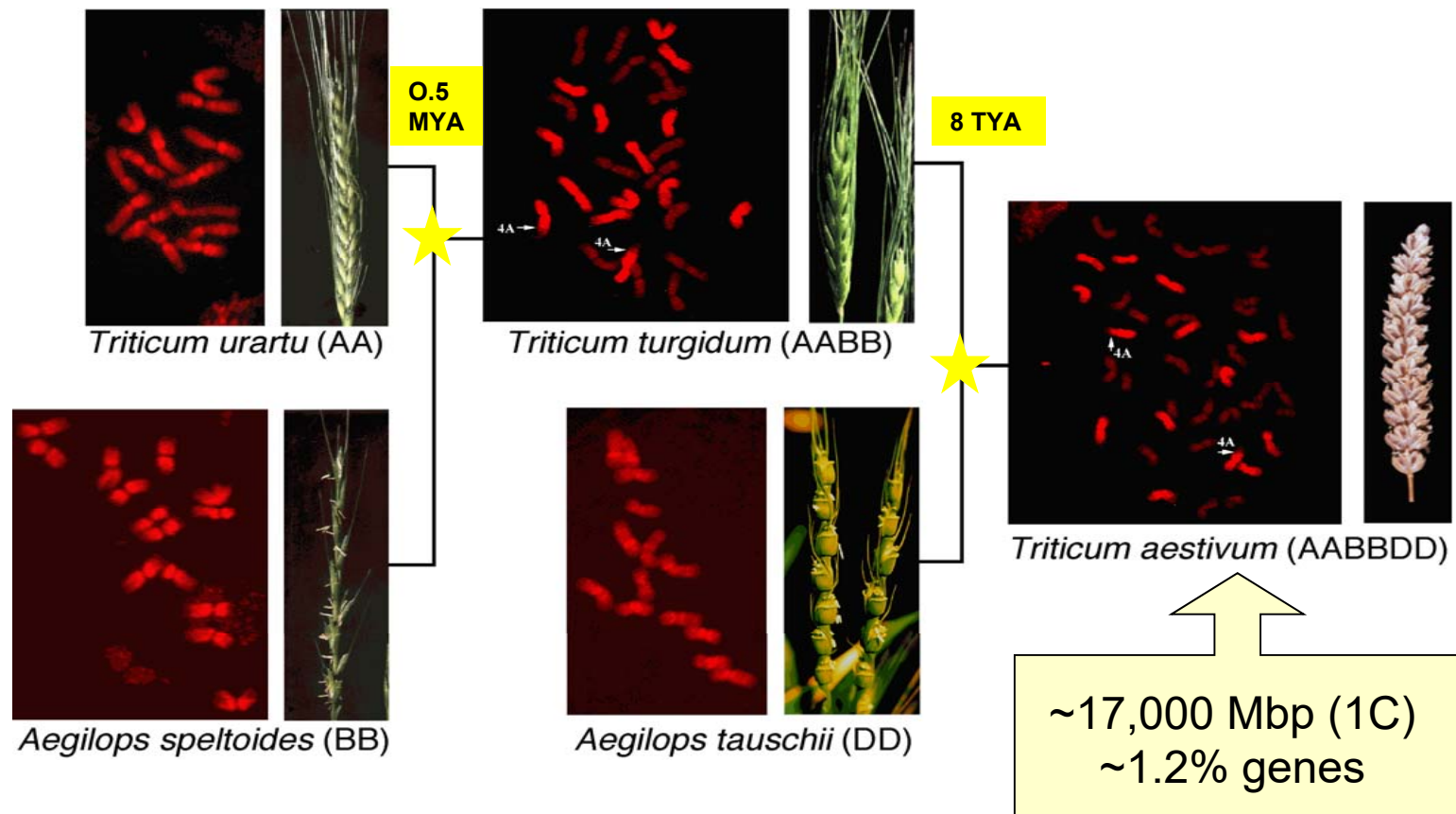
The development of wheat as a food source is deeply linked to the history of modern civilization ...

The fertile soil of the Fertile Crescent enabled humans to invent farming, cities, trade, and writing ...

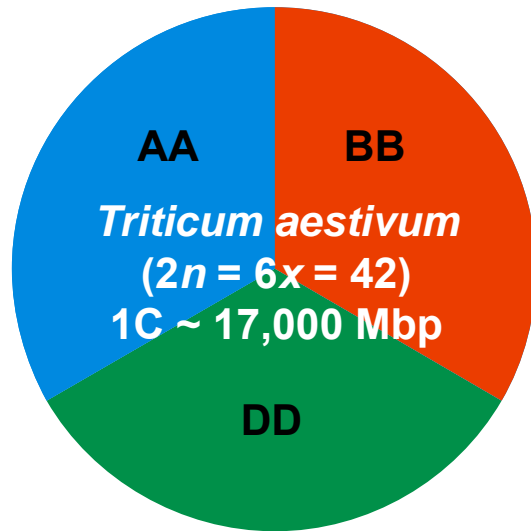


Nuclear genome of bread wheat is complex

- Allohexaploid species ($2n = 6x = 42$, AABBDD genome)
- Resulted from two independent hybridization events

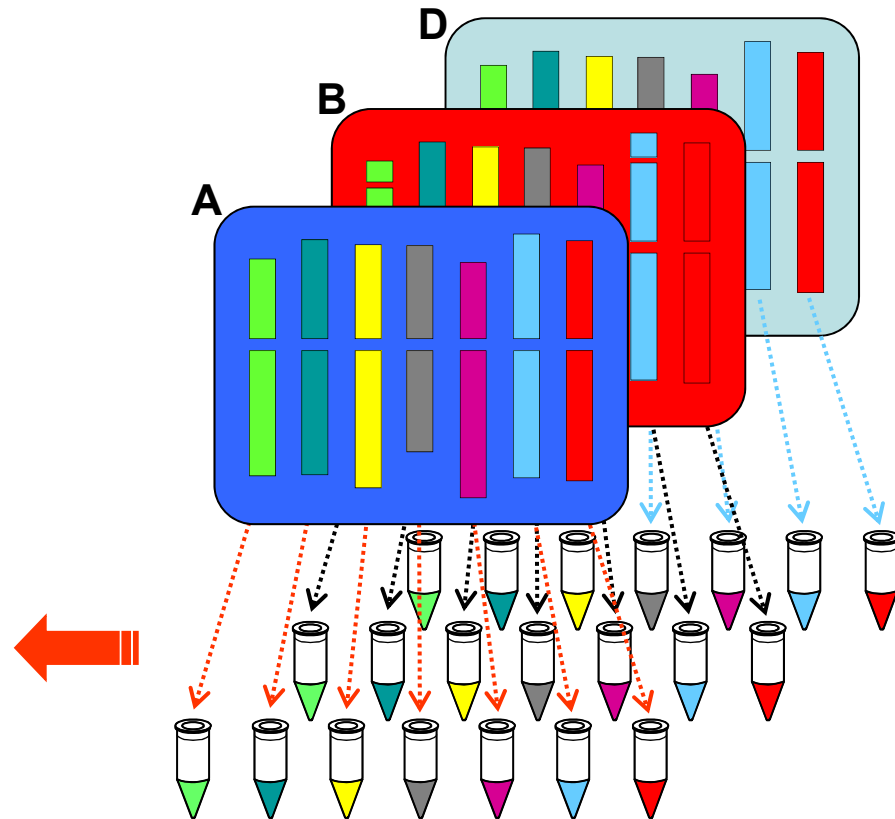


Divide and sequence



- Chromosomes: 605 - 995 Mbp (3.6 – 5.9% of the genome)
- Chromosome arms: 225 - 585 Mbp (1.3 – 3.4% of the genome)

Three genomes of hexaploid wheat



Integrating flow cytogenetics and genomics

Critical requirements

- Preparation of aqueous suspensions of mitotic chromosomes
- Preservation of chromosome integrity and intact DNA
- Discrimination of individual chromosome types
- Sorting chromosomes in large quantities



Chromosome sample for flow cytometry

A sample must be in a form of liquid suspension of single particles

The procedure

Cell cycle synchronisation
in root-tip meristems



Accumulation of mitotic cells
in metaphase



Extraction of chromosomes



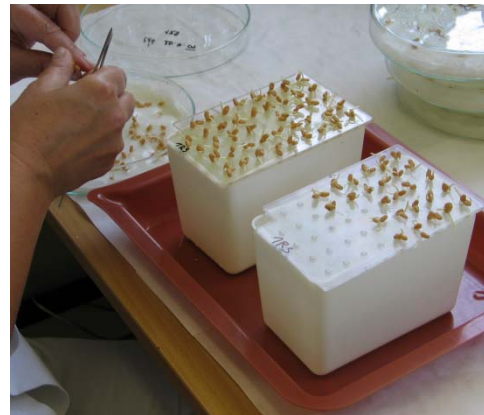
Fluorescent staining
of chromosomal DNA



Flow cytometric analysis

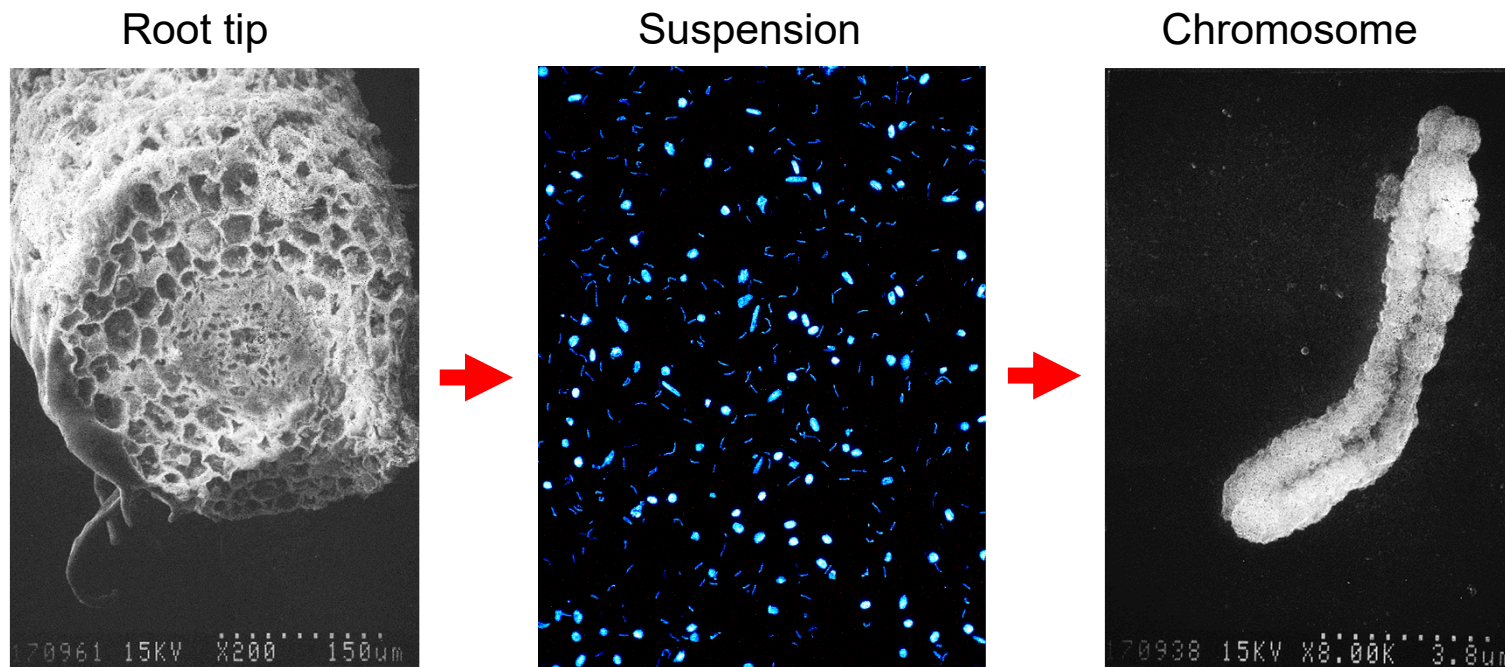


Chromosome sorting



Isolation of intact chromosomes

- Mild fixation of synchronized root tips in formaldehyde
- Release of chromosomes by mechanical homogenization
- Removal of large debris and tissue fragments by filtration



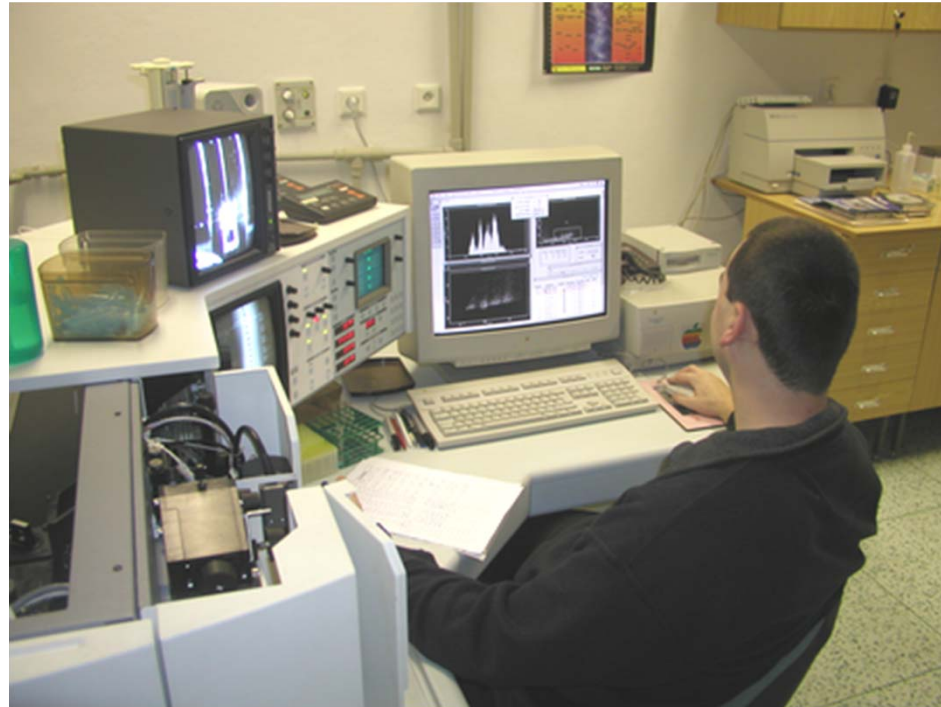
Development of flow cytogenetics at IEB

Species list:

- Field bean
- Garden pea
- Chickpea
- Garden vetch

- Barley
- Bread wheat
- Durum wheat
- Rye
- Oats

- Norway spruce
- White campion

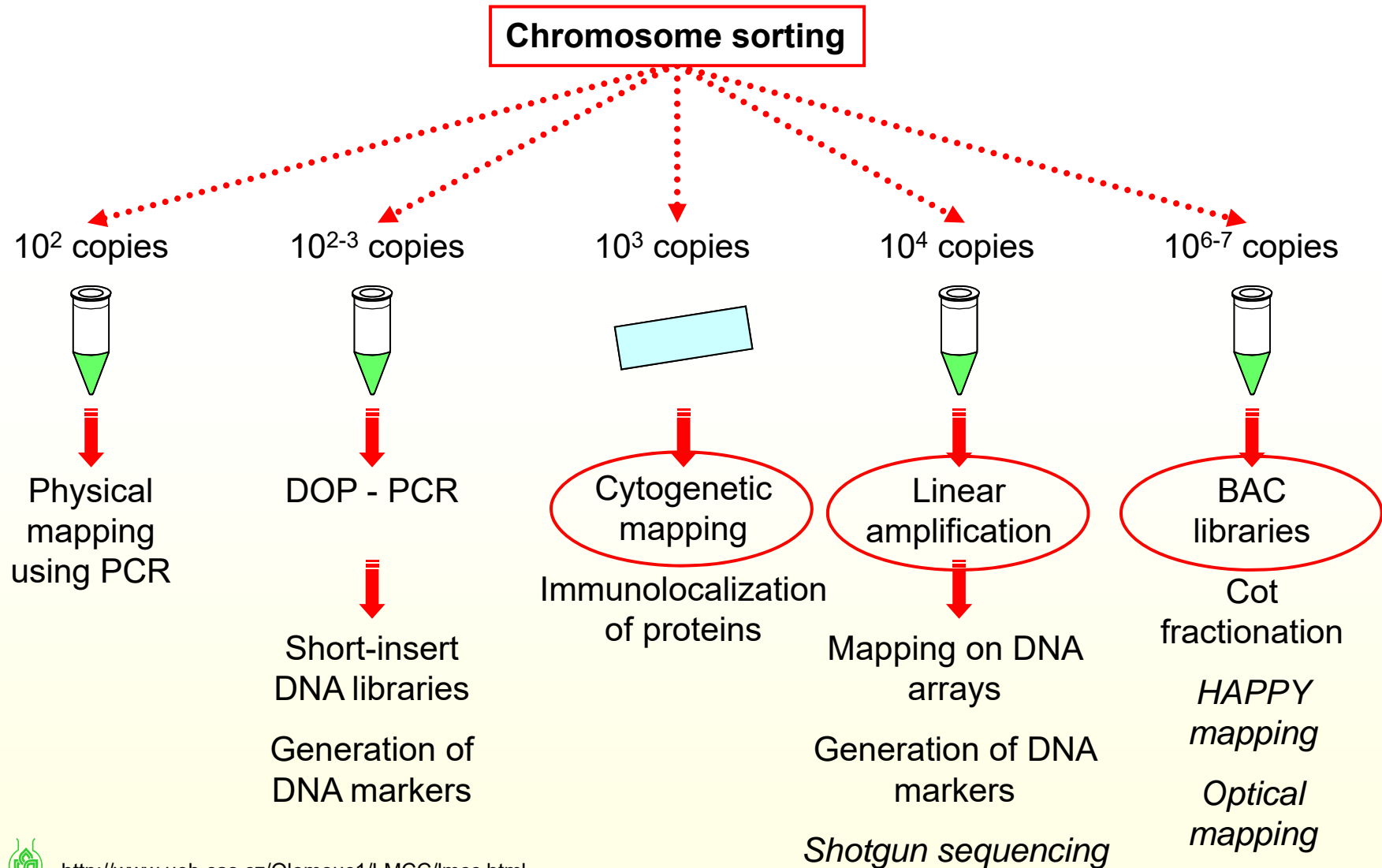


BD FACSVantage SE high-speed flow sorter

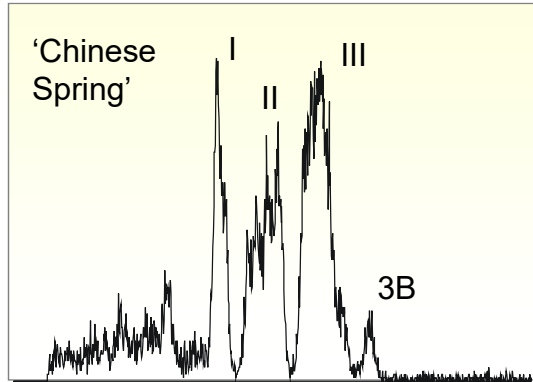
- Sample rate: 500 – 1000 chromosomes / sec
- Sort rate: 15 - 30 chromosomes / sec



The uses of flow-sorted chromosomes



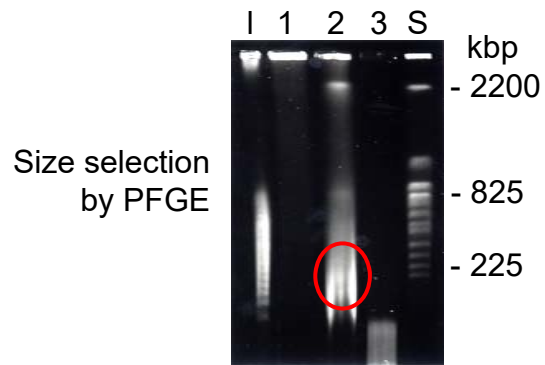
Chromosome-specific BAC libraries



Chromosome analysis and sorting

$2 \times 10^6 - 10^7$ flow-sorted chromosomes (~8 weeks of sorting)

Partial digestion



Size selection by PFGE

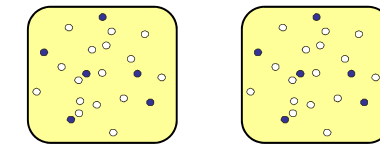
Major challenges:

- Quantity of DNA (micrograms DNA)
- Quality of DNA (HMW)
- Cloning efficacy
- Insert size

E. coli transformation

Ligation into a dephosphorylated BAC vector

Colonies

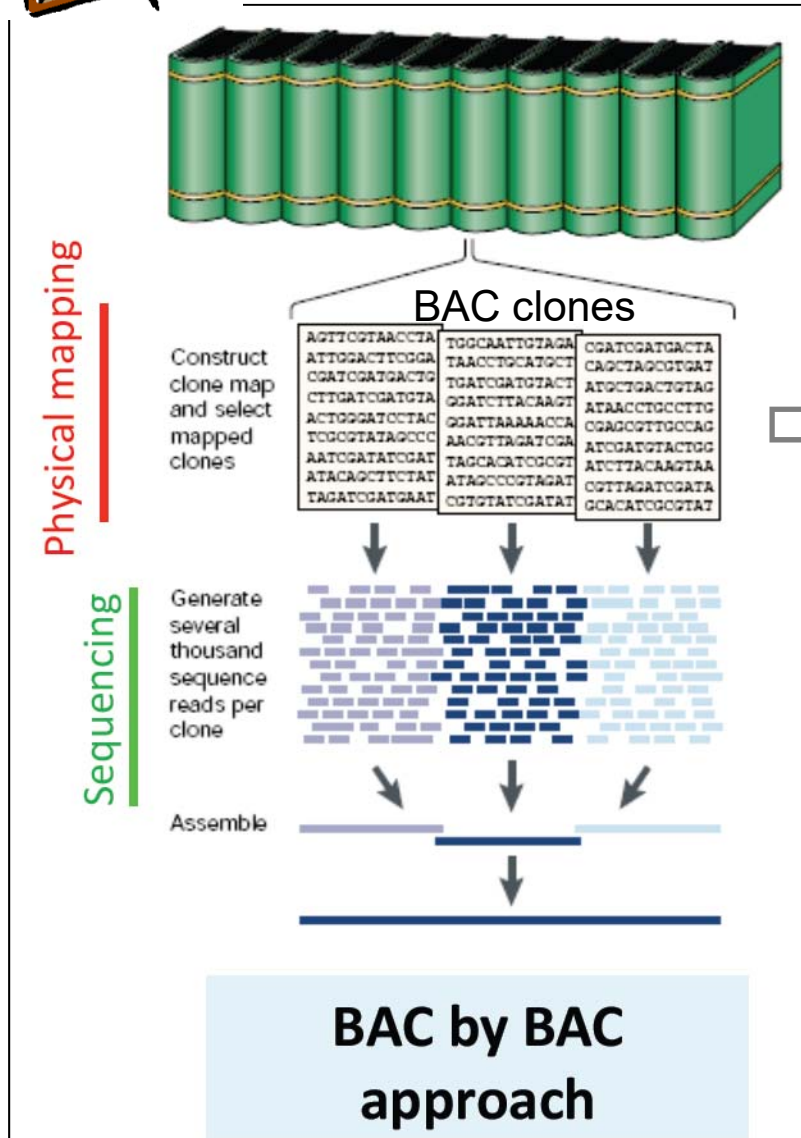


Ordering into 384-well plates

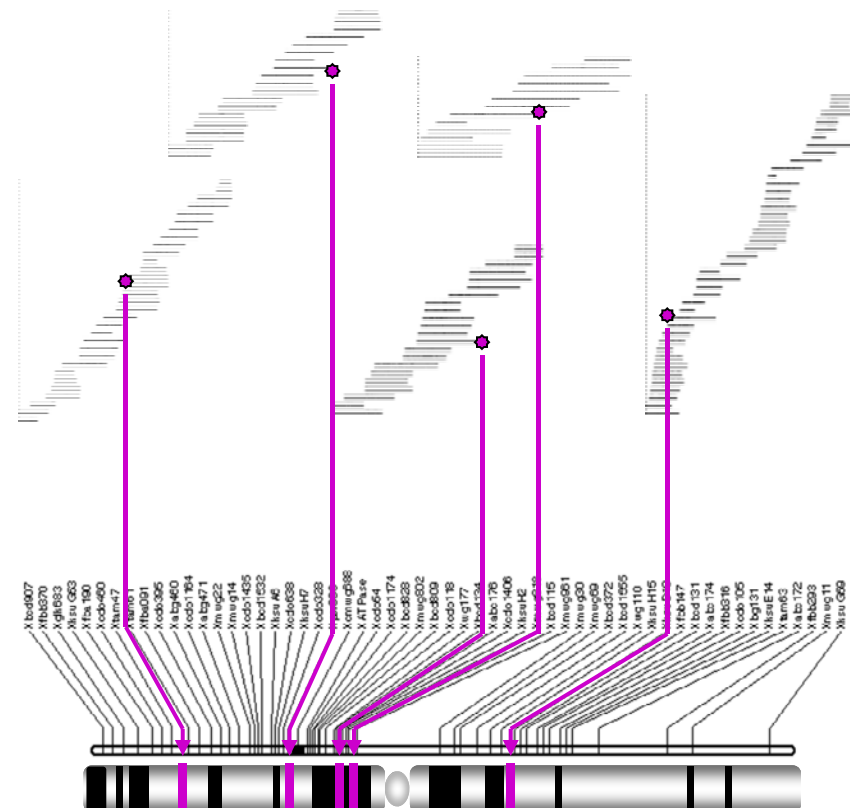




BAC-BY-BAC SEQUENCING

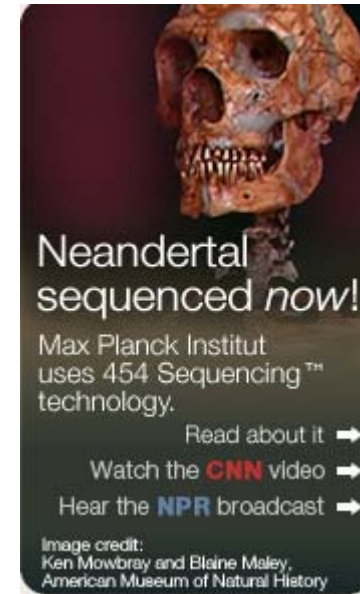


- **Physical map** is composed of contigs of overlapping BAC clones
- BAC contigs are landed on the chromosome through markers comprised in the contigs



Genome Sequencer 20 System 454 pyrosequencing (2005)

- <http://www.454.com>

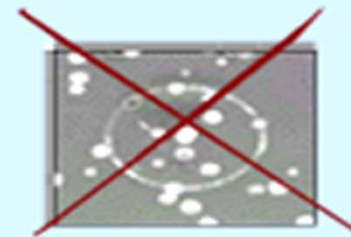


DNA library preparation

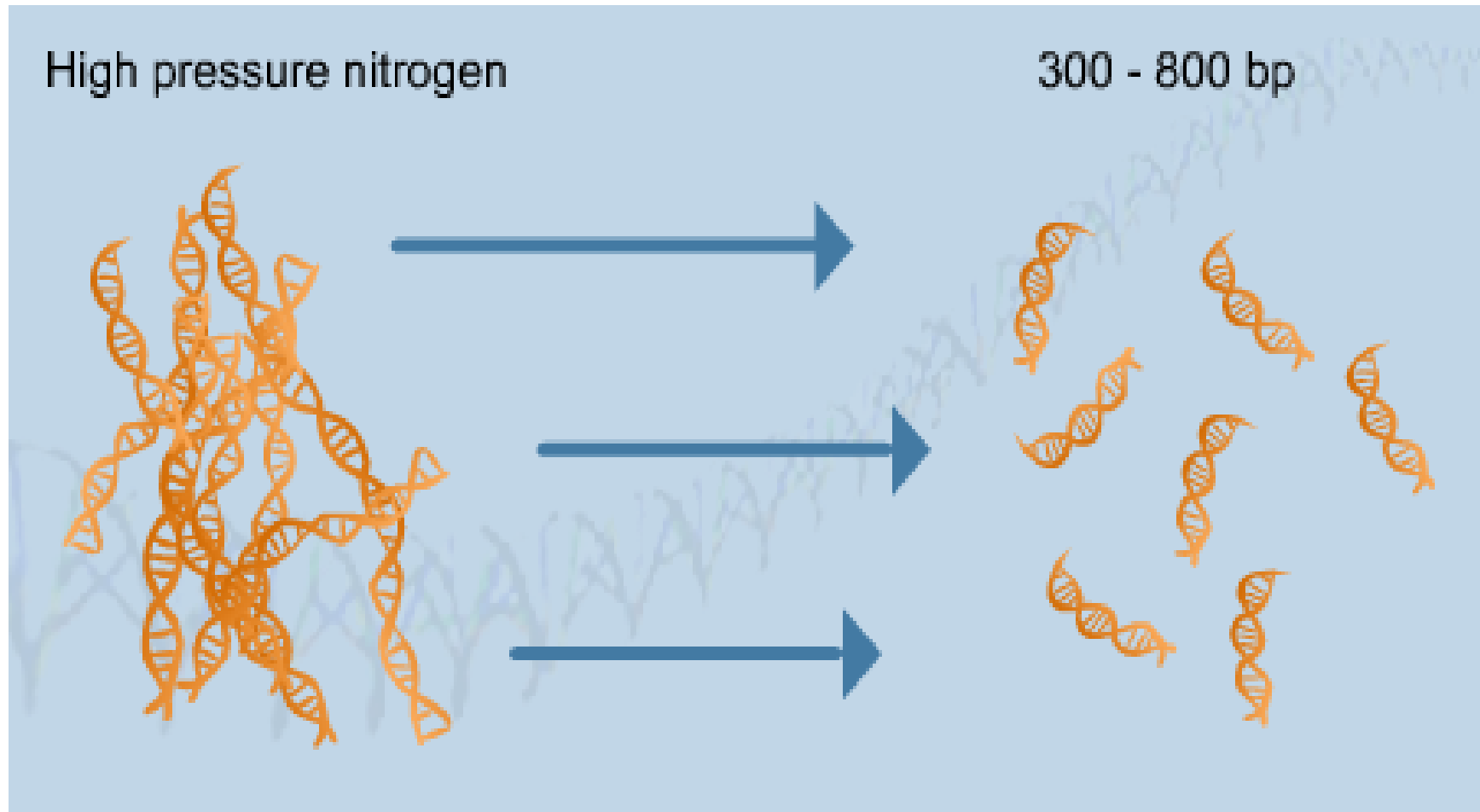
One sample preparation per genome

No Cloning

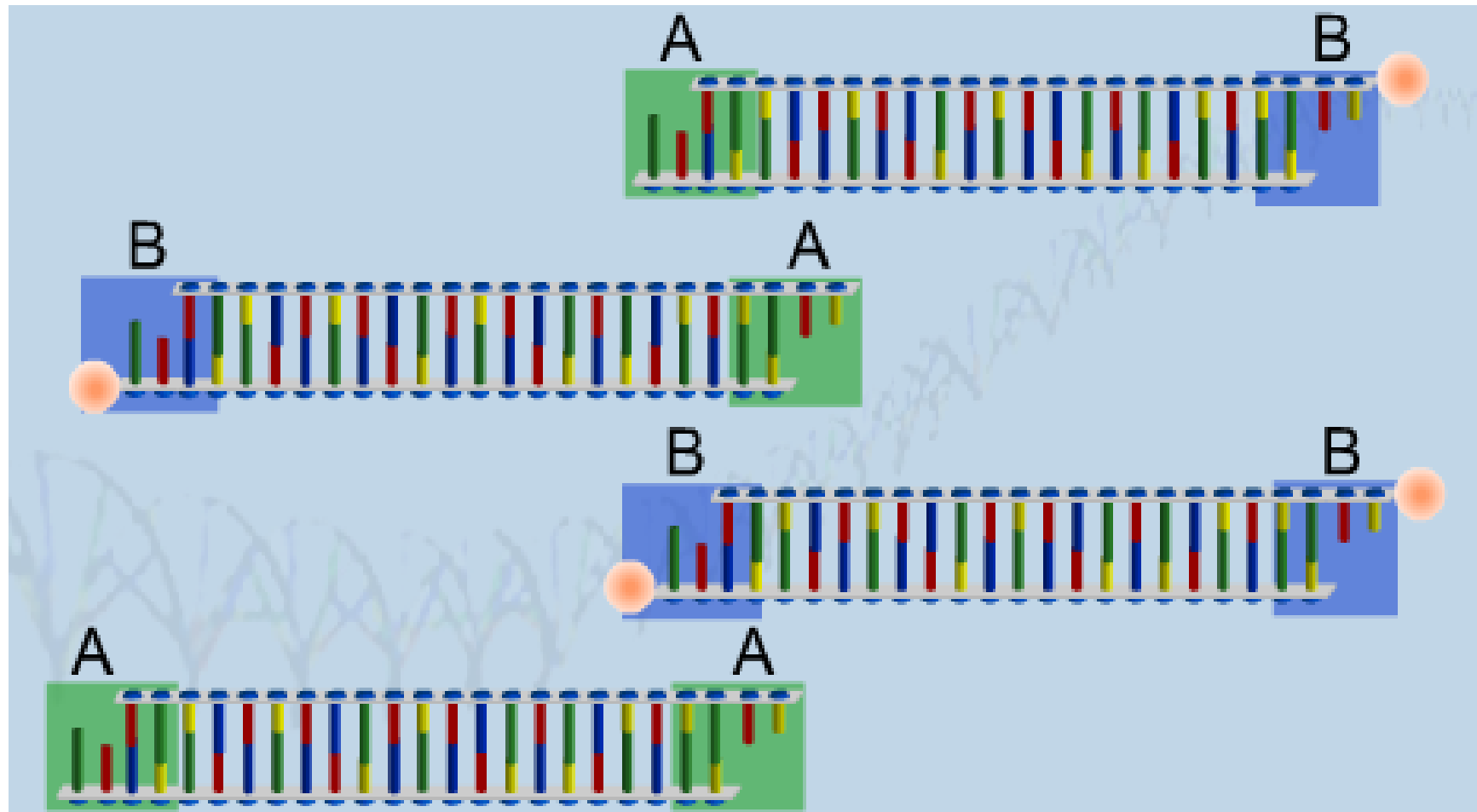
No Colony Picking



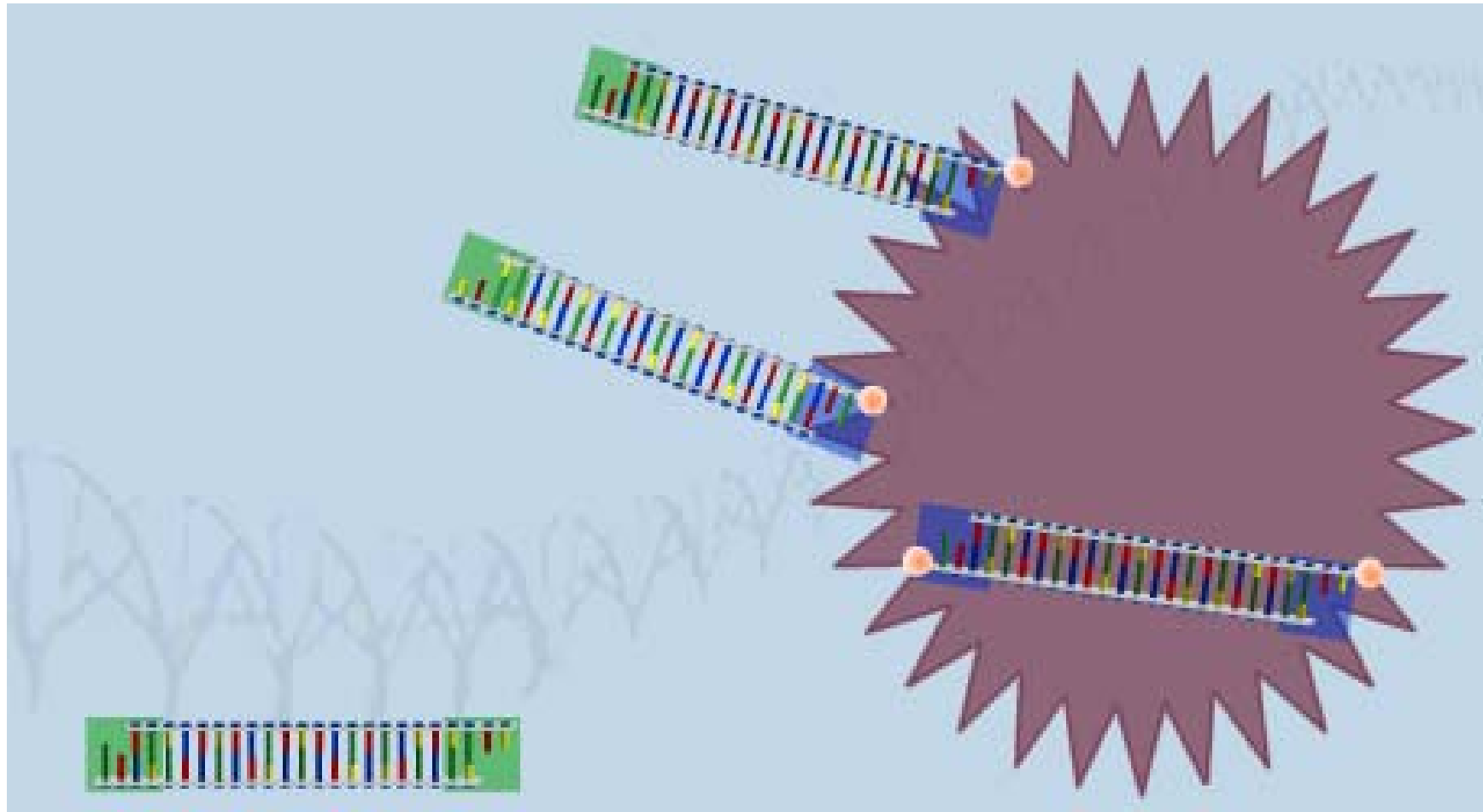
Fragmentace DNA



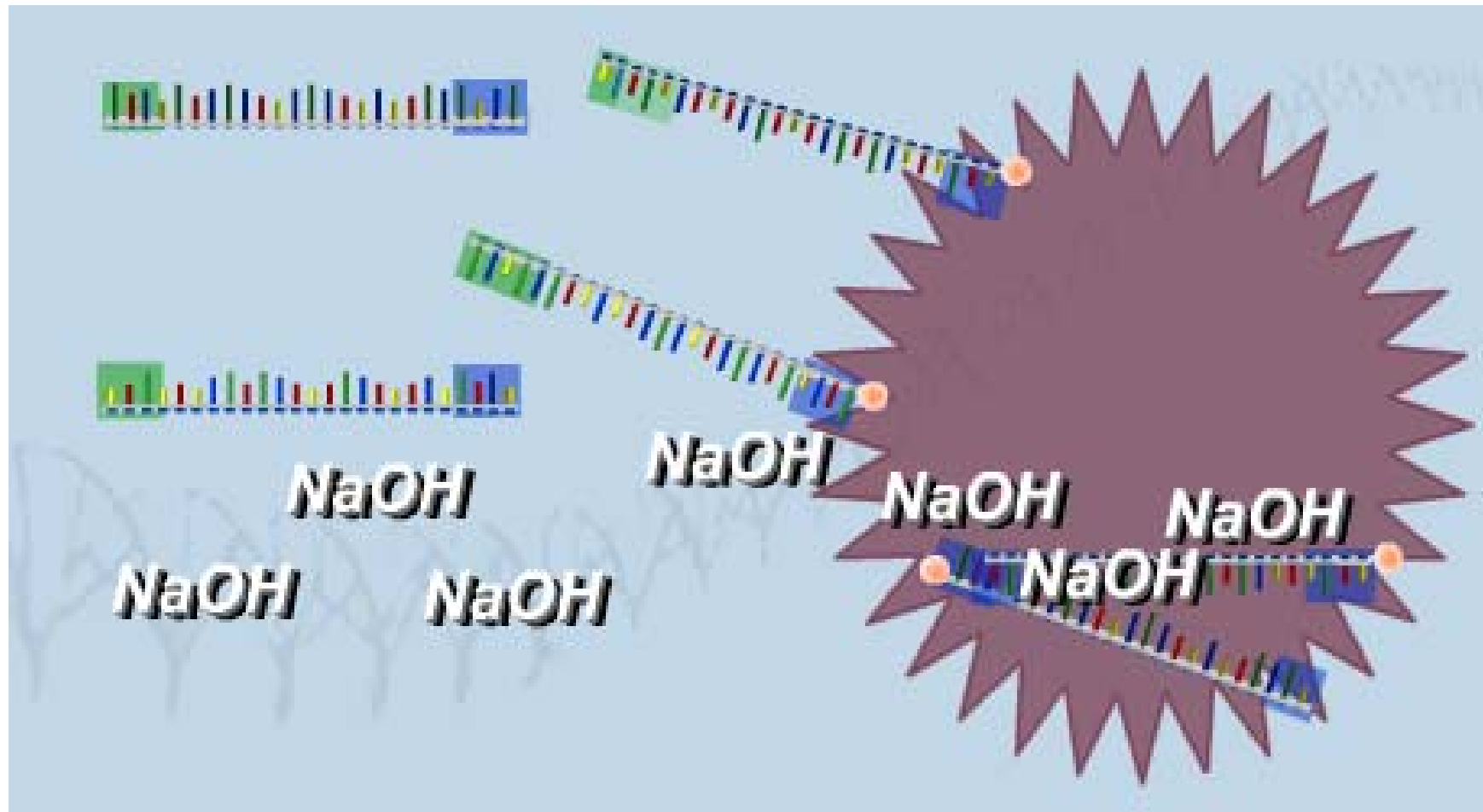
Ligace adaptoru

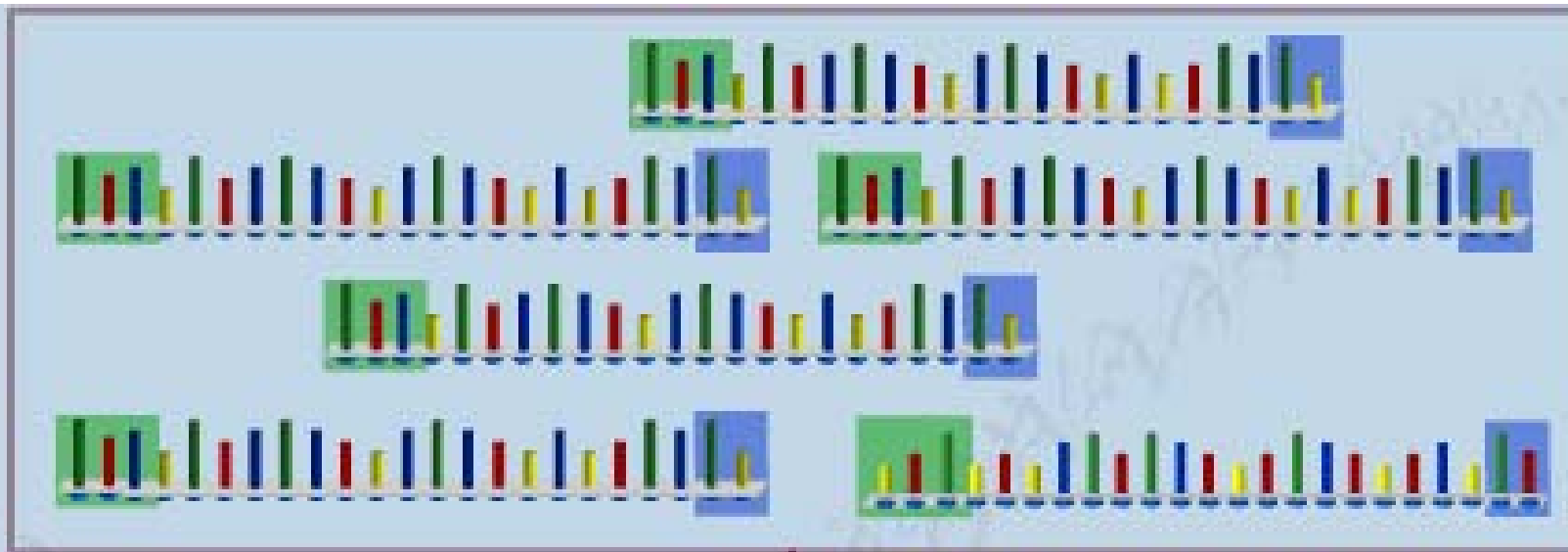


Vychytání DNA molekul



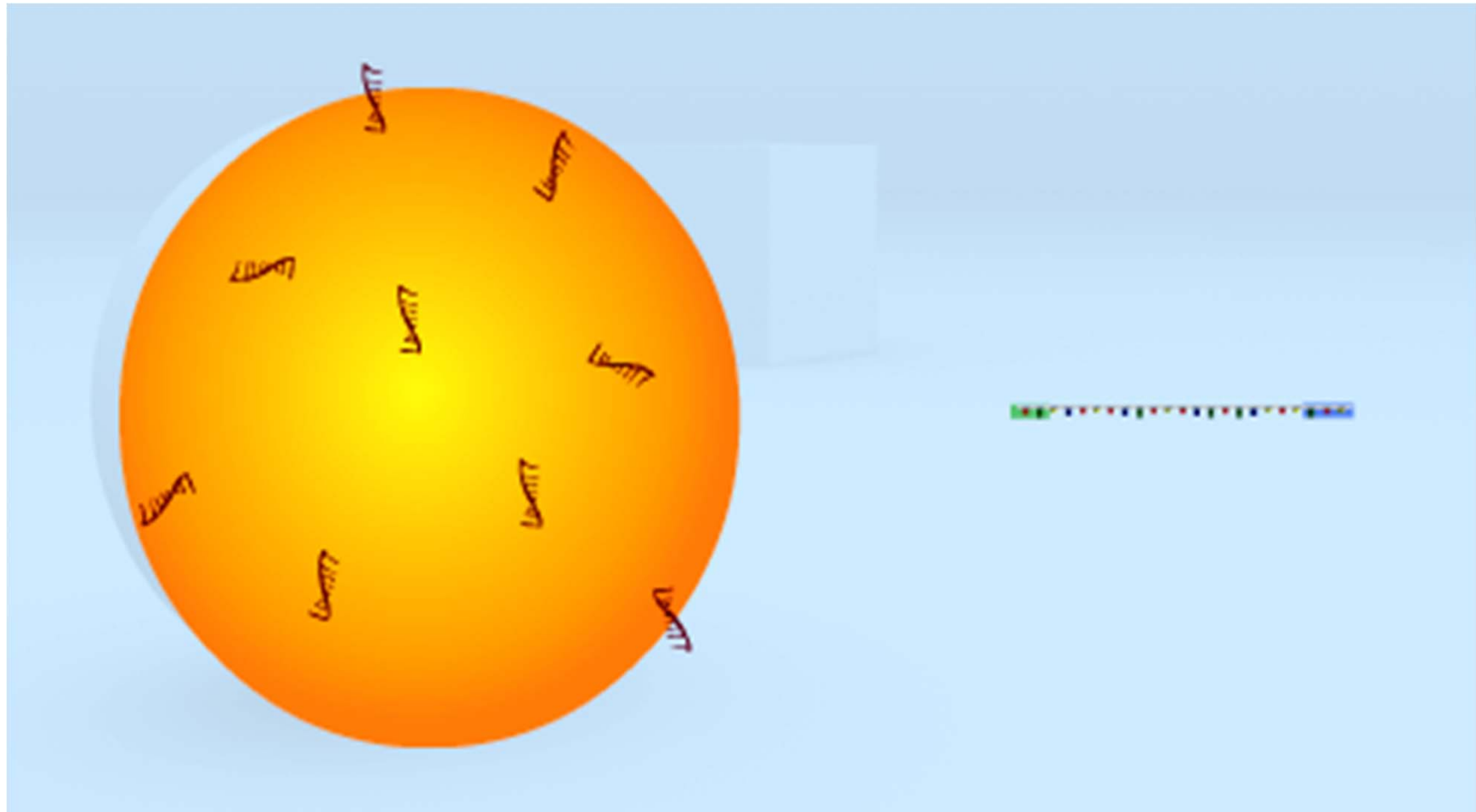
denaturace



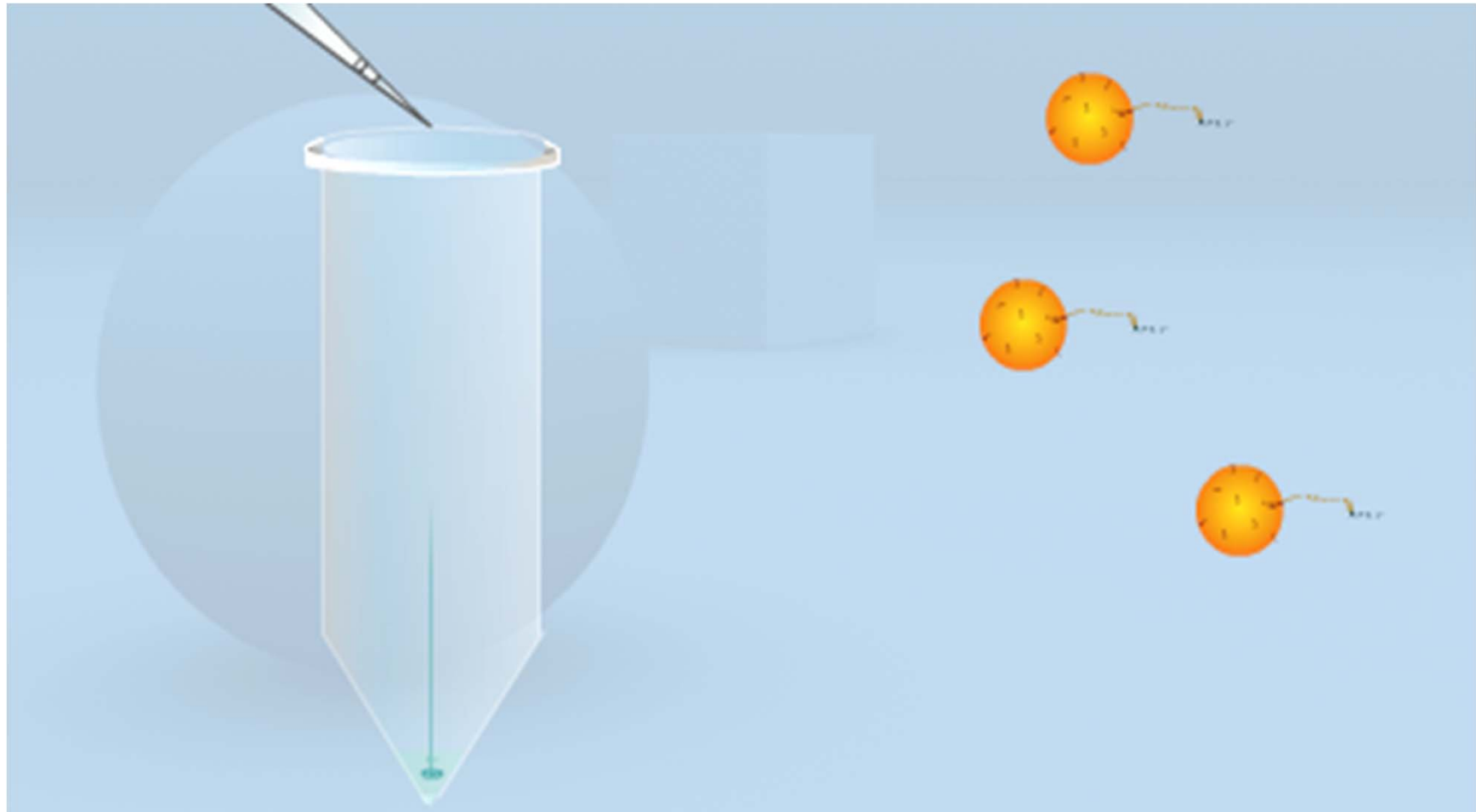


Single-stranded
template DNA
sstDNA

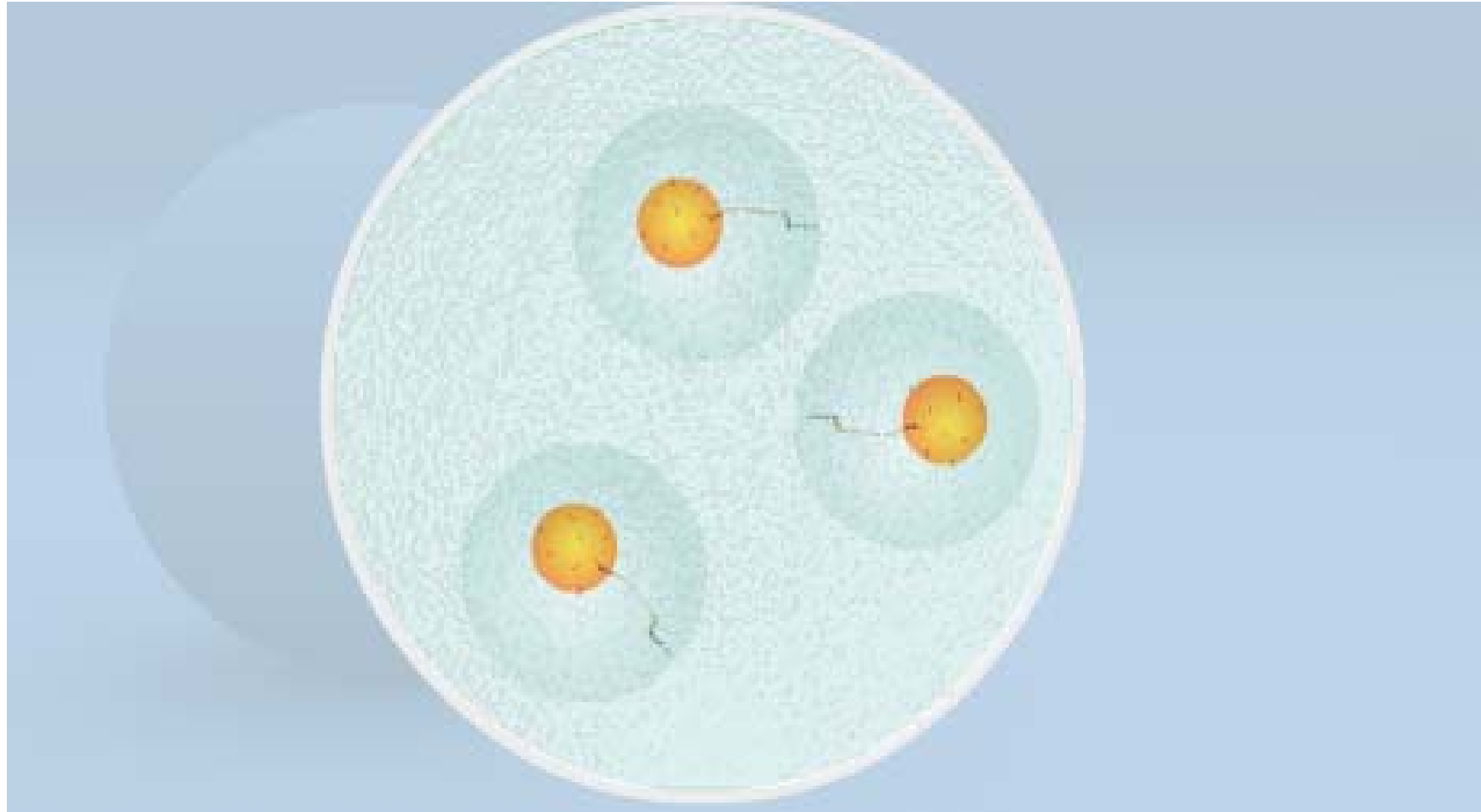
emPCR



Vznik emulze (olej)



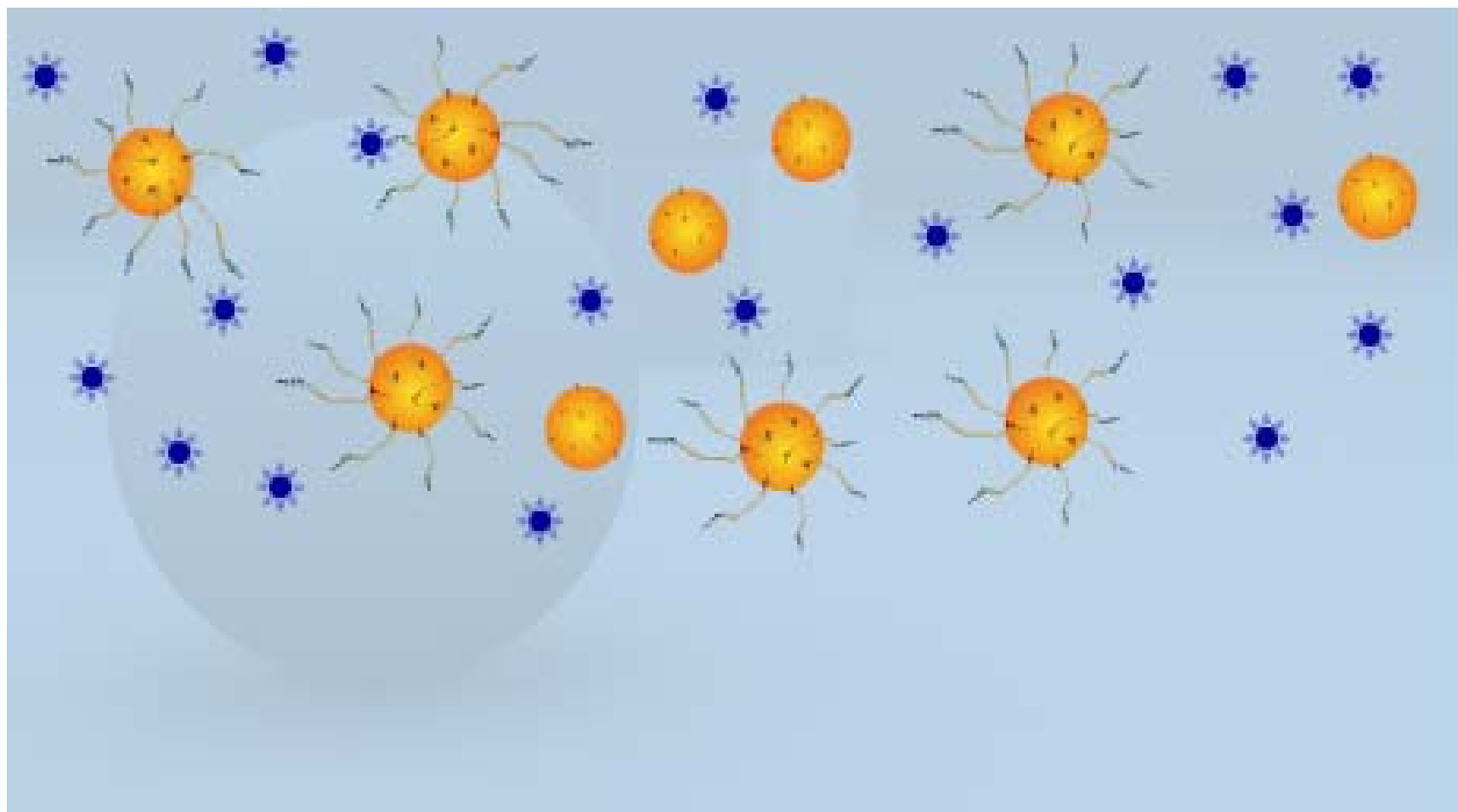
emPCR



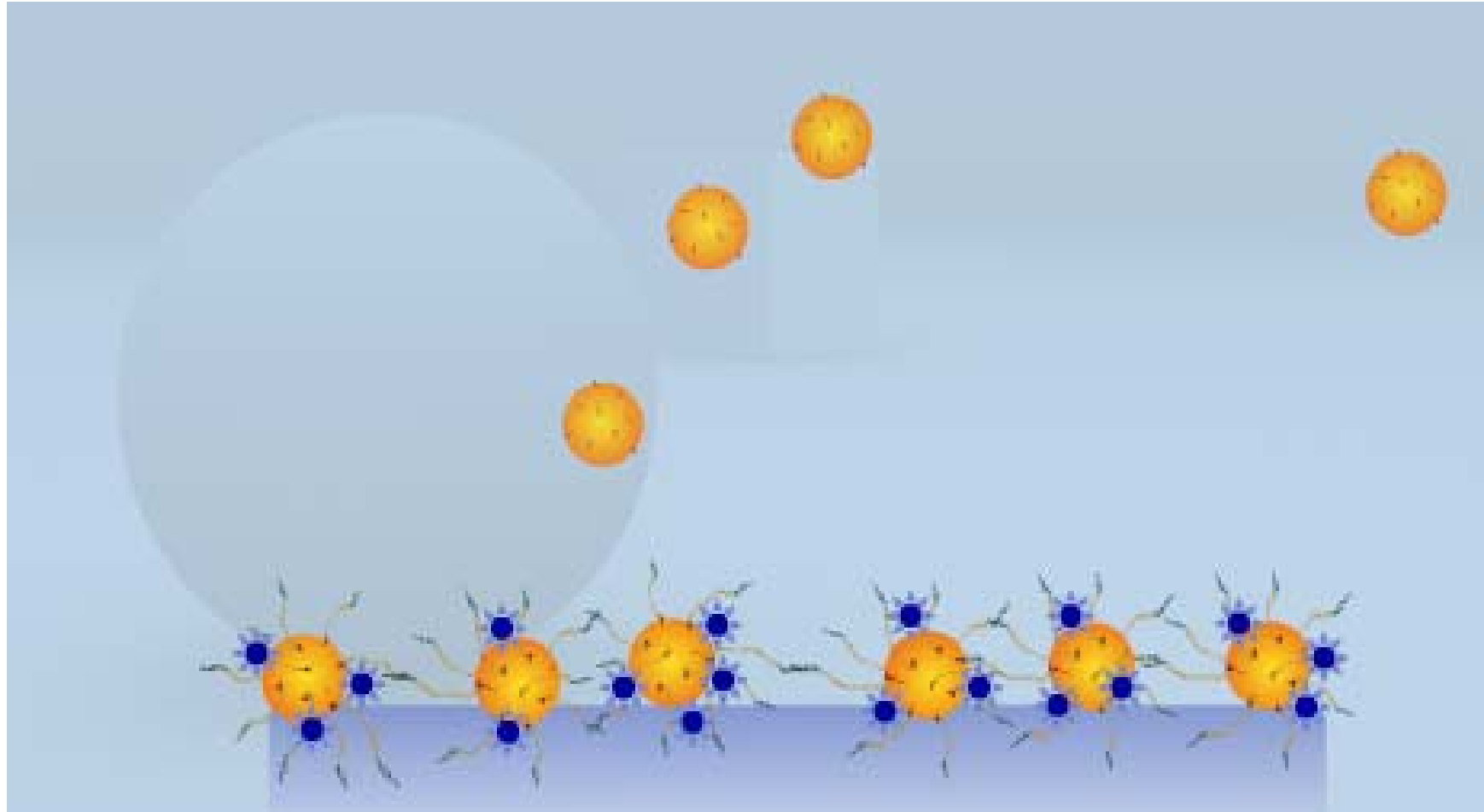
emPCR



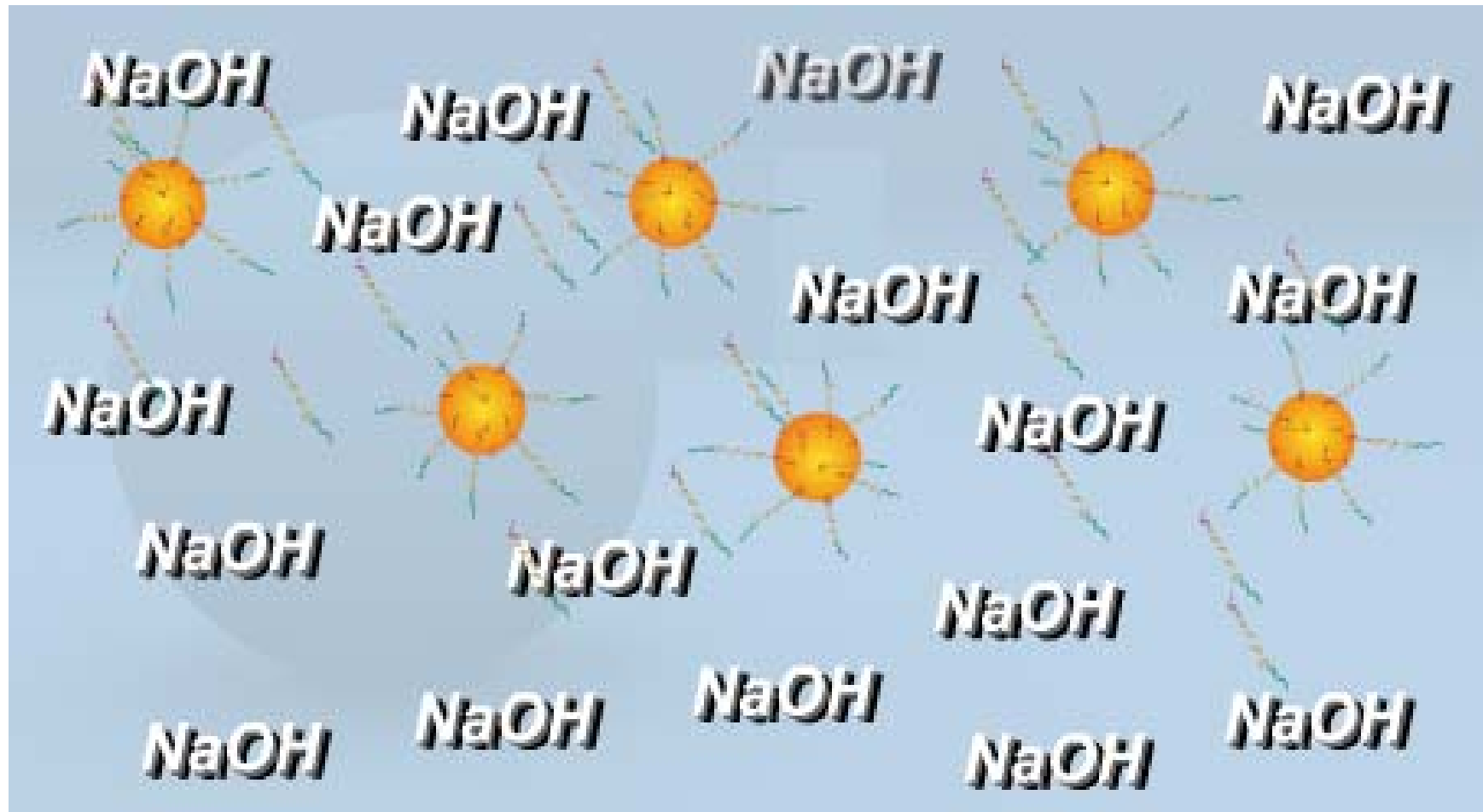
Vychytání kuliček



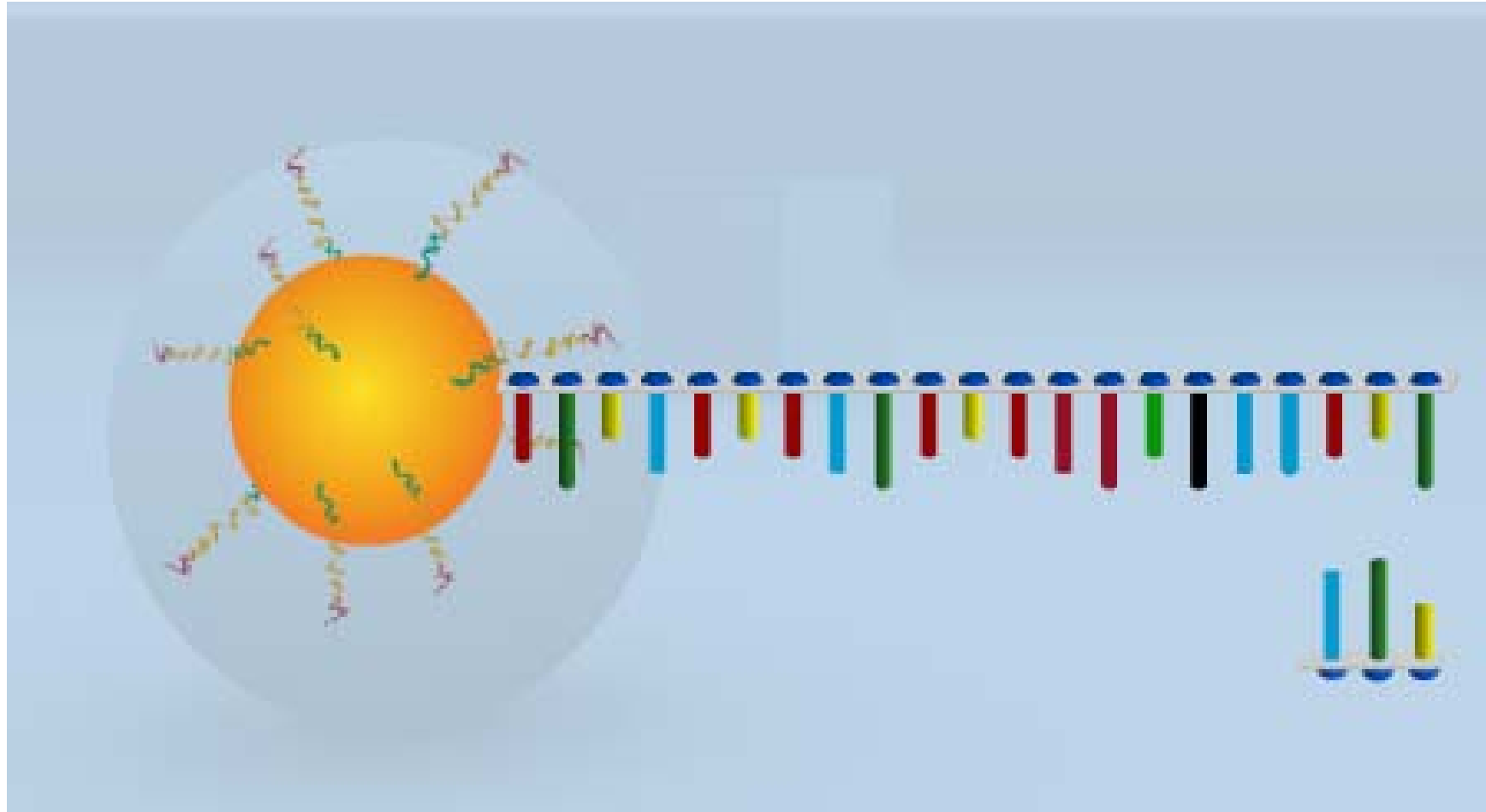
Vychytání kuliček



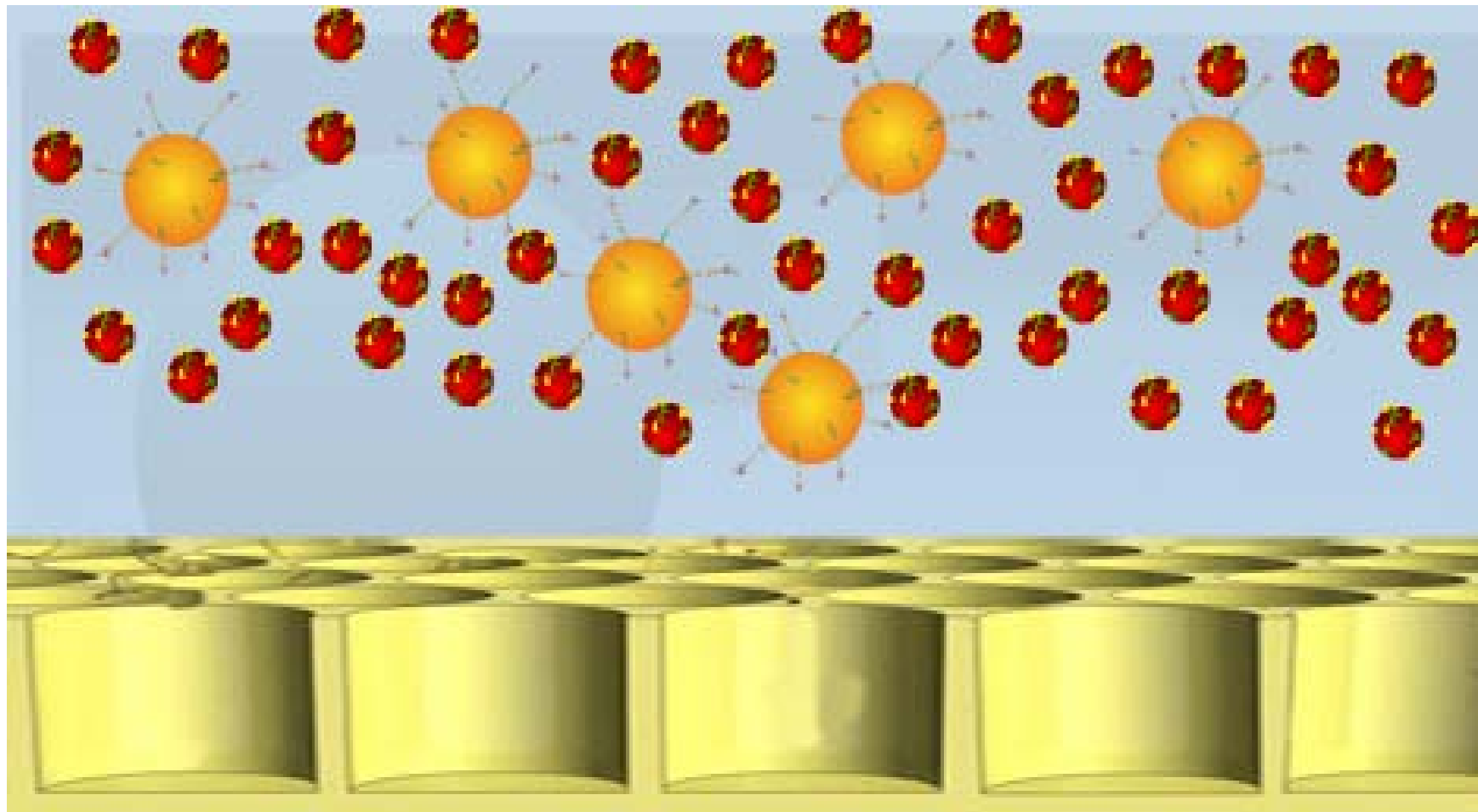
denaturace



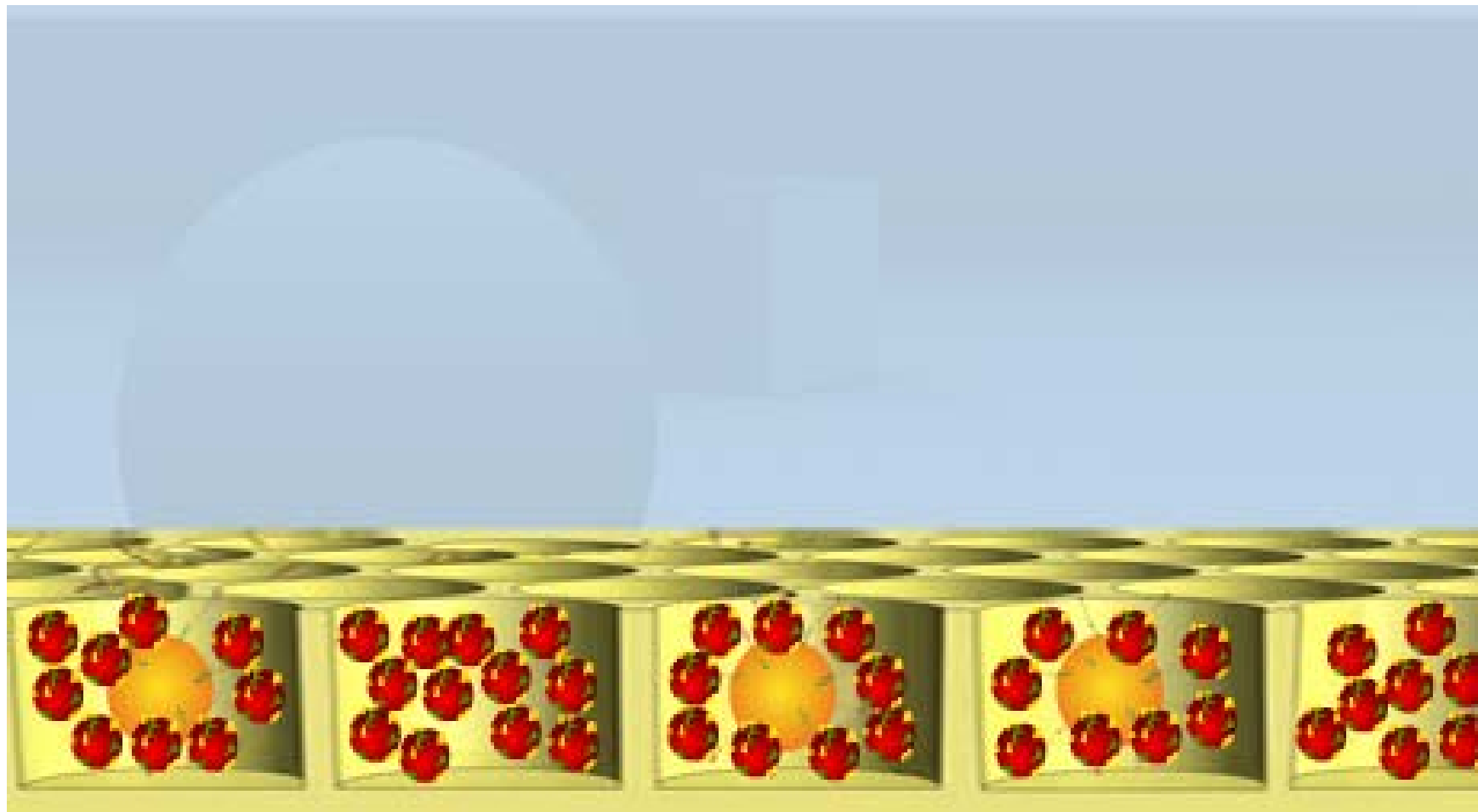
Sekvenační primer



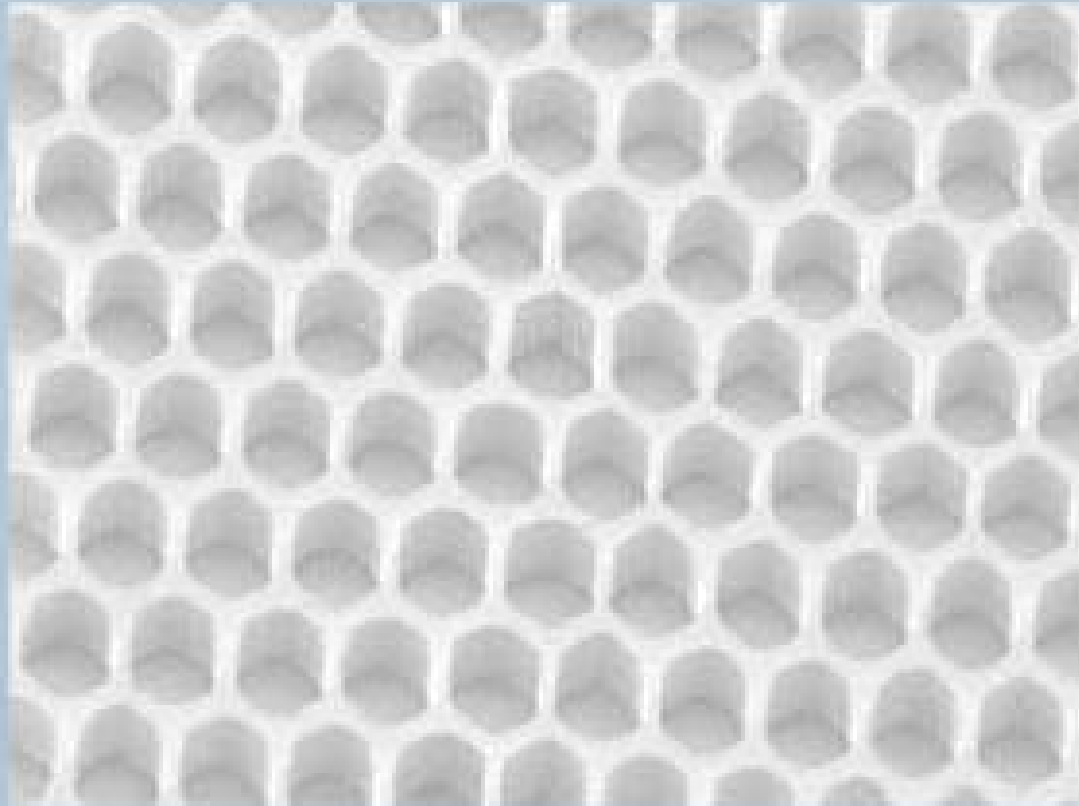
Disperze na sklíčko



Disperze na sklíčko



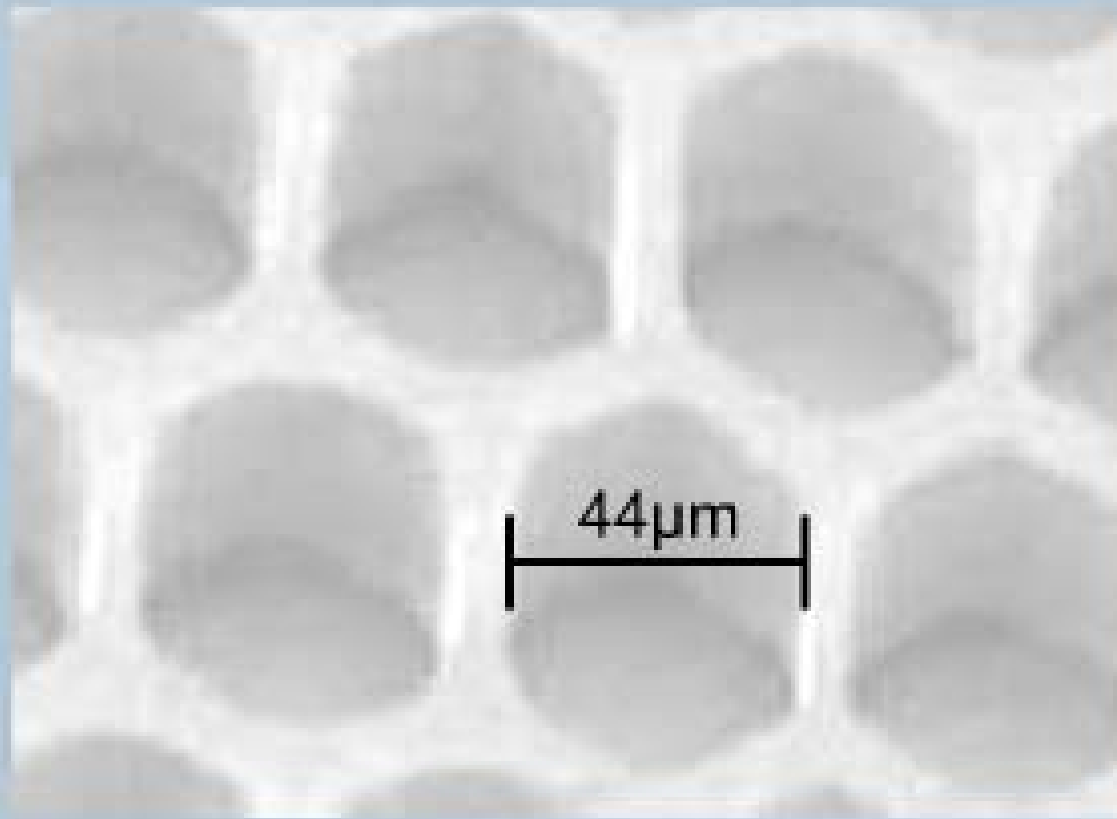
Parametry mikroreaktorů



1.6 million
wells

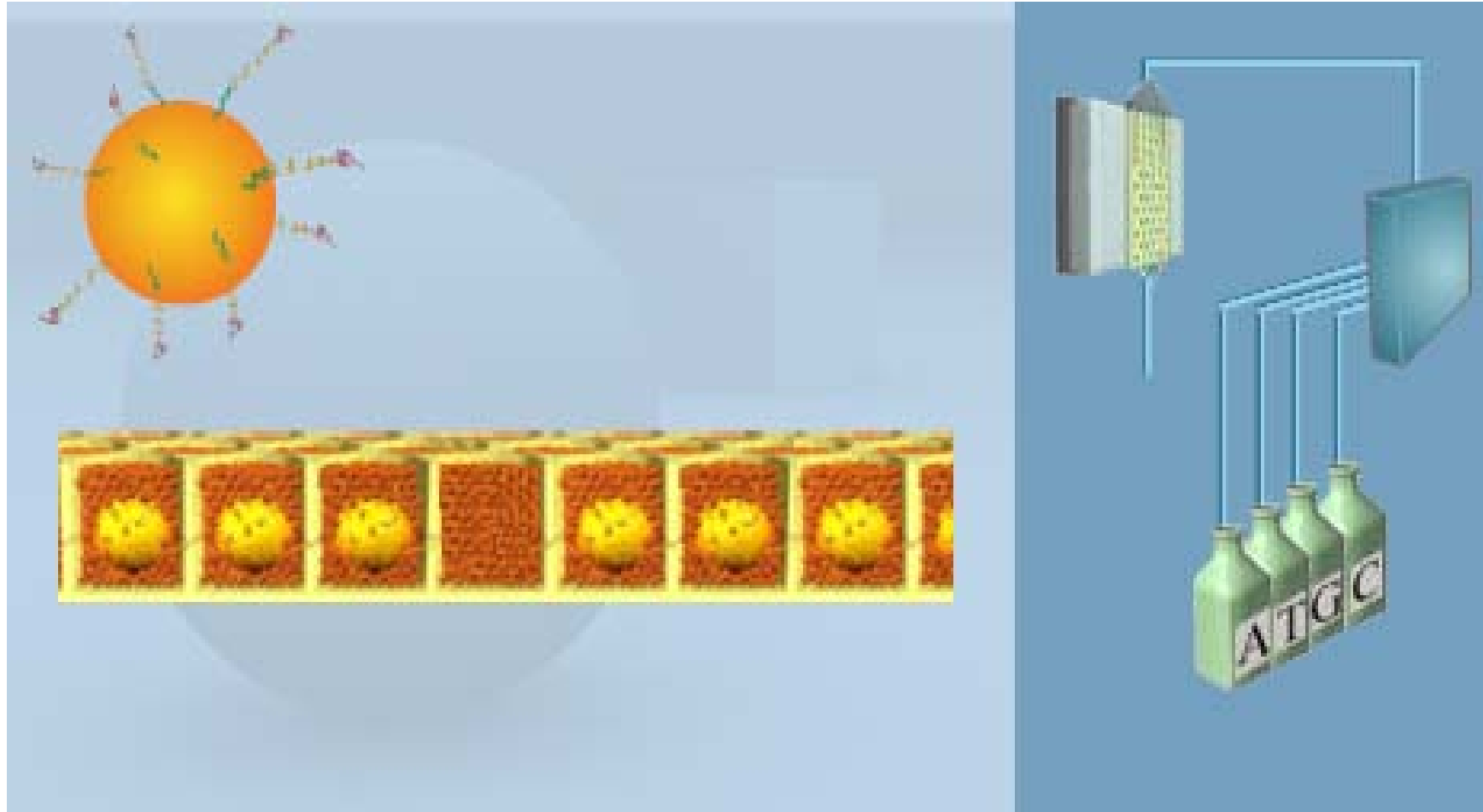
PicoTiterPlate device

Parametry mikroreaktorů

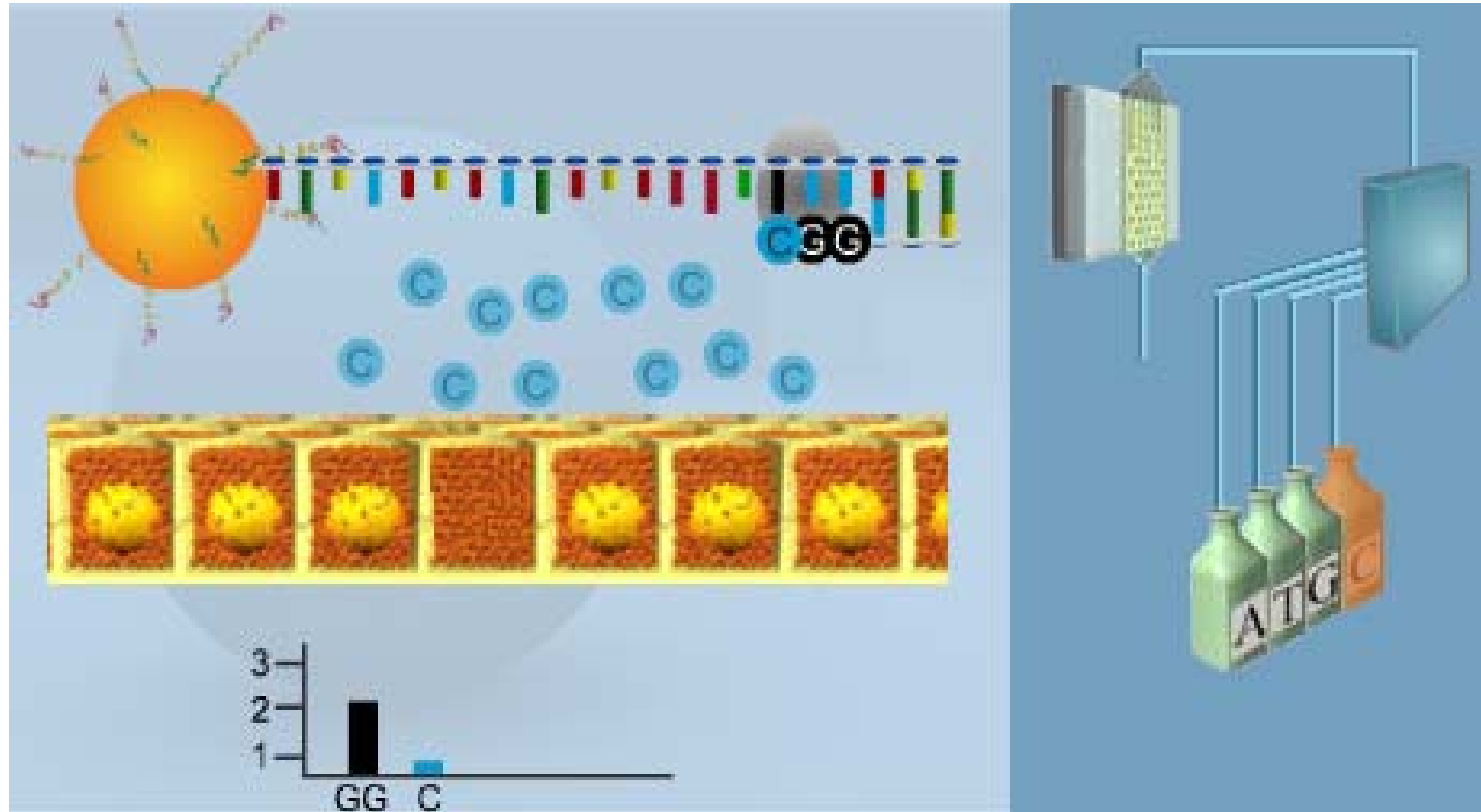


PicoTiterPlate device

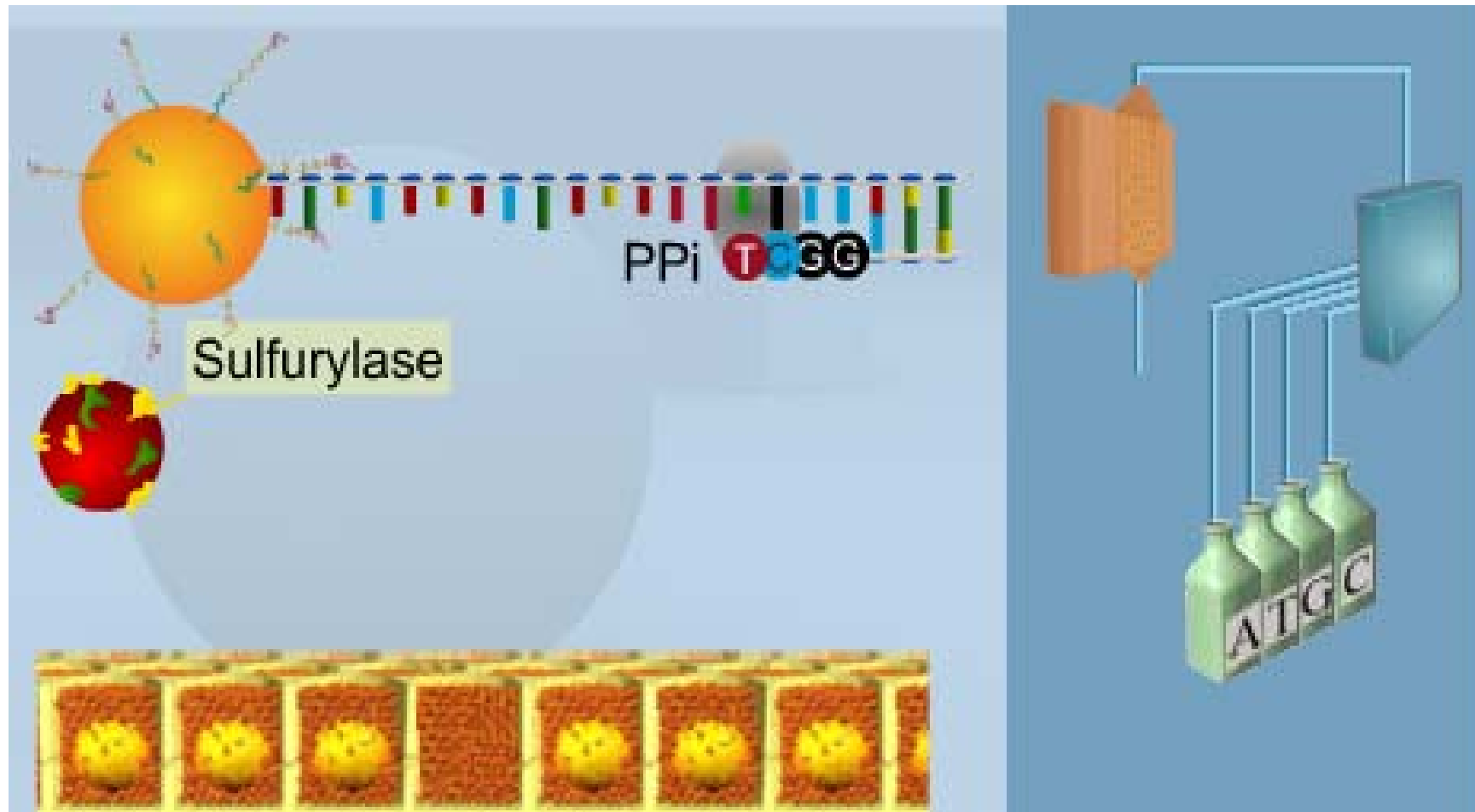
sekvenace



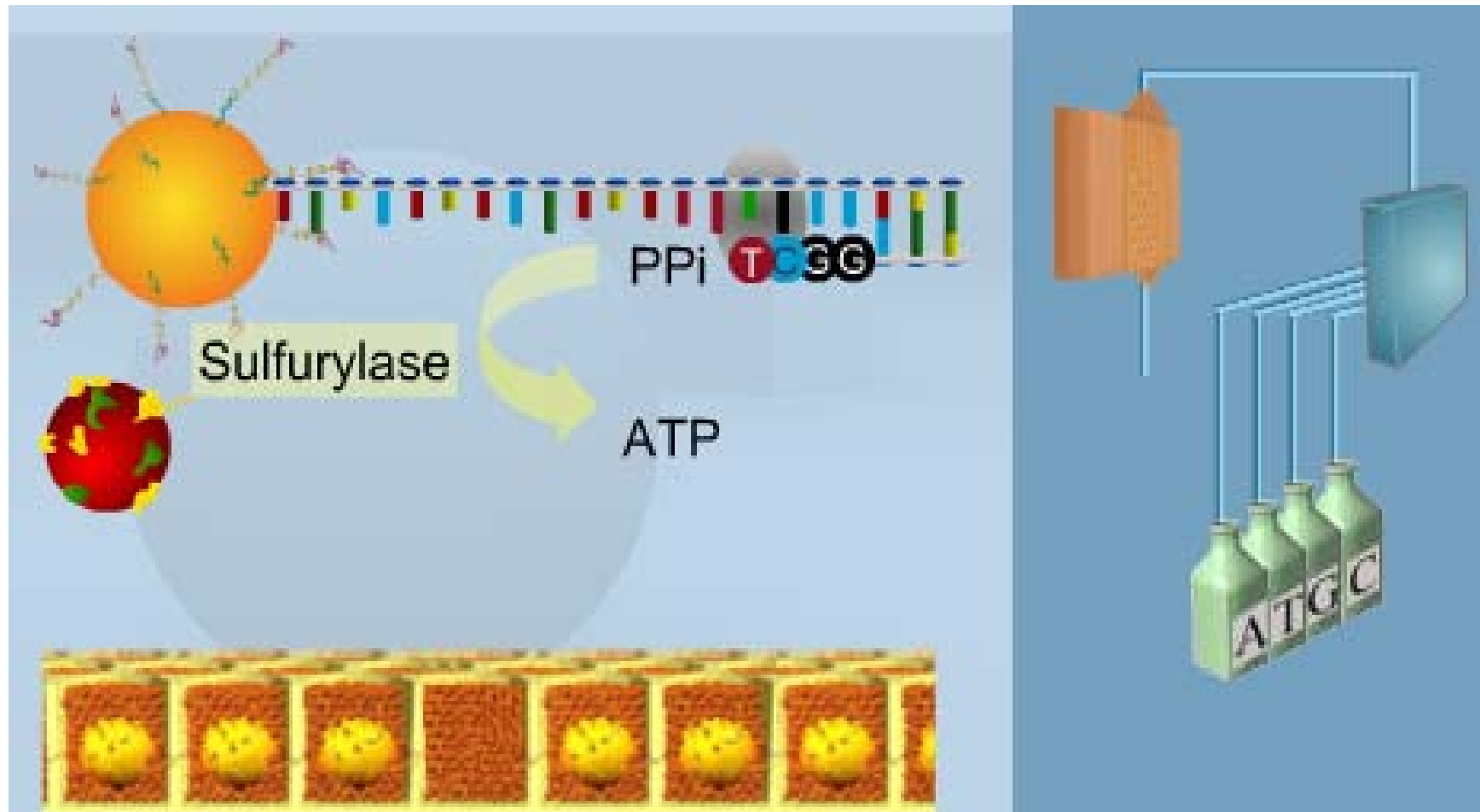
sekvenace



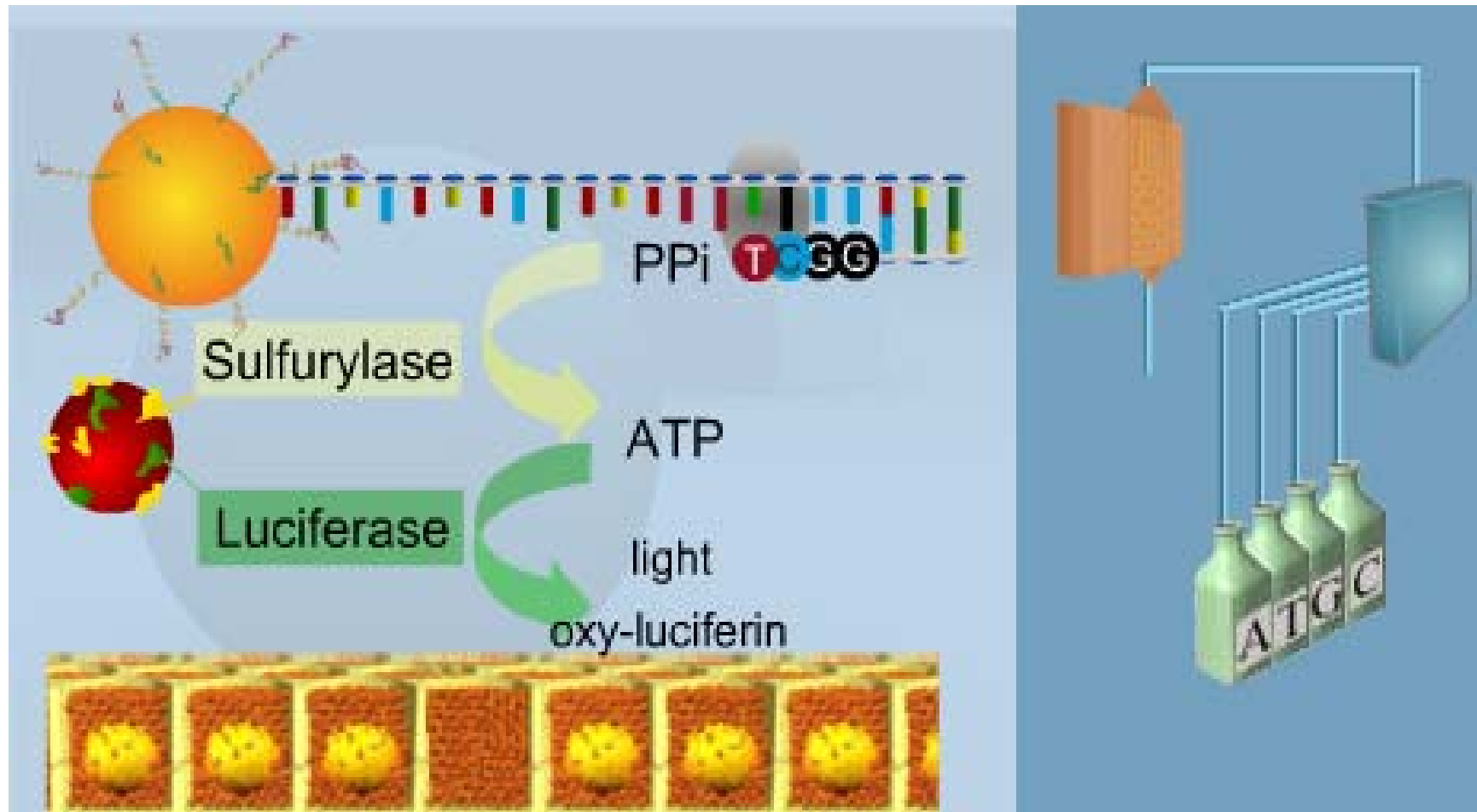
sekvenace



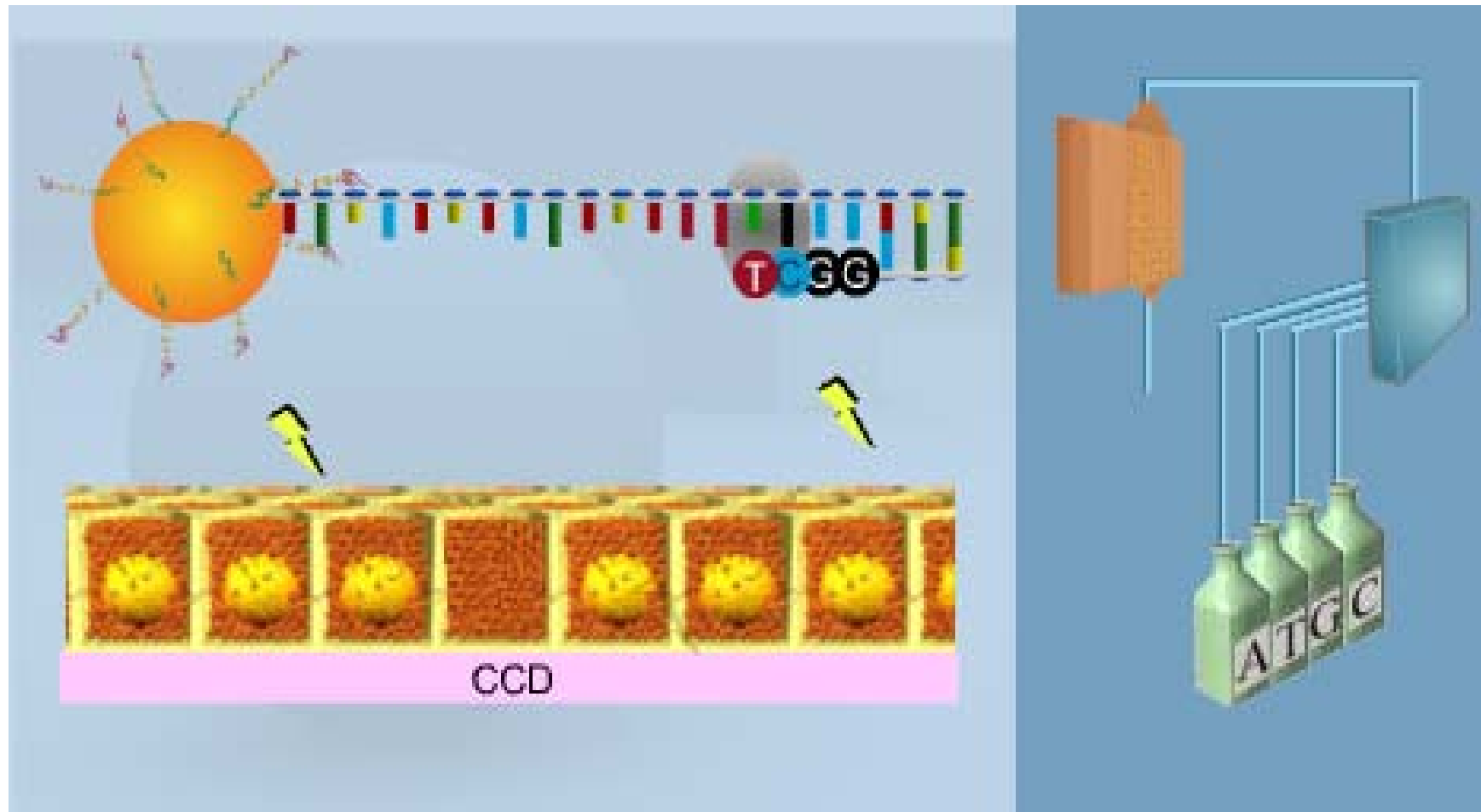
sekvenace



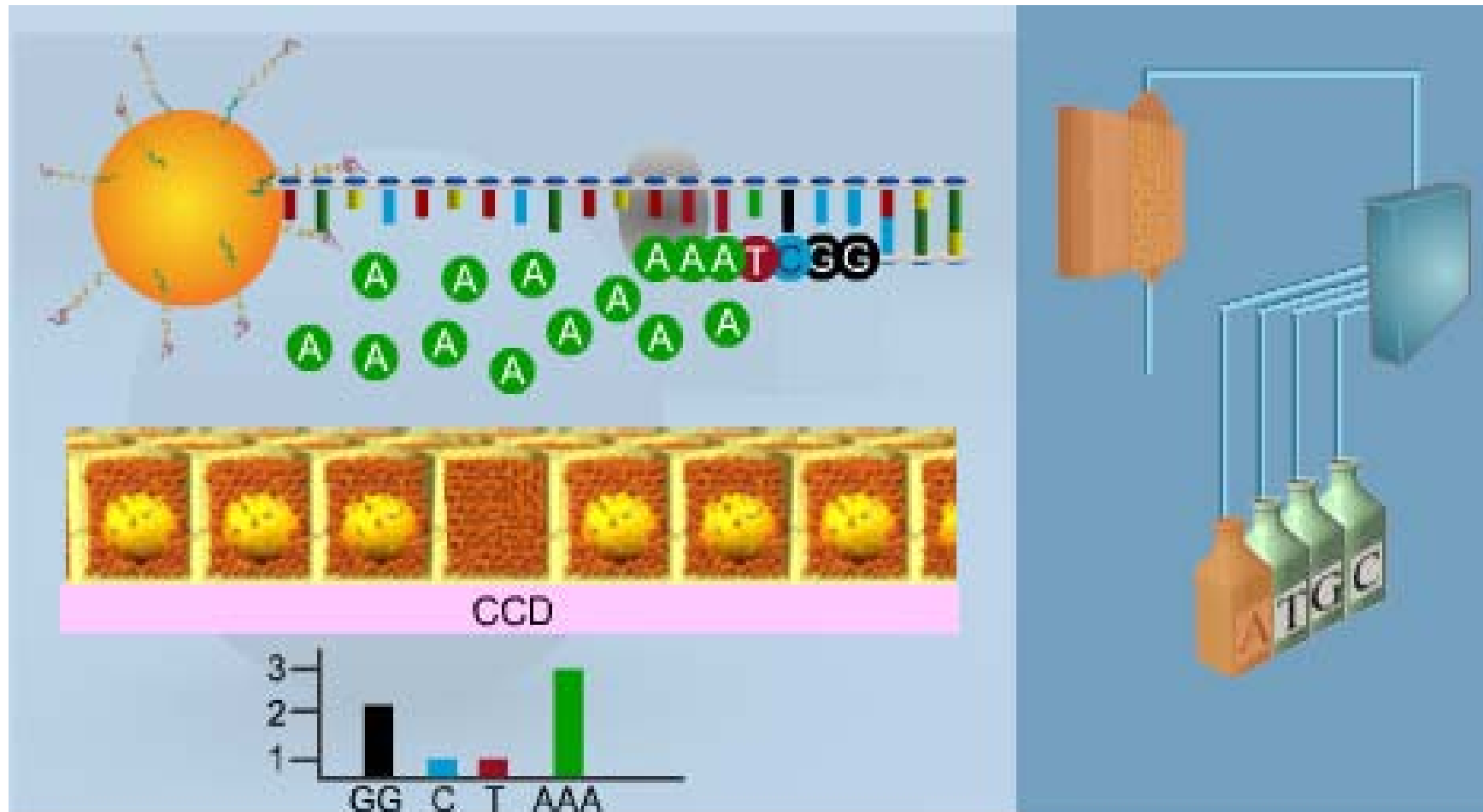
sekvenace



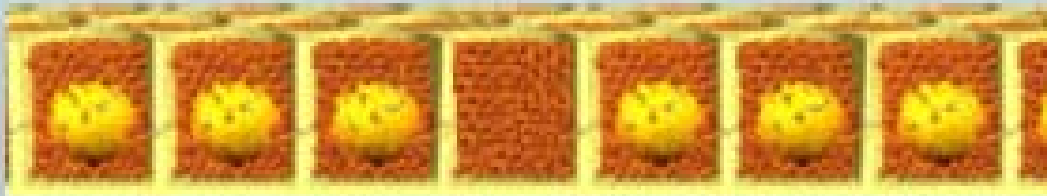
sekvenace



sekvenace



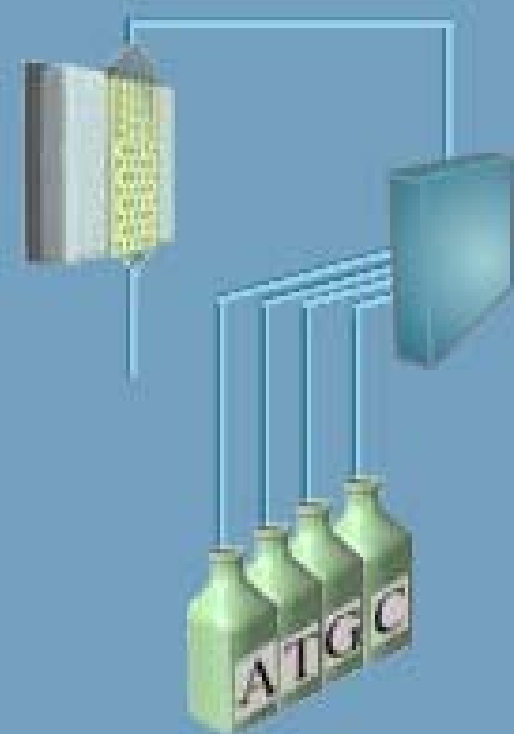
sekvenace



Massive parallelization of sequencing reactions

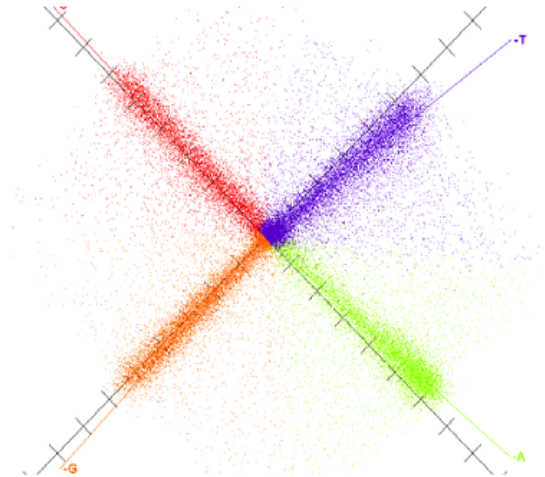
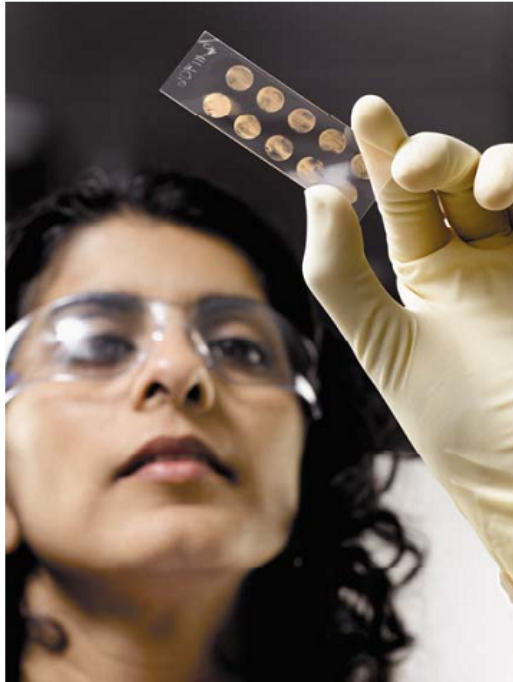
100 bases read length
X
200 000

20 Million Bases



SOLID (Sequencing by Oligonucleotide Ligation and Detection)

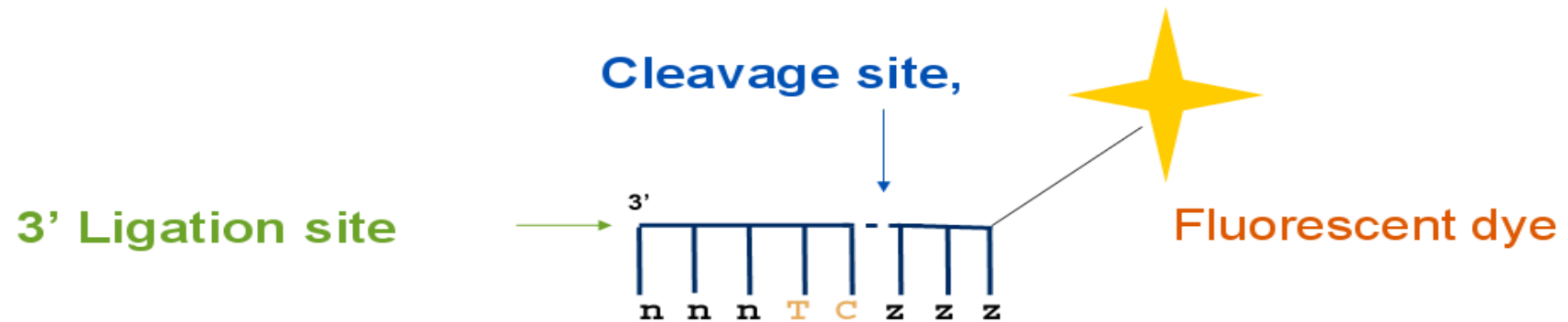
2-base encoding sequencing (2007)



SOLiD™ System
Sequencing by Oligonucleotide Ligation and Detection

Properties of the Probes

Spatial separation among dye, ligation & cleavage sites



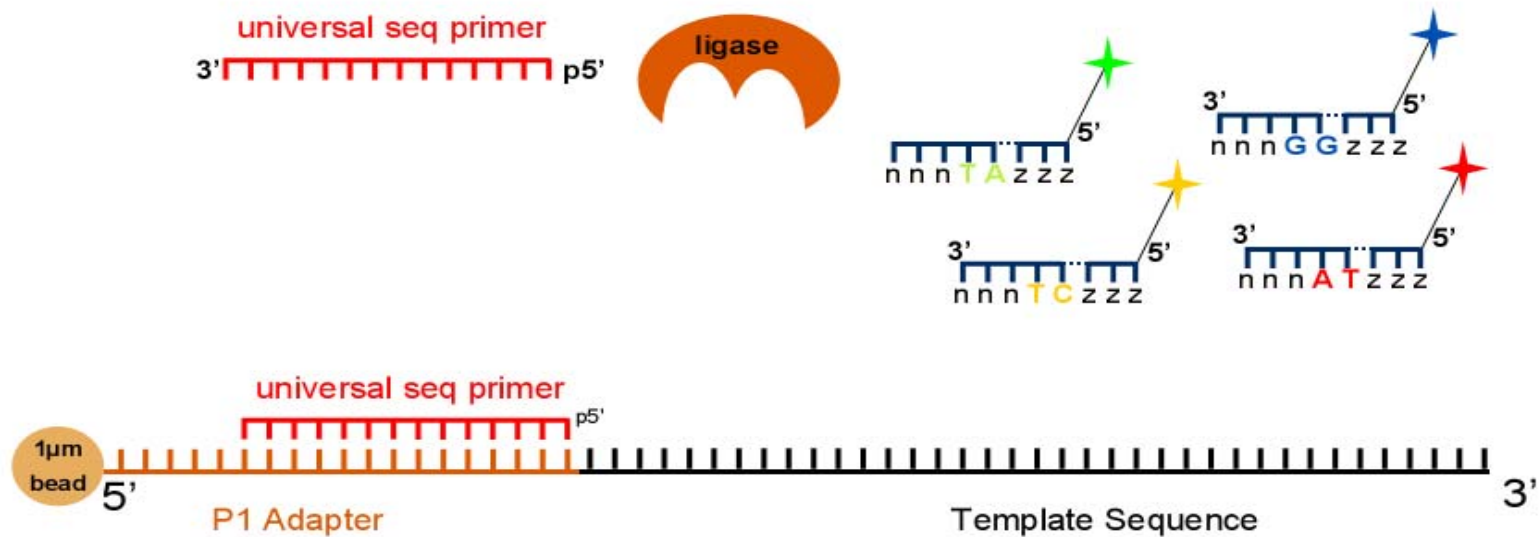
1,024 Octamer Probes (4^5)

4 Dyes, 4 dinucleotides, 256 probes per dye

N= degenerate bases Z= Universal bases

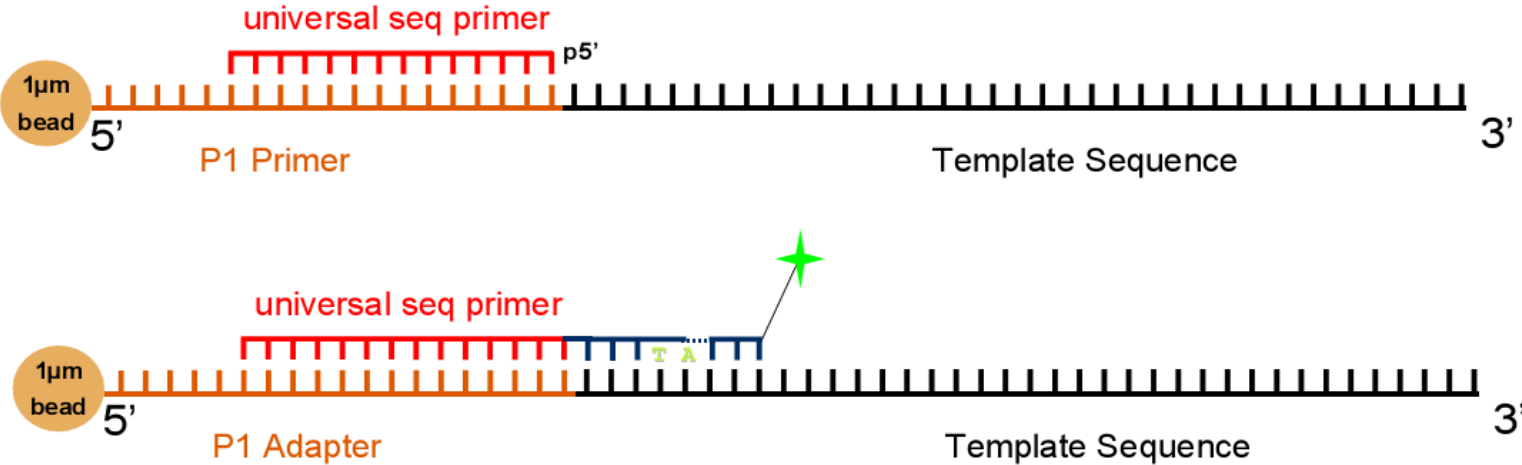
SOLiD Chemistry System 4-color ligation

Ligation reaction

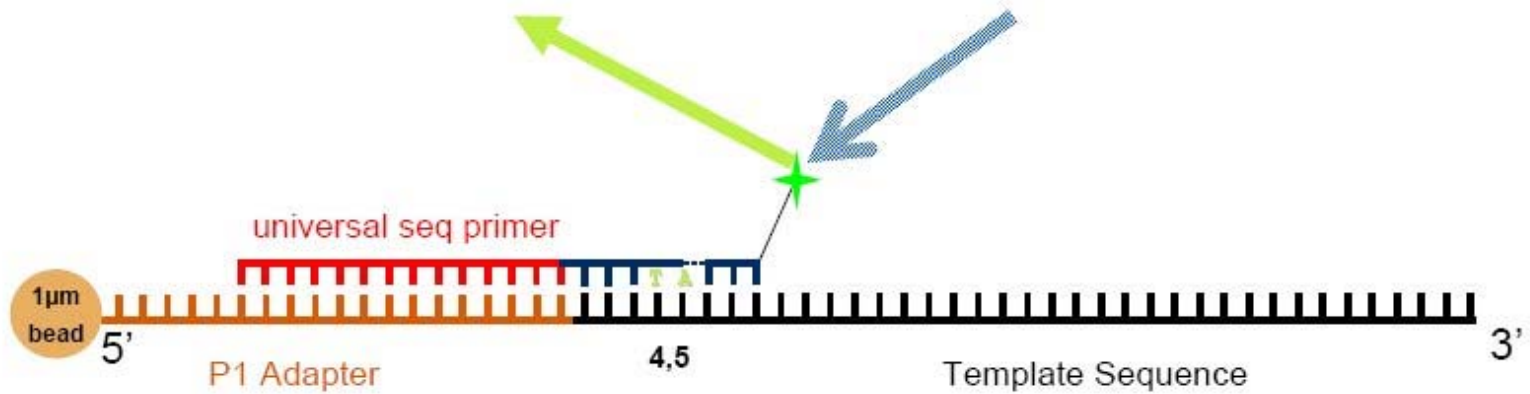


SOLiD Chemistry System 4-color ligation

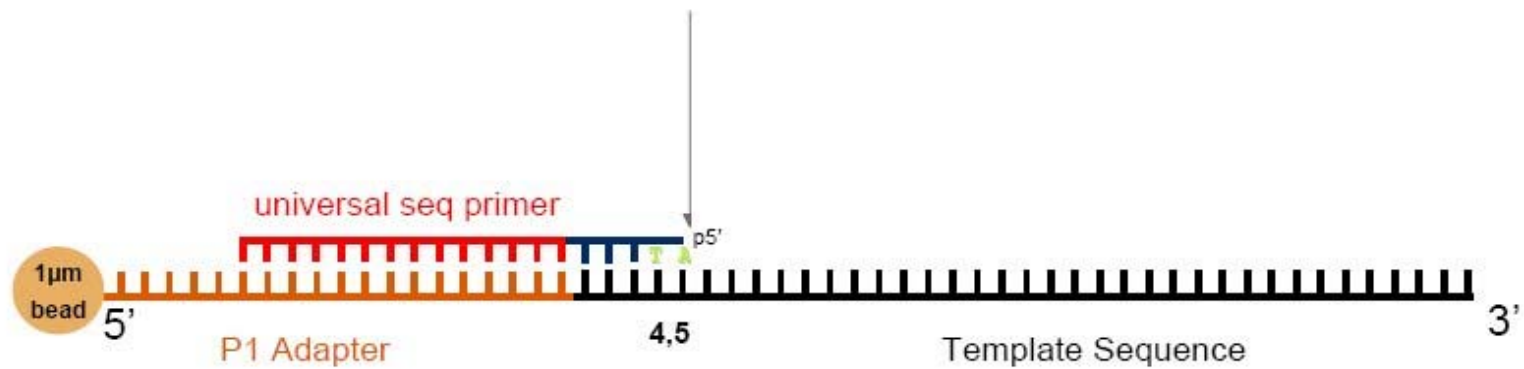
De-Phosphorylation



SOLiD Chemistry System 4-color ligation Visualization

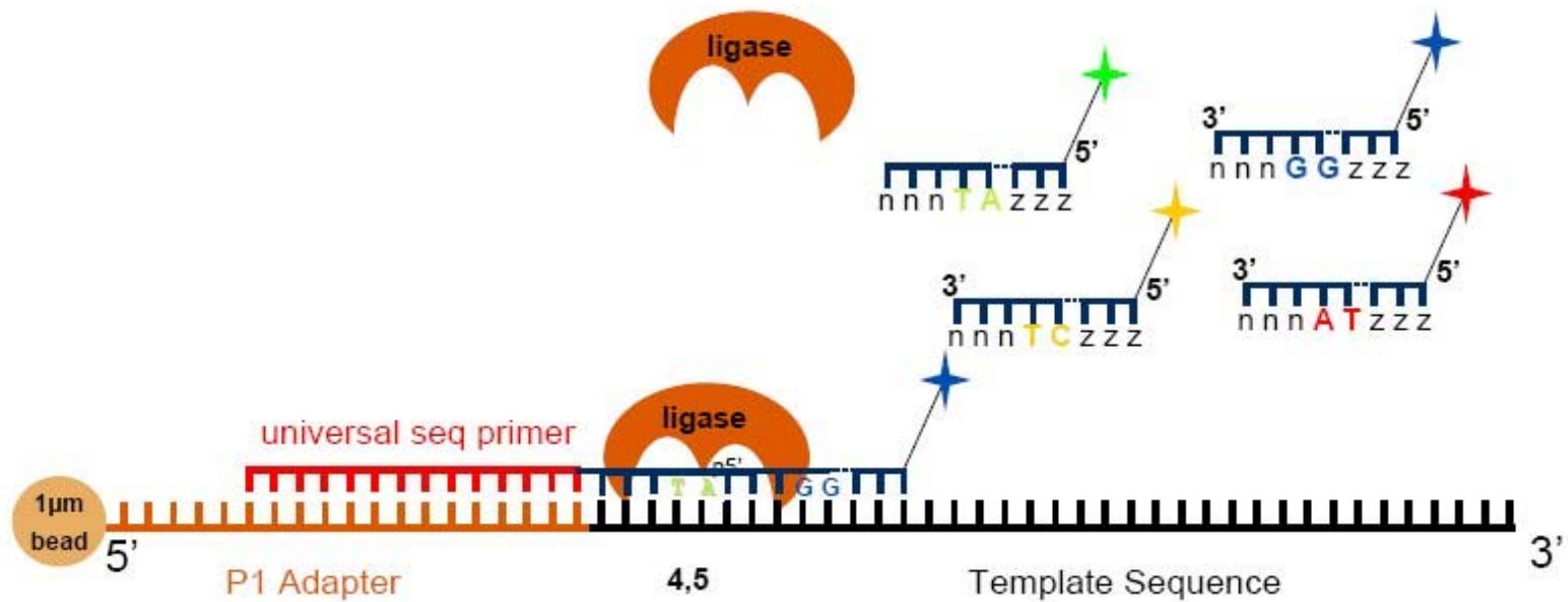


SOLiD Chemistry System 4-color ligation Cleavage

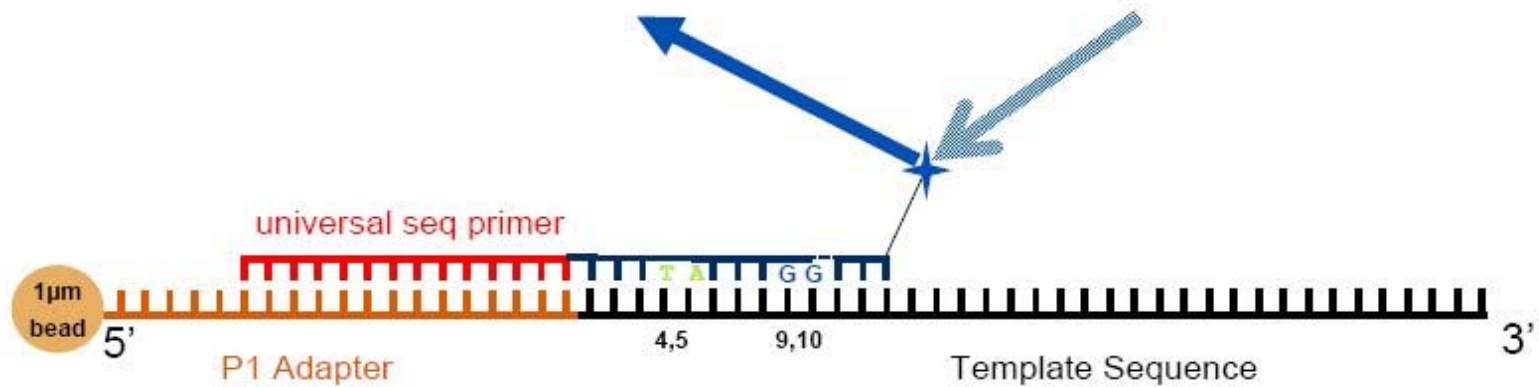


SOLiD Chemistry System 4-color ligation

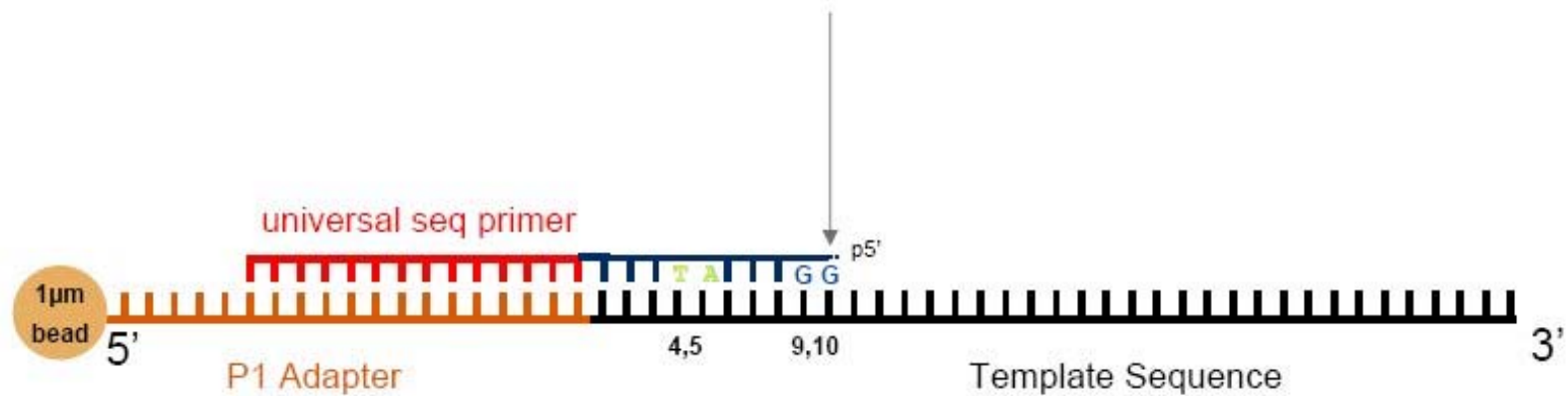
Ligation (2nd cycle)



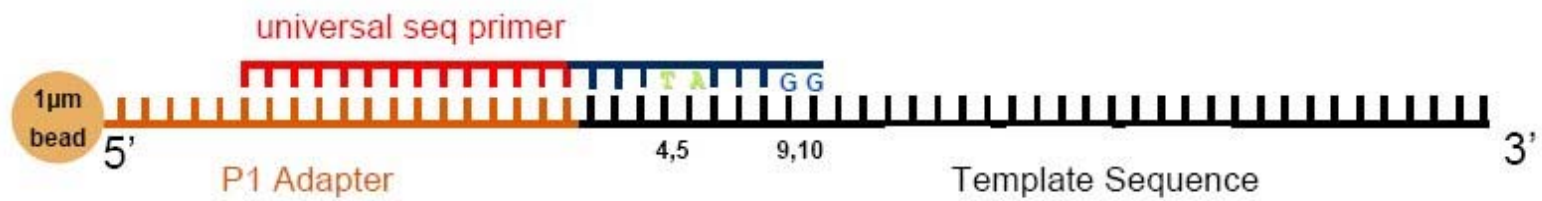
SOLiD Chemistry System 4-color ligation Visualization (2nd cycle)



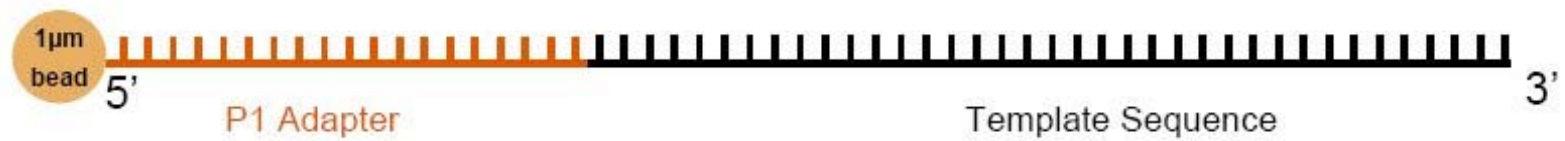
SOLiD Chemistry System 4-color ligation Cleavage (2nd cycle)



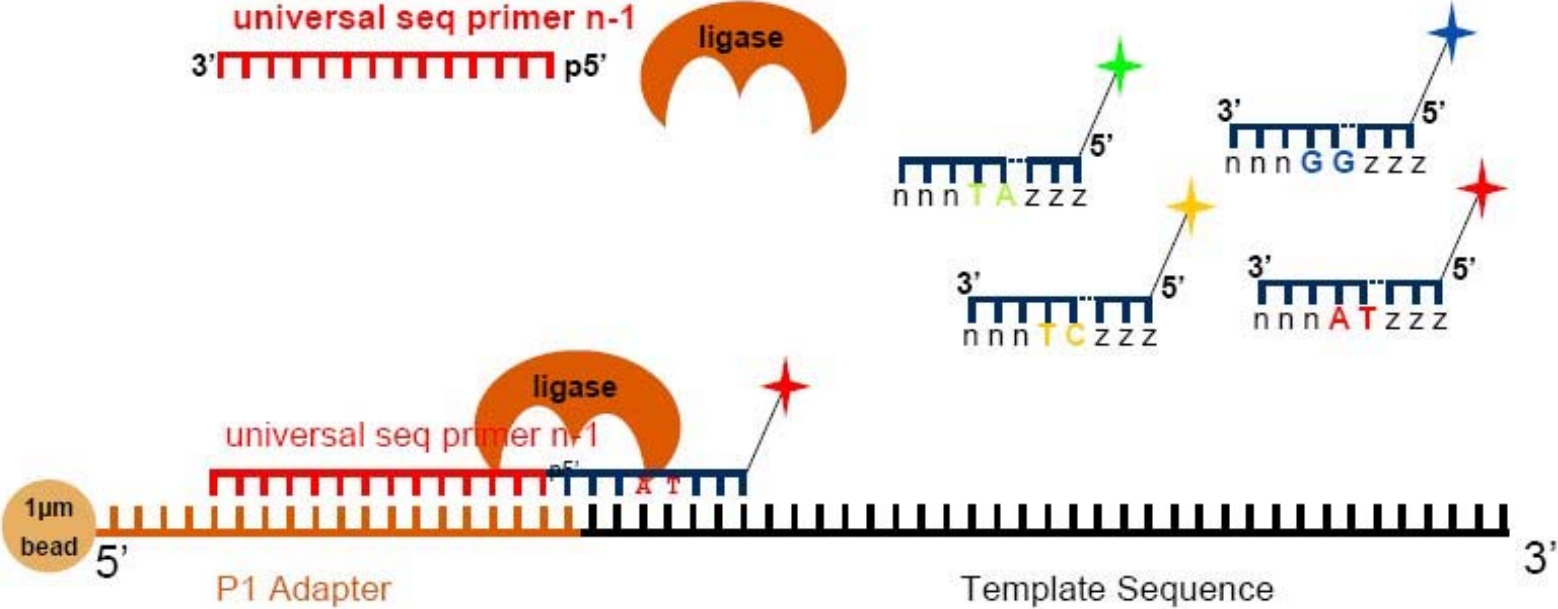
SOLiD Chemistry System 4-color ligation interrogates every 5th base



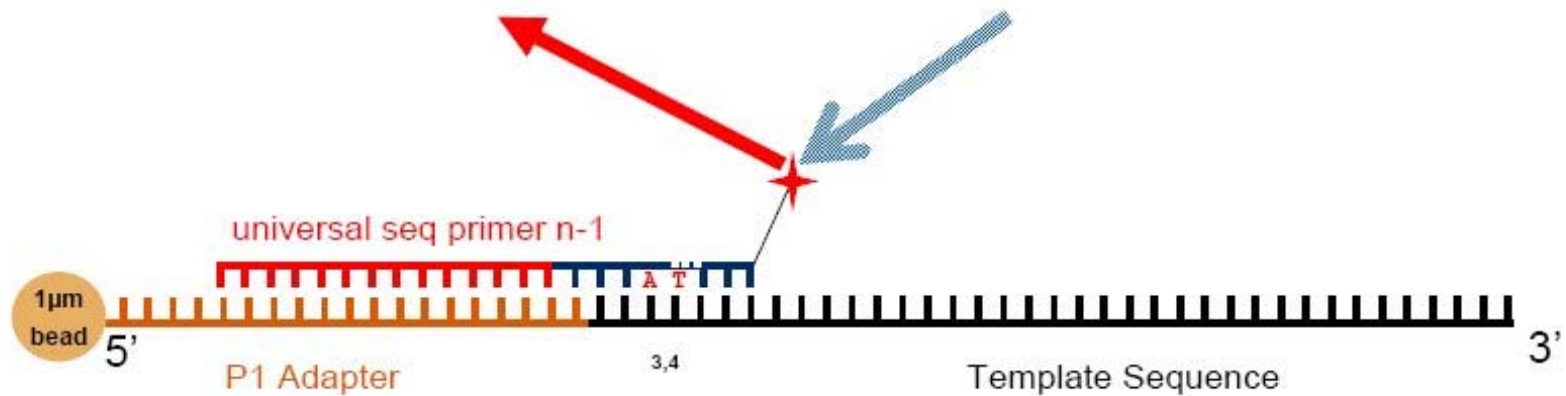
SOLiD Chemistry System 4-color ligation Reset



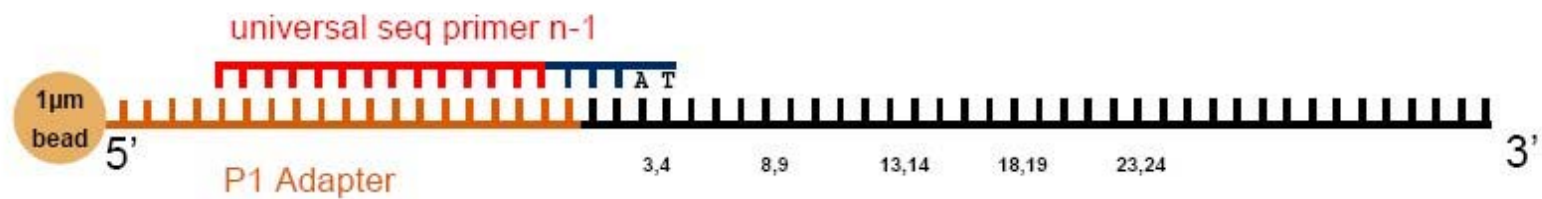
SOLiD Chemistry System 4-color ligation (1st cycle after reset)



SOLiD Chemistry System 4-color ligation (1st cycle after reset)

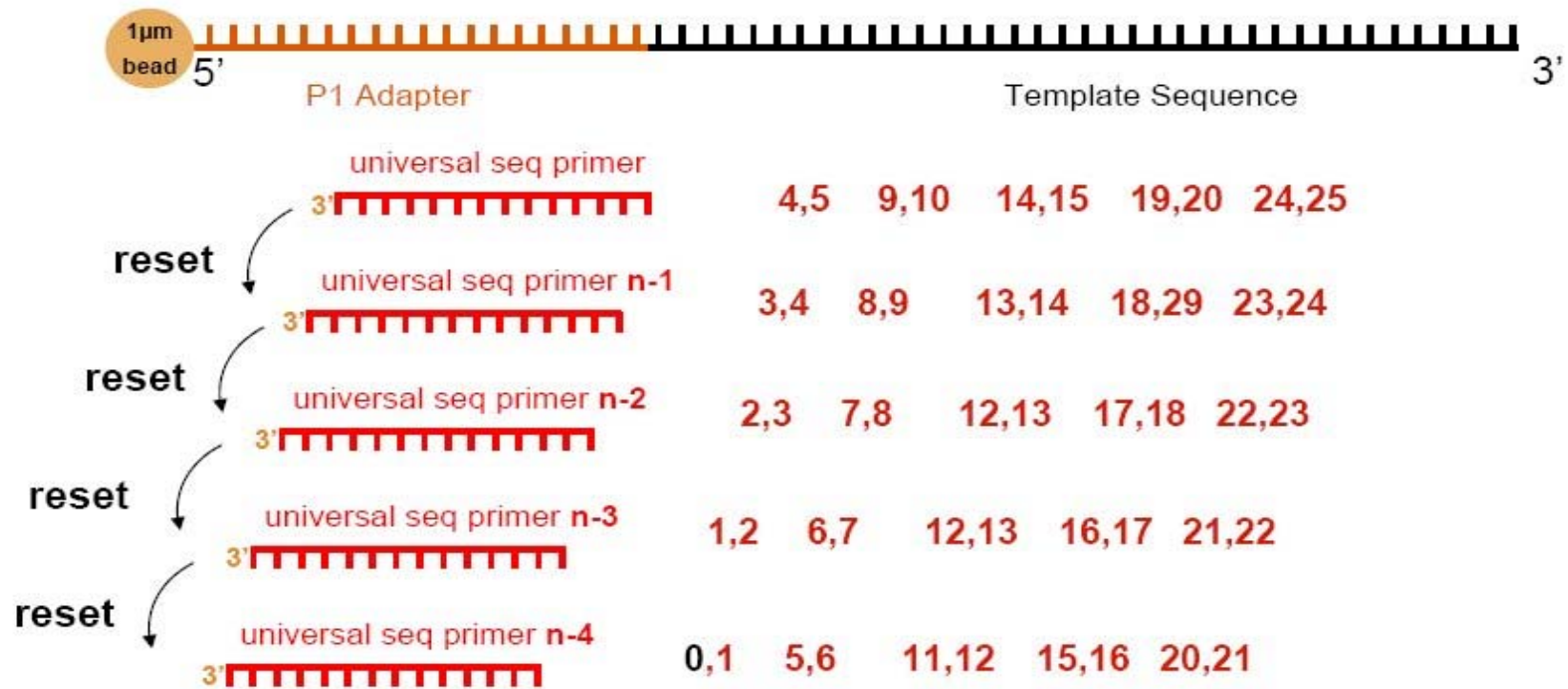


SOLiD Chemistry System 4-color ligation (2nd Round)



Sequential rounds of sequencing

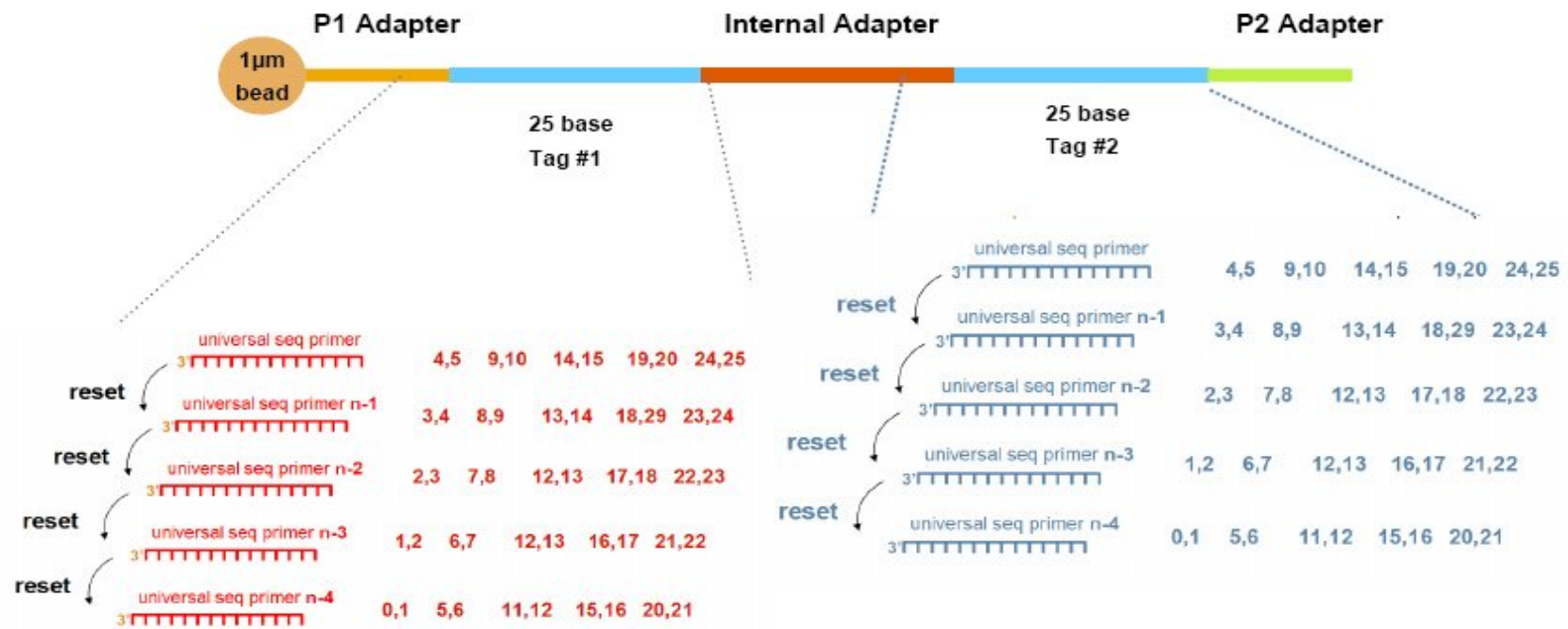
Multiple cycles per round



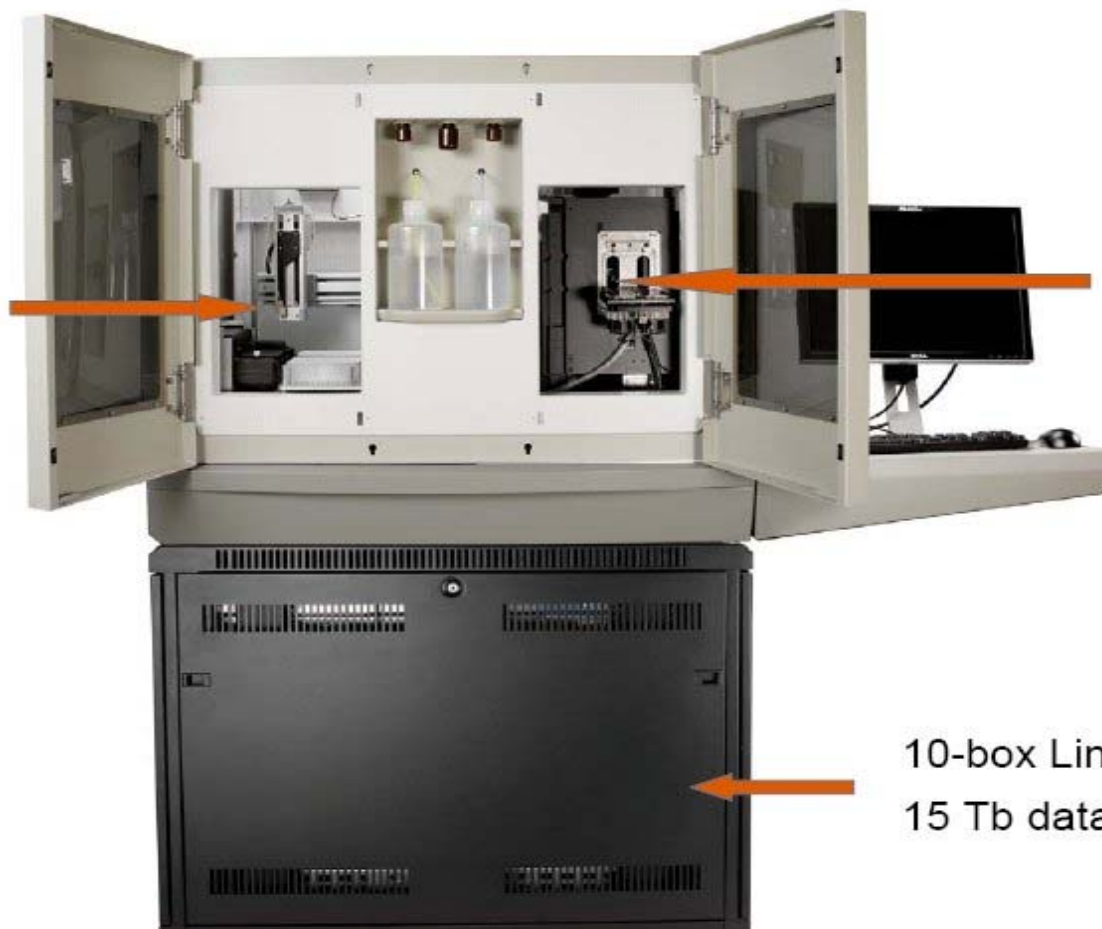
Paired End two sequences generated

Sequential rounds of sequencing

Multiple cycles per round



Reagent
handling

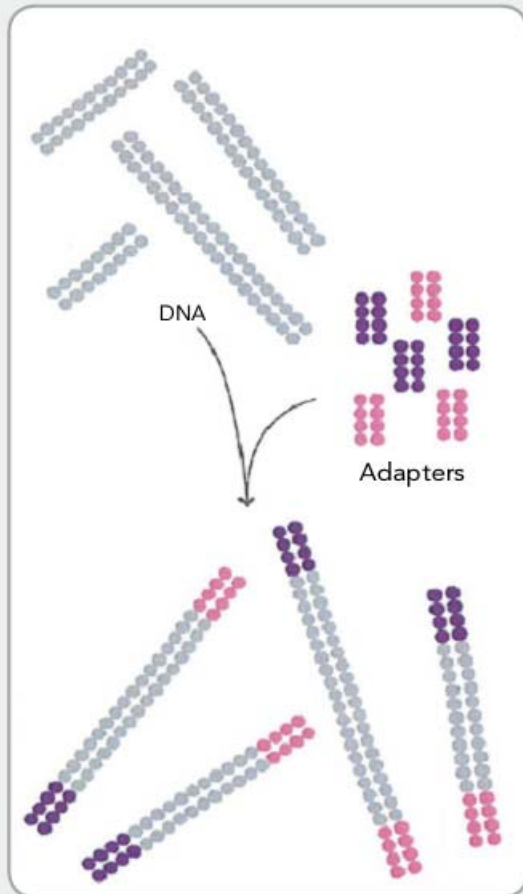


Dual Flow
Cell

10-box Linux Cluster
15 Tb data storage

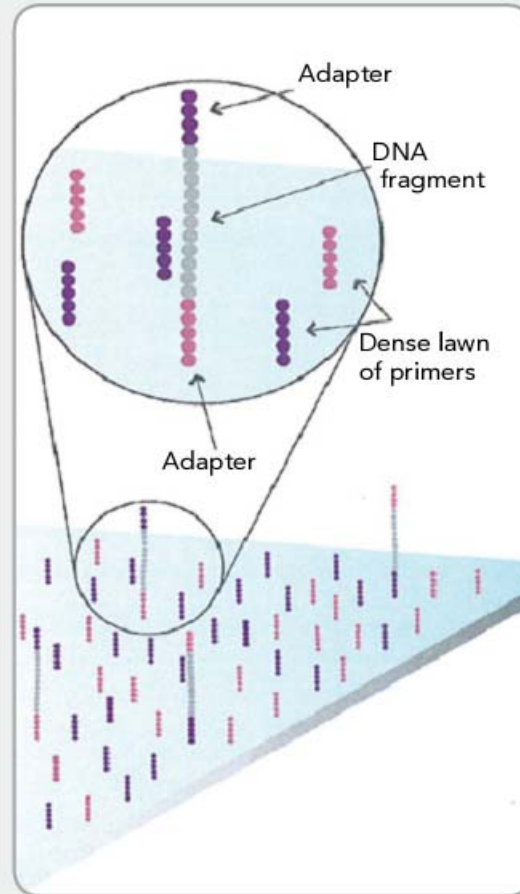
Solexa (2007)

1. PREPARE GENOMIC DNA SAMPLE



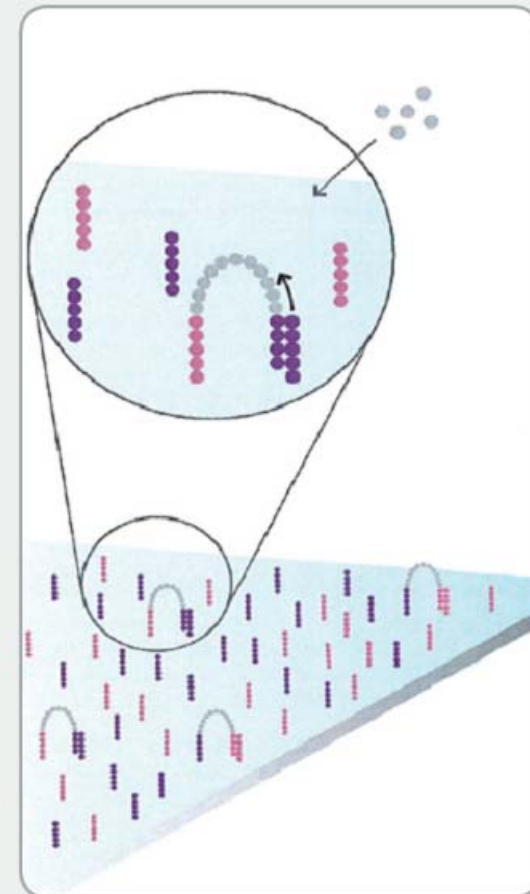
Randomly fragment genomic DNA and ligate adapters to both ends of the fragments.

2. ATTACH DNA TO SURFACE



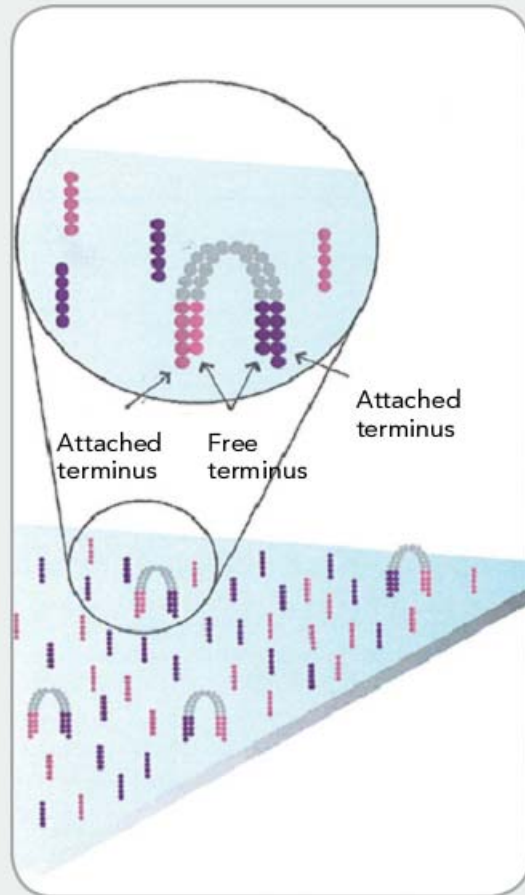
Bind single-stranded fragments randomly to the inside surface of the flow cell channels.

3. BRIDGE AMPLIFICATION



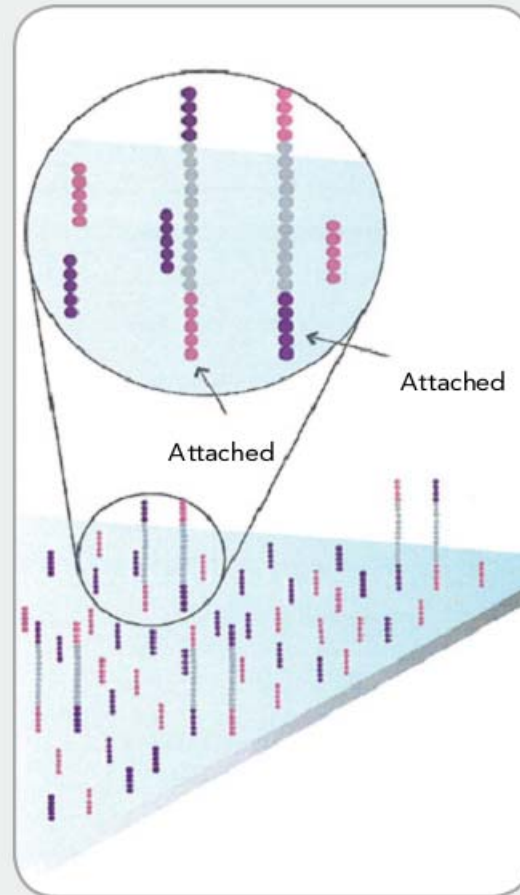
Add unlabeled nucleotides and enzyme to initiate solid-phase bridge amplification.

4. FRAGMENTS BECOME DOUBLE STRANDED



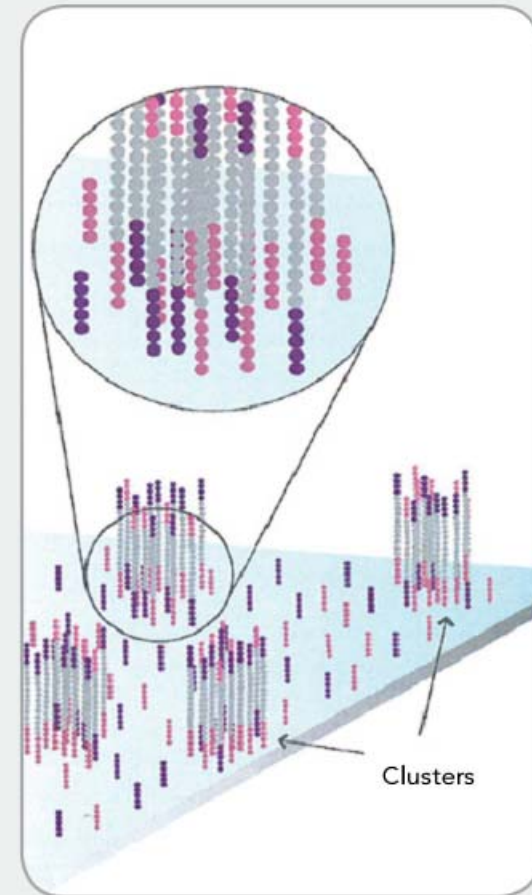
The enzyme incorporates nucleotides to build double-stranded bridges on the solid-phase substrate.

5. DENATURE THE DOUBLE-STRANDED MOLECULES



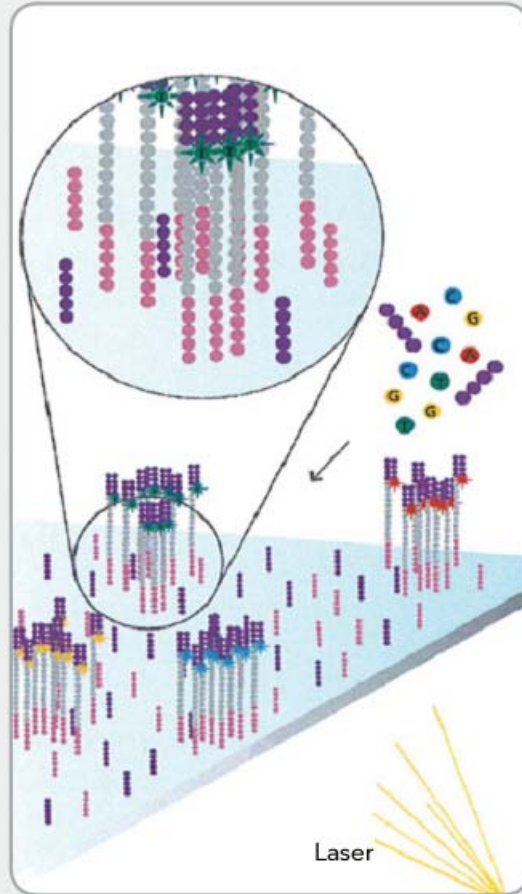
Denaturation leaves single-stranded templates anchored to the substrate.

6. COMPLETE AMPLIFICATION



Several million dense clusters of double-stranded DNA are generated in each channel of the flow cell.

7. DETERMINE FIRST BASE



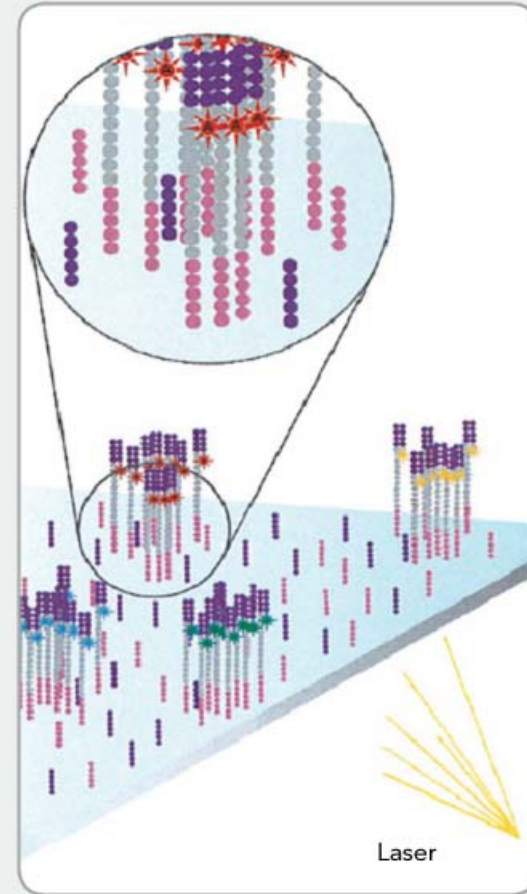
First chemistry cycle: to initiate the first sequencing cycle, add all four labeled reversible terminators, primers and DNA polymerase enzyme to the flow cell.

8. IMAGE FIRST BASE



After laser excitation, capture the image of emitted fluorescence from each cluster on the flow cell. Record the identity of the first base for each cluster.

9. DETERMINE SECOND BASE

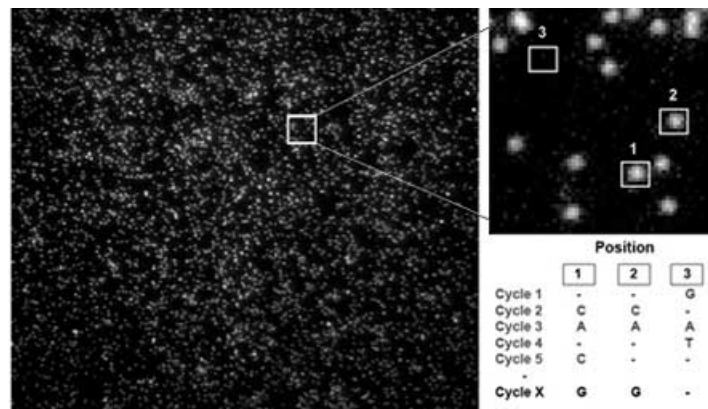
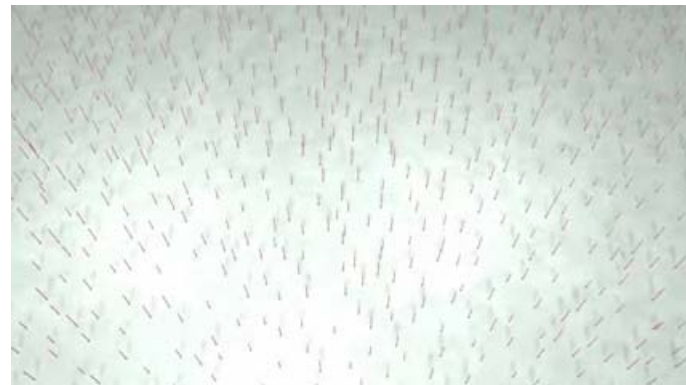
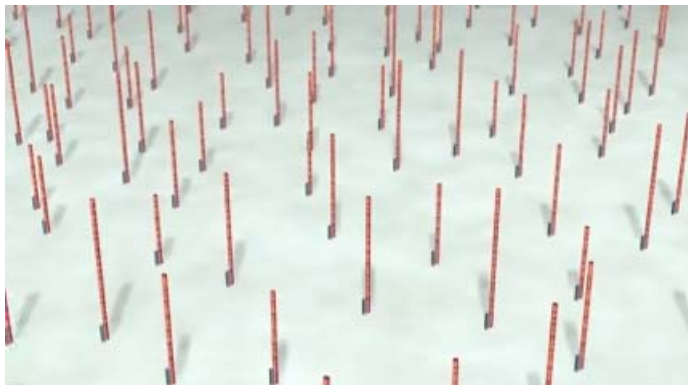


Second chemistry cycle: to initiate the next sequencing cycle, add all four labeled reversible terminators and enzyme to the flow cell.

HELICOS (2008)



True Single Molecule Sequencing (tSMS)

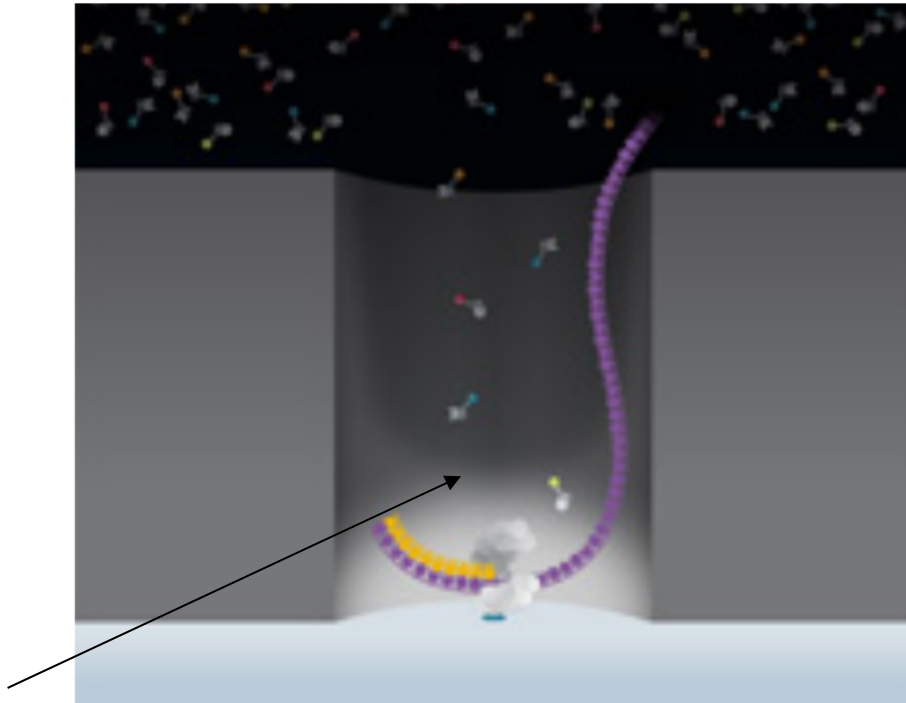


Single Molecule Real-Time (SMRT)

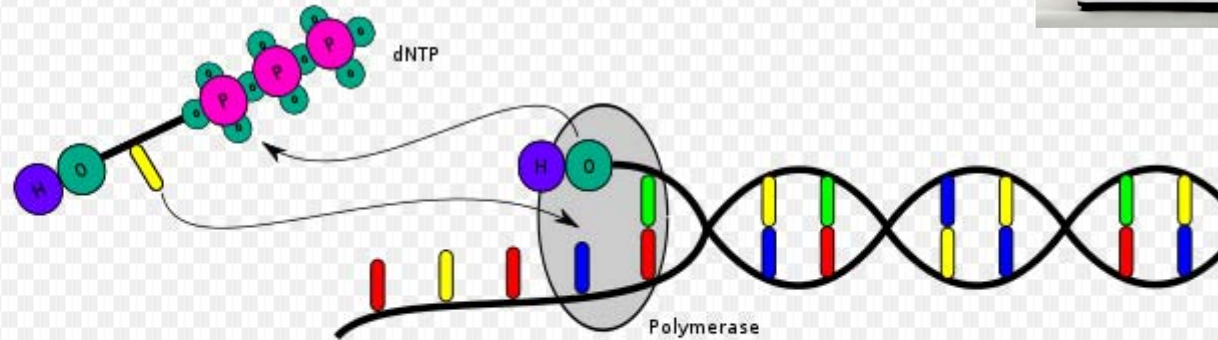
Pacific Biosciences



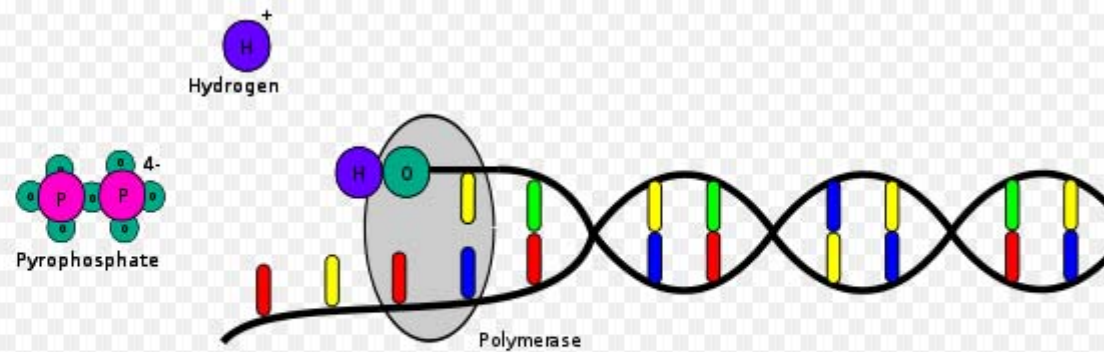
20 zeptolitru



Ion Torrent

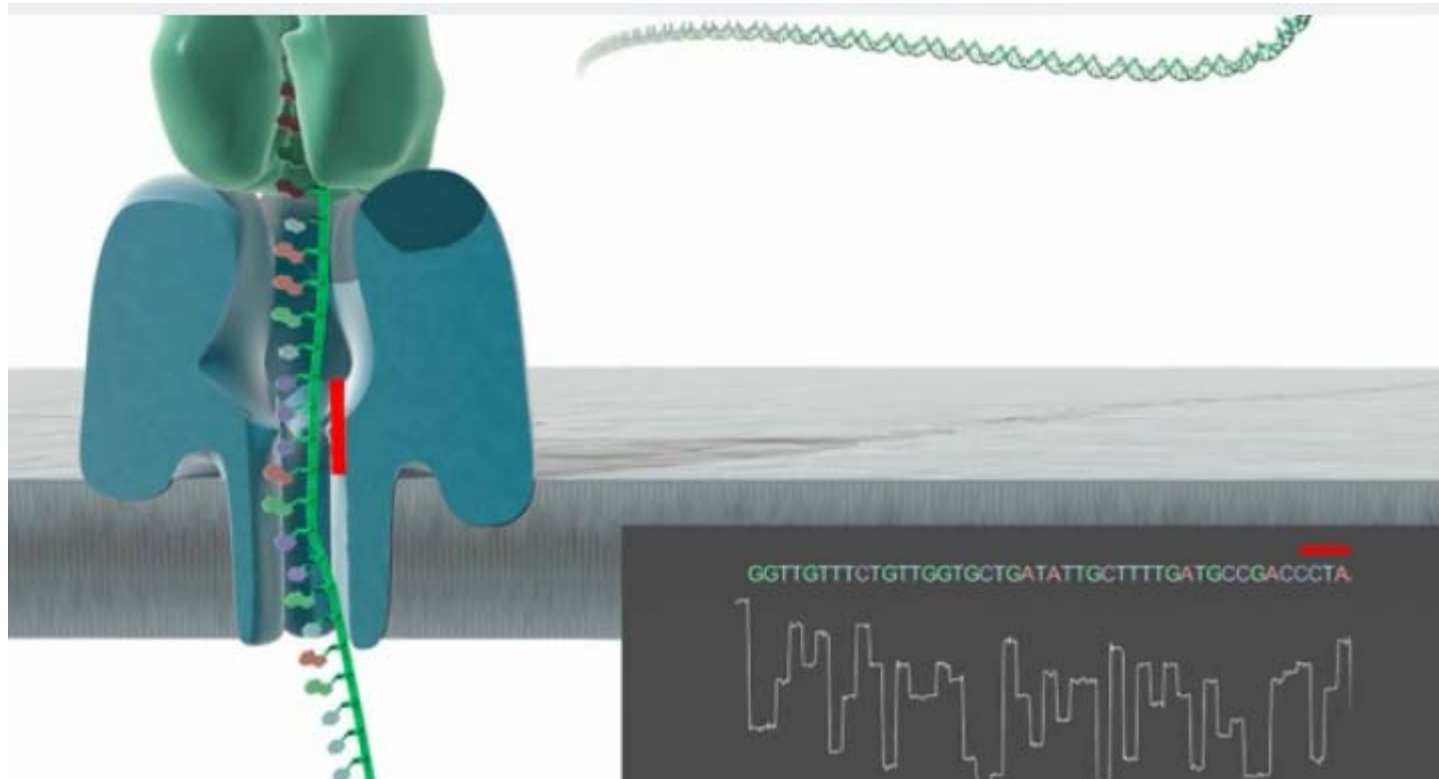


Polymerase integrates a nucleotide.



Hydrogen and pyrophosphate are released.

Oxford nanopore



Další technologie

- Mikroelektroforéza
- Sekvenování na bázi microarray