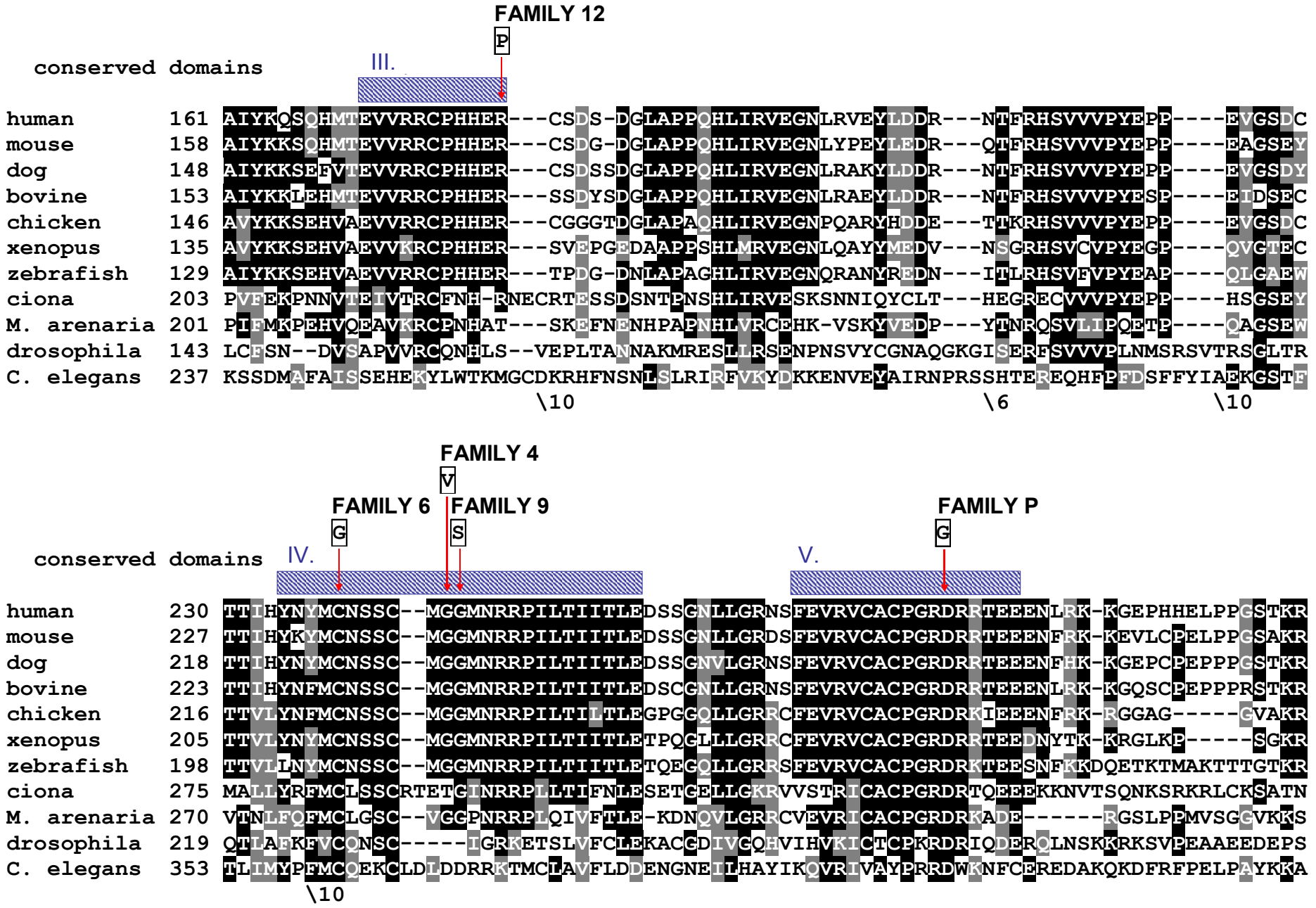

FAMILY 12
P
conserved domains
III.
human 161 AIYKQSQHMTEVVRRCPHHER---CSDS-DGLAPPQHLIRVEGNLRVEYLDDR---NTFRHSVVVPYEPP----EVGSDC
mouse 158 AIYKKSQHMTEVVRRCPHHER---CSDG-DGLAPPQHLIRVEGNLYPEYLEDR---QTFRHSVVVPYEPP----EAGSEY
dog 148 AIYKKSEFVTEVVRRCPHHER---CSDSSDGLAPPQHLIRVEGNLRAKYLDDR---NTFRHSVVVPYEPP----EVGSDY
bovine 153 AIYKKLEHMTEVVRRCPHHER---SSDYSDGLAPPQHLIRVEGNLRAEYLDDR---NTFRHSVVVPYESP----EIDSEC
chicken 146 AVYKKSEHVAEVVRRCPHHER---CGGGTDGLAPAQHLIRVEGNPQARYHDDE---TTKRHSVVVPYEPP----EVGSDC
xenopus 135 AVYKKSEHVAEVVKRCPHHER---SVEPGEDAAPPSHLMRVEGNLQAYYMEDV---NSGRHSVCVPYEGP----QVGTEC
zebrafish 129 AIYKKSEHVAEVVRRCPHHER---TPDG-DNLAPAGHLIRVEGNQRANYREDN---ITLRHSVFVPYEAP----QLGAEW
ciona 203 PVEEKPNNVTEIVTRCFNH-RNECRTESSDSNTPNSHLIRVESKSNNIQYCLT---HEGRECVVVPYEPP----HSGSEY
M. arenaria 201 PIEMKPEHVQEAVKRCPNHAT---SKEFNENHPAPNHLVRCEHK-VSKYVEDP---YTNRQSVLIPQETP----QAGSEW
drosophila 143 LCESN--DVSAPVVRCQNHLS--VEPLTANNAKMRESLLRSENPNSVYCGNAQGKGISERFSVVVPLNMSRSVTRSGLTR
C. elegans 237 KSSDMAFAISSEHEKYLWTKMGCDKRHFNSNLSLRIRFVKYDKKENVEYAIRNPRSSHTEREQHFPFDSFFYIAEKGSTF
\10
\6
\10
FAMILY 4
V
FAMILY 6
FAMILY 9
FAMILY P
G
S
G
conserved domains
IV.
V.
human 230 TTIHYNYMCNSSC--MGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGRDRRTEEENLRK-KGEPHHELPPGSTKR
mouse 227 TTIHYKYMCNSSC--MGGMNRRPILTIITLEDSSGNLLGRDSFEVRVCACPGRDRRTEEENFRK-KEVLCPELPPGSAKR
dog 218 TTIHYNYMCNSSC--MGGMNRRPILTIITLEDSSGNVLGRNSFEVRVCACPGRDRRTEEENFHK-KGEPCPEPPPGSTKR
bovine 223 TTIHYNFMCNSSC--MGGMNRRPILTIITLEDSCGNLLGRNSFEVRVCACPGRDRRTEEENLRK-KGQSCPEPPPRSTKR
chicken 216 TTVLYNFMCNSSC--MGGMNRRPILTILTLEGPGGQLLGRRCFEVRVCACPGRDRKIEEENFRK-RGGAG-----GVAKR
xenopus 205 TTVLYNYMCNSSC--MGGMNRRPILTIITLETPQGLLLGRRCFEVRVCACPGRDRRTEEDNYTK-KRGLKP-----SGKR
zebrafish 198 TTVLLNYMCNSSC--MGGMNRRPILTIITLETQEGQLLGRRSFEVRVCACPGRDRKTEESNFKKDQETKTMAKTTTGTKR
ciona 275 MALLYRFMCLSSCRTETGINRRPLLTIFNLESETGELLGKRVVSTRICACPGRDRTQEEEKKNVTSQNKSRKRLCKSATN
M. arenaria 270 VTNLFQFMCLGSC--VGGPNRRPLQIVFTLE-KDNQVLGRRCVEVRICACPGRDRKADE------RGSLPPMVSGGVKKS
drosophila 219 QTLAFKFVCQNSC-----IGRKETSLVFCLEKACGDIVGQHVIHVKICTCPKRDRIQDERQLNSKKRKSVPEAAEEDEPS
C. elegans 353 TLIMYPFMCQEKCLDLDDRRKTMCLAVFLDDENGNEILHAYIKQVRIVAYPRRDWKNFCEREDAKQKDFRFPELPAYKKA
\10

# definice života

živý organismus je
přirozeně se vyskytující
sám sebe reprodukující systém,
který vykonává řízené manipulace
s hmotou, energií a informací

složitá organizace a řád

regulace a udržování vnitřní homeostázy
získávání a využití energie,
    výměna látek a energie s prostředím
schopnost reagovat na vnější podněty
reprodukce,
    dědičnost a proměnlivost (variabilita)
vývoj a růst
adaptace na prostředí

# život v prostoru: prostorová hierarchie živých systémů

biosféra
ekosystém
společenstva
populace
organismus
orgány a orgánové systémy
tkáně
buňky
organely
molekuly

kontinuita života je zajištěna předáváním genetické informace

## život v čase 1: evoluce živých systémů (evolution)

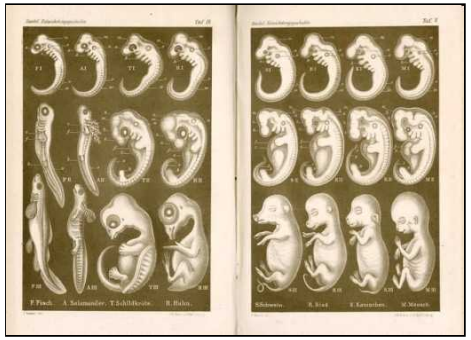
časové měřítko cca 3.8 mld let od vzniku života na planetě

http://rainbow.ldeo.columbia.edu/courses/v1001/arch.berl.gif

## život v čase 2: vývoj živých systémů (development)

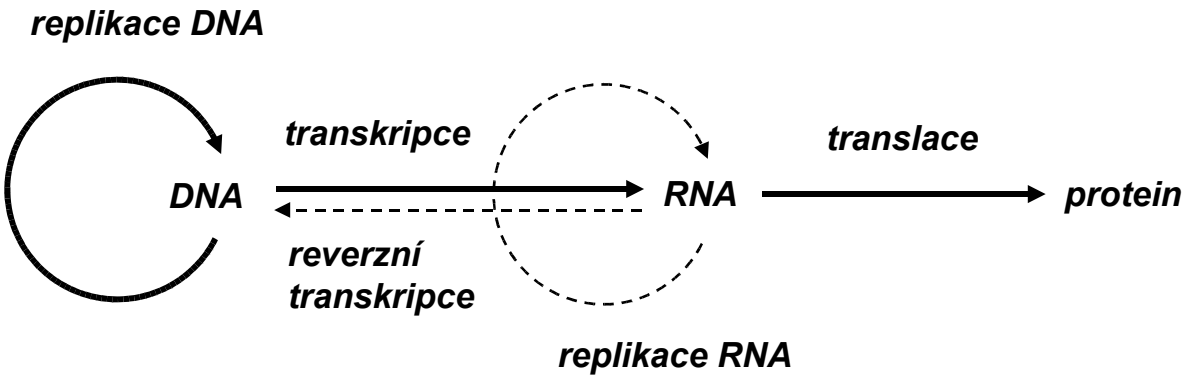
časové měřítko mezi vznikem a zánikem jedince

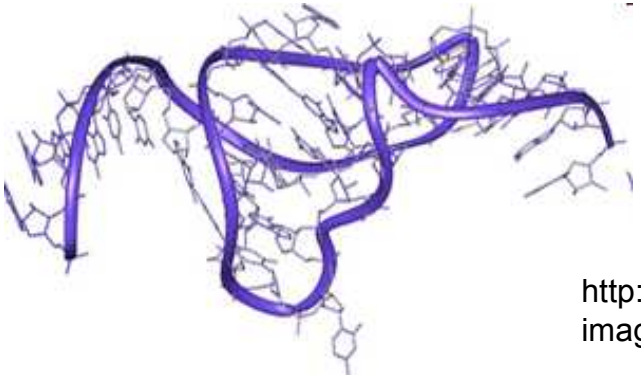
http://www.wellcome.ac.uk/stellent/groups/corporatesite/@msh_publishing_group/documents/image/wtx054619.jpg



kontinuita života je zajištěna předáváním genetické informace

# tok genetické informace: centrální dogma



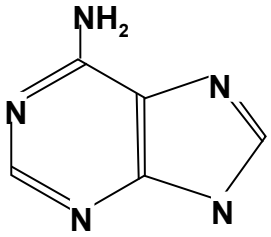



http://evolution.berkeley.edu/evolibrary/images/interviews/rnastructure.gif

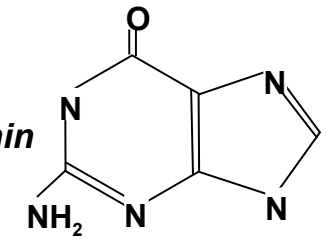
# DNA

***purinové báze***

***adenin***

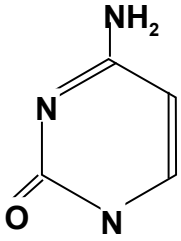



***guanin***

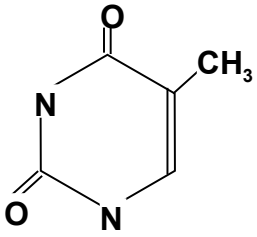



***pyrimidinové báze***

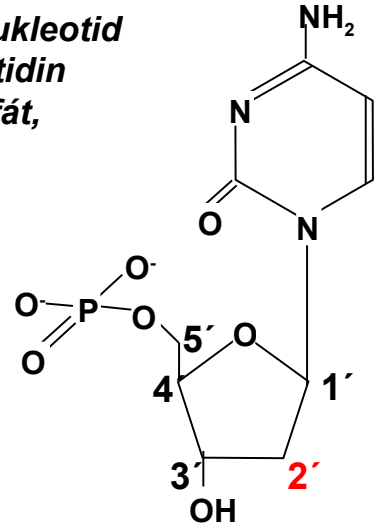
***cytosin***




***thymin***

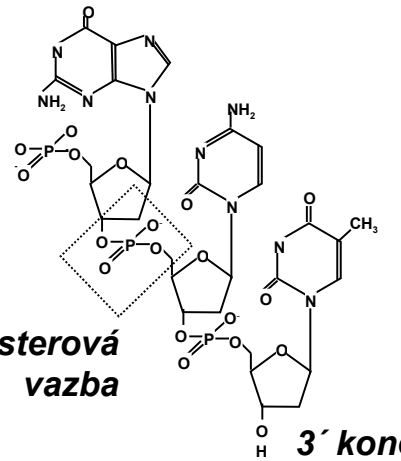



***deoxyribonukleotid (2´ deoxycytidin 5´ monofosfát, dCMP)***

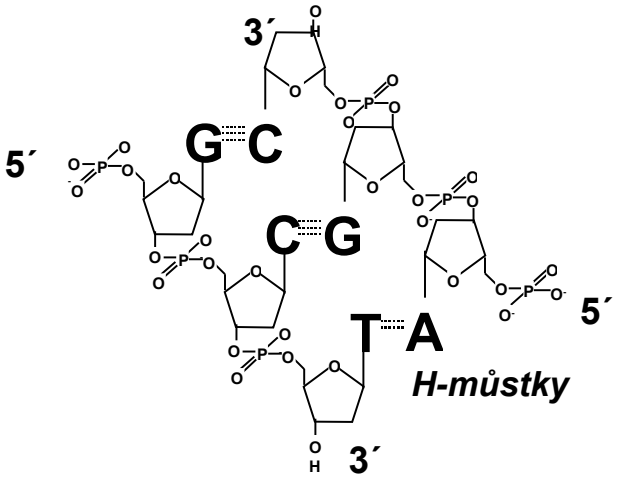


# DNA

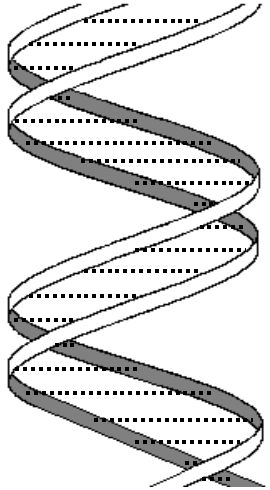
***jednořetězec DNA***
***(sekvence 5´ GCT 3´)***



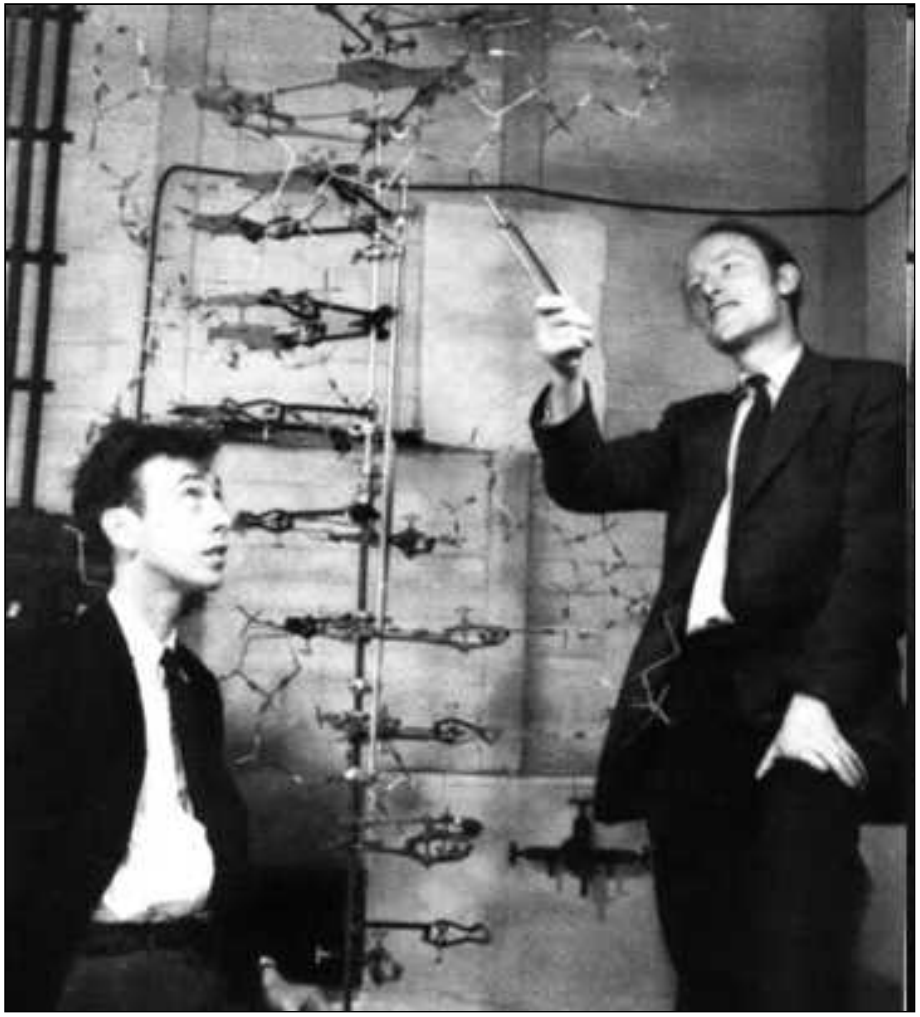

***dvouřetězec DNA***




***dvojitá spirála***



# DNA



April 25, 1953 NATURE 737

## MOLECULAR STRUCTURE OF NUCLEIC ACIDS

### A Structure for Deoxyribose Nucleic Acid

We wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A structure for nucleic acid has already been proposed by Pauling and Corey[1]. They kindly made their manuscript available to us in advance of publication. Their model consists of three intertwined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons: (1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

Another three-chain structure has also been suggested by Fraser (in the press). In his model the phosphates are on the outside and the bases on the inside, linked together by hydrogen bonds. This structure as described is rather ill-defined, and for this reason we shall not comment on it.

We wish to put forward a radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate diester groups joining β-D-deoxyribofuranose residues with 3',5' linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite directions. Each chain, loosely resembles Furberg's[2] model No. 1; that is, the bases are on the inside of the helix and the phosphates on the outside. The configuration of the sugars and the atoms near it is close to Furberg's 'standard configuration', the sugar being roughly perpendicular to the attached base. There is a residue on each chain every 3·4 A. in the z-direction. We have assumed an angle of 36° between adjacent residues in the same chain, so that the structure repeats after 10 residues on each chain, that is, after 34 A. The distance of a phosphorus atom from the fibre axis is 10 A. As the phosphates are on the outside, cations have easy access to them.

The structure is an open one, and its water content is rather high. At lower water contents we would expect the bases to tilt so that the structures could become more compact.

The novel feature of the structure is the manner in which the two chains are held together by the purine and pyrimidine bases. The planes of the bases are perpendicular to the fibre axis. They are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other chain, so that the two lie side by side with identical z-coordinates. One of the pair must be a purine and the other a pyrimidine for bonding to occur. The hydrogen bonds are made as follows: purine position 1 to pyrimidine position 1; purine position 6 to pyrimidine position 6.

If it is assumed that the bases only occur in the structure in the most plausible tautomeric forms (that is, with the keto rather than the enol configurations) it is found that only specific pairs of bases can bond together. These pairs are: adenine (purine) with thymine (pyrimidine), and guanine (purine) with cytosine (pyrimidine).

In other words, if an adenine forms one member of a pair, on either chain, then on these assumptions the other member must be thymine; similarly for guanine and cytosine. The sequence of bases on a single chain does not appear to be restricted in any way. However, if only specific pairs of bases can be formed, it follows that if the sequence of bases on one chain is given, then the sequence on the other chain is automatically determined.

It has been found experimentally[3,4] that the ratio of the amounts of adenine to thymine, and the ratio of guanine to cytosine, are always very close to unity for deoxyribose nucleic acid.

It is probably impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact.

The preliminary published X-ray data[5,6] on deoxyribose nucleic acid are insufficient for a rigorous test of our structure. So far as we can tell, it is roughly compatible with the experimental data, but it must be regarded as unproved until it has been checked against more exact results. Some of these are given in the following communications. We were not aware of the details of the results presented there when we devised our structure, which rests mainly though not entirely on published experimental data and stereochemical arguments.

It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.

Full details of the structure, including the conditions assumed in building it, together with a set of co-ordinates for the atoms, will be published elsewhere.

We are much indebted to Dr. Jerry Donohue for constant advice and criticism, especially on interatomic distances. We have also been stimulated by a knowledge of the general nature of the unpublished experimental results and ideas of Dr. M. H. F. Wilkins, Dr. R. E. Franklin and their co-workers at King's College, London. One of us (J. D. W.) has been aided by a fellowship from the National Foundation for Infantile Paralysis.

J. D. WATSON
F. H. C. CRICK

Medical Research Council Unit for the Study of the Molecular Structure of Biological Systems,
Cavendish Laboratory, Cambridge.
April 2


1 Pauling, L., and Corey, R. B., *Nature*, this issue, p. 346; and *Proc. U.S. Nat. Acad. Sci.*, **39**, 84 (1953).

2 Furberg, S., *Acta Chem. Scand.*, **6**, 634 (1952).

3 Chargaff, E., this volume, p. 334; and Zamenhof, S., Brawerman, G., and Chargaff, E., *Biochim. et Biophys. Acta*, **9**, 402 (1952).

4 Wyatt, G. R., *J. Gen. Physiol.*, **36**, 201 (1952).

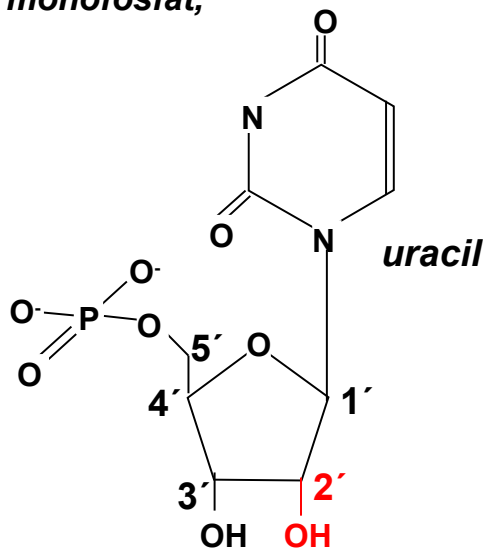
5 Astbury, W. T., *Symp. Soc. Exp. Biol.* **1**, Nucleic Acid, 66 (Camb. Univ. Press, 1947).

6 Wilkins, M. H. F., and Randall, J. T., *Biochim. et Biophys. Acta*, **10**, 192 (1953).

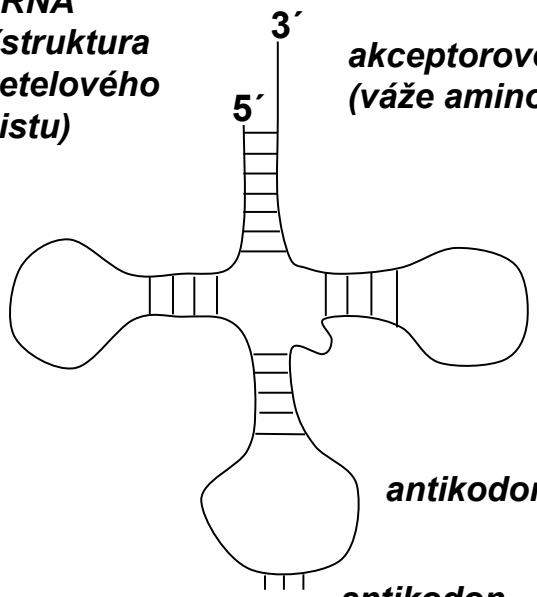

http://web.virginia.edu/Heidi/chapter30/Images/30_01.jpg

# RNA

***ribonukleotid (uridin 5´ monofosfát, UMP)***




***tRNA (struktura jetelového listu)***



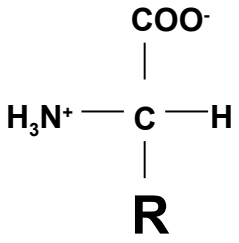

***akceptorové rameno (váže aminokyselinu)***

***antikodonové rameno***

***antikodon***

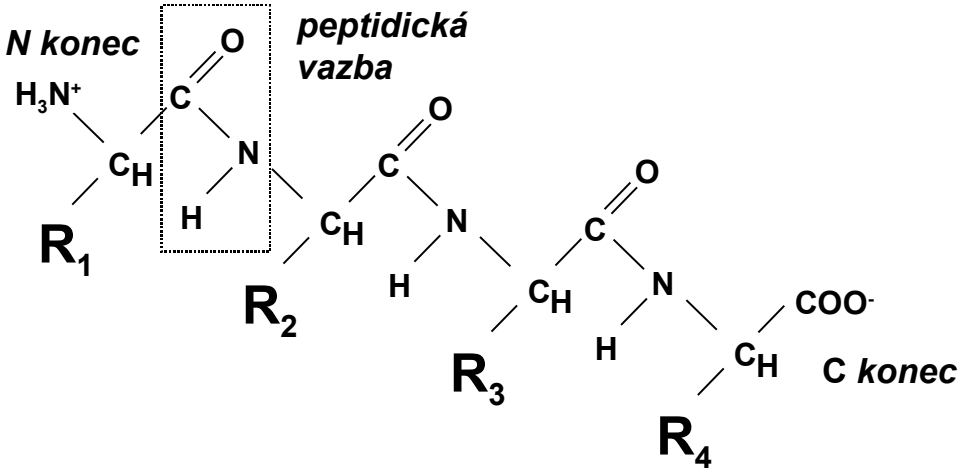
# proteiny

***aminokyselina***




***postranní řetězec***

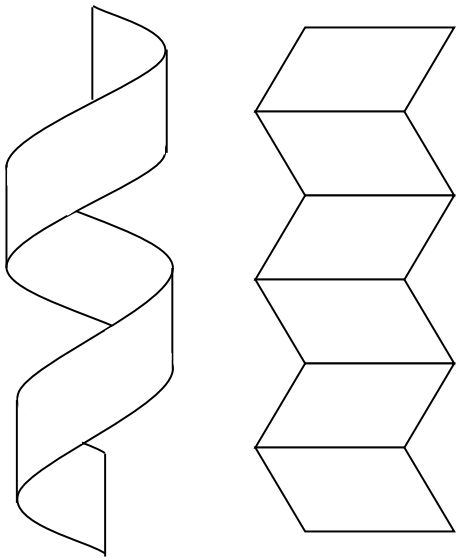
***polypeptidický řetězec***



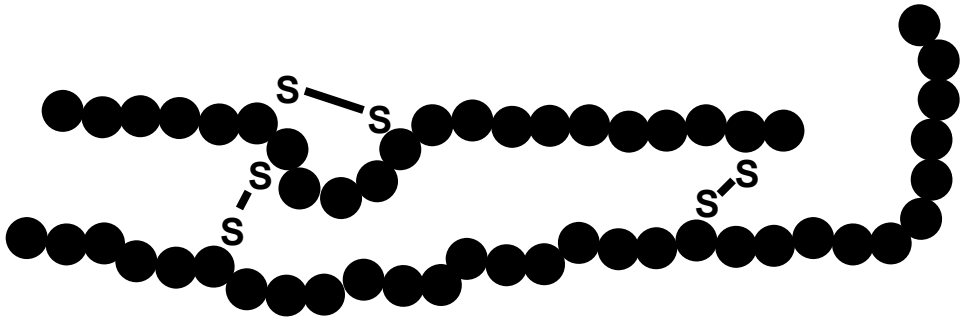
# proteiny

***sekundární struktura proteinů***

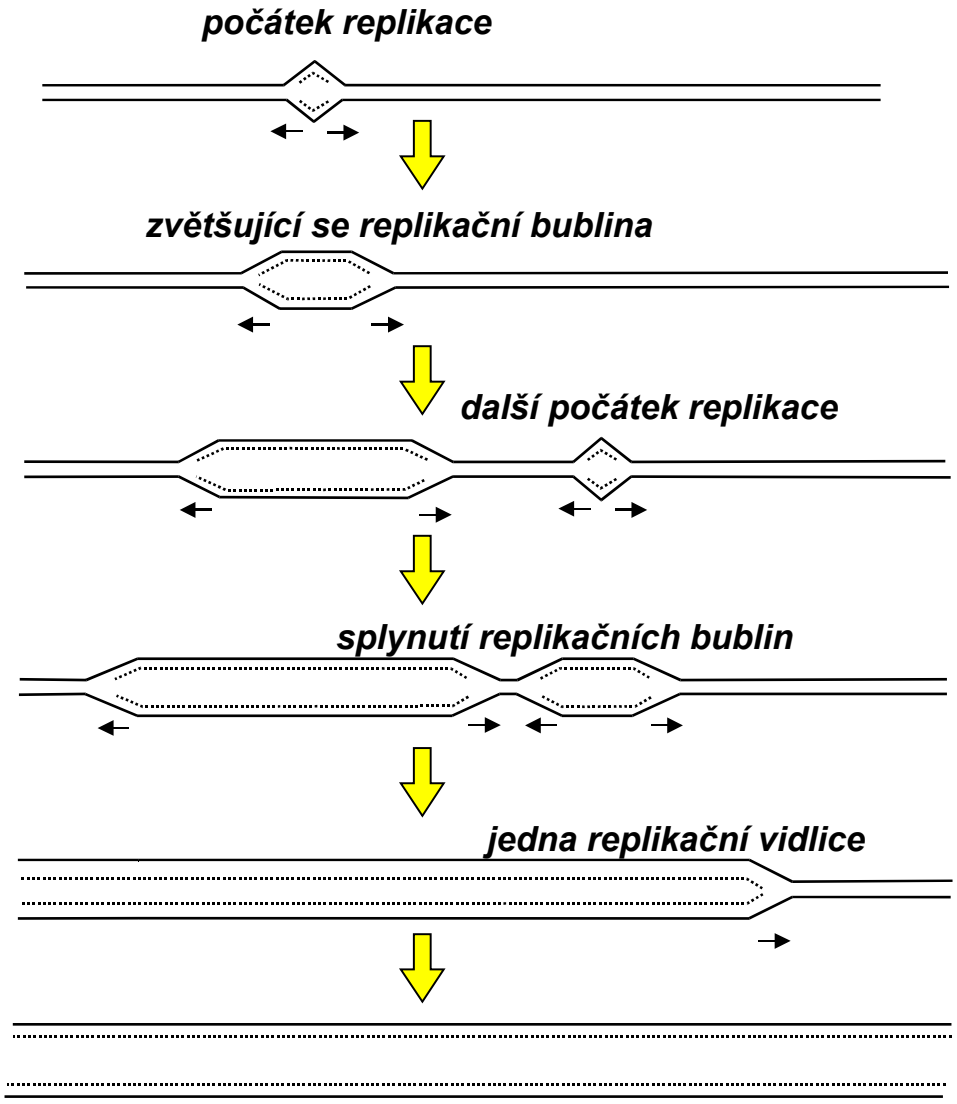
***α-helix*** ***β-skládaný list***

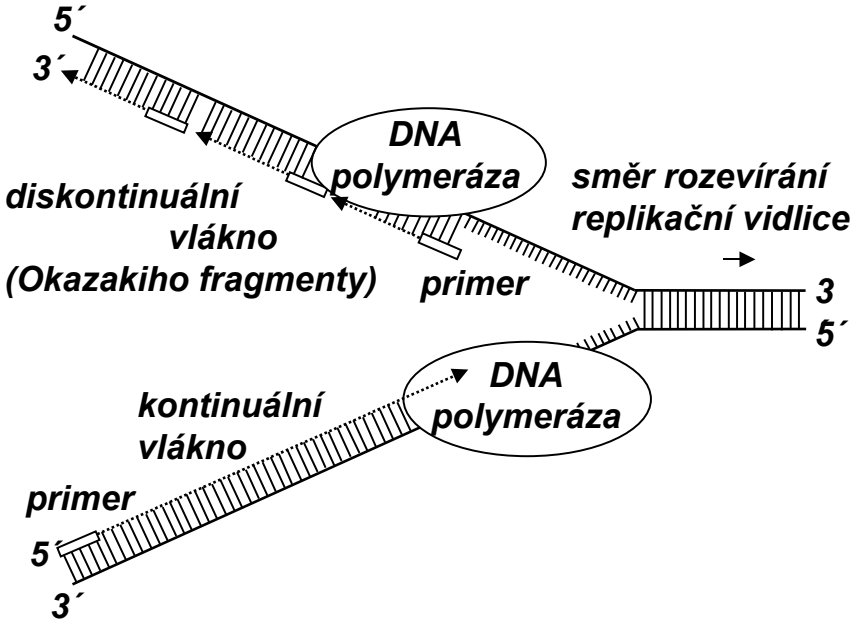


***disulfidické můstky v řetězcích A a B lidského inzulínu***



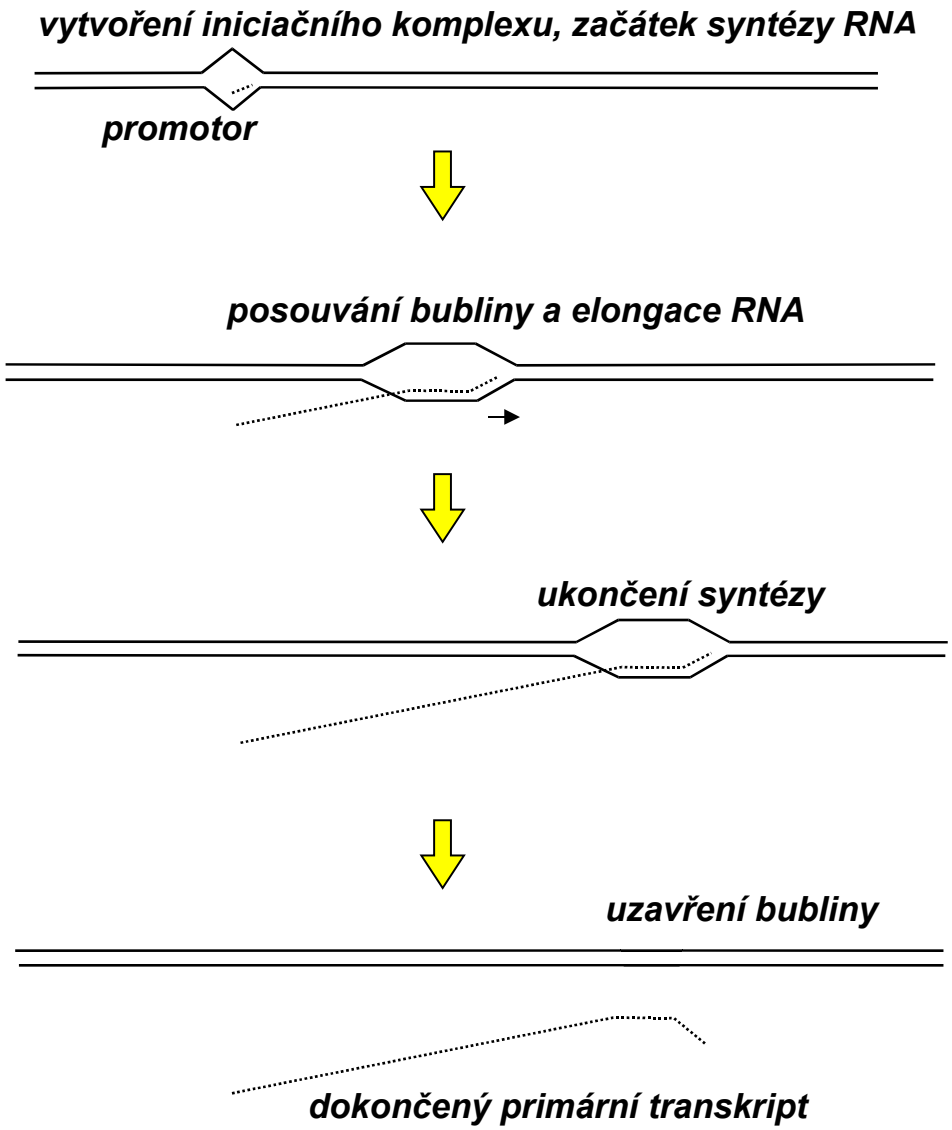
# replikace DNA

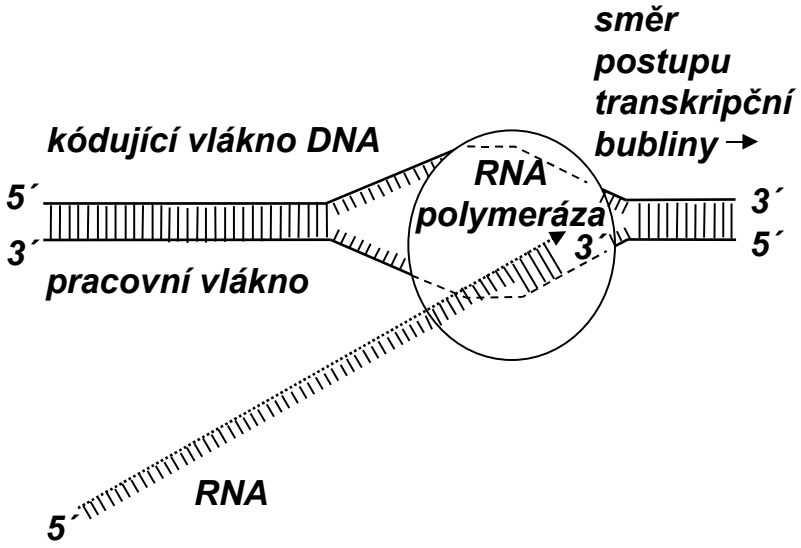


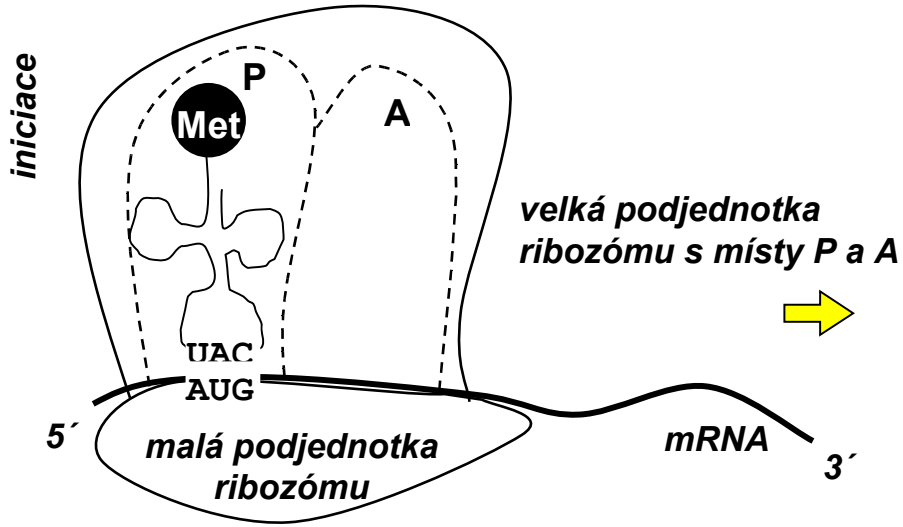

dceřinné molekuly DNA - jeden starý a jeden nový řetězec

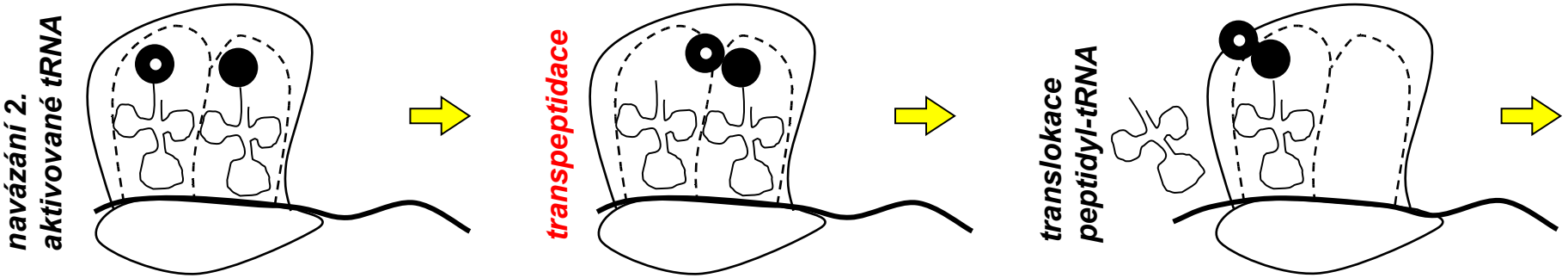
# transkripce RNA

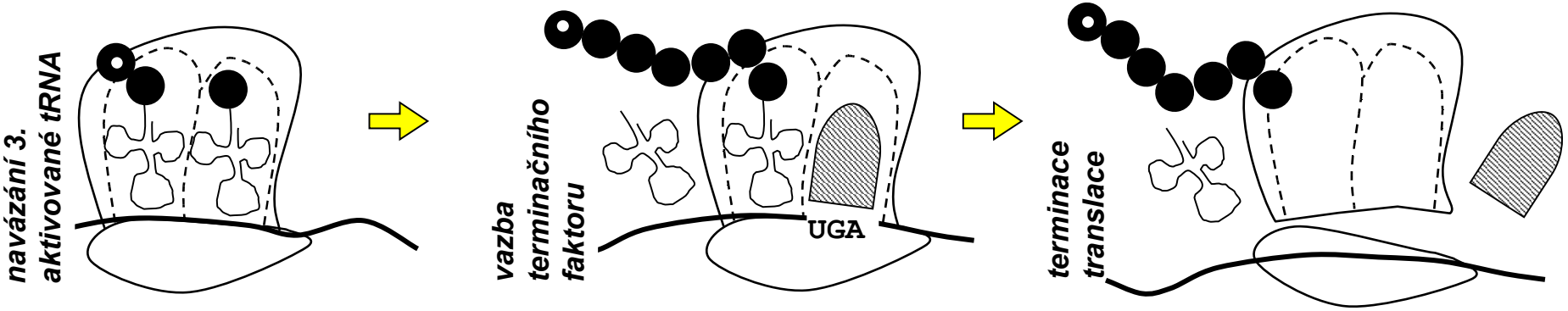


# translace


iniciace
P
Met
A
UAC
AUG
5´
malá podjednotka ribozómu
mRNA
3´
velká podjednotka ribozómu s místy P a A

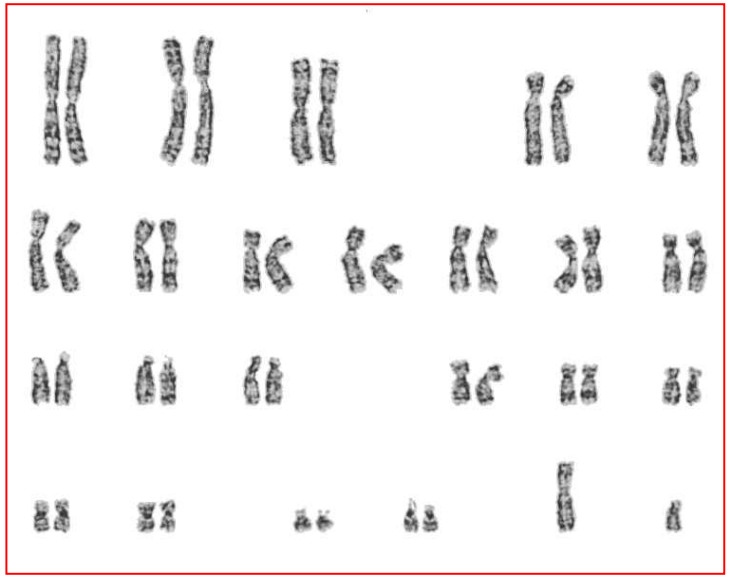

navázání 2. aktivované tRNA
transpeptidace
translokace peptidyl-tRNA

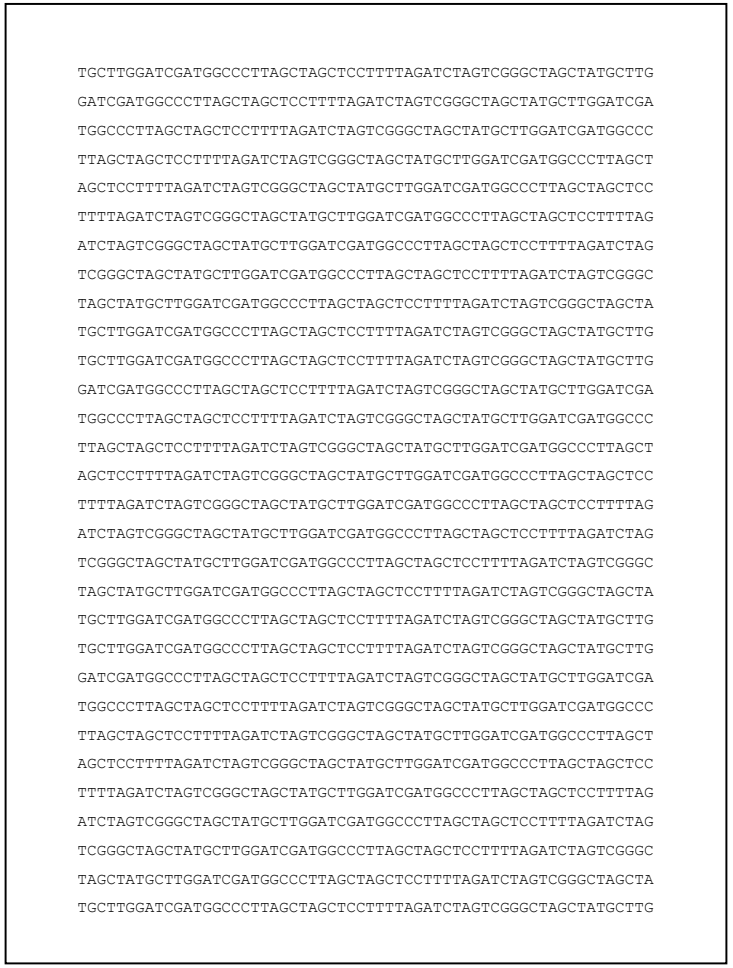

navázání 3. aktivované tRNA
vazba terminačního faktoru
UGA
terminace translace

# genetický kód

| 1. pozice kodonu | 2. pozice kodonu | | | | 3. pozice kodonu |
|---|---|---|---|---|---|
| | U | C | A | G | |
| U | UUU Phe | UCU Ser | UAU Tyr | UGU Cys | U |
| | UUC Phe | UCC Ser | UAC Tyr | UGC Cys | C |
| | UUA Leu | UCA Ser | UAA STOP | UGA STOP | A |
| | UUG Leu | UCG Ser | UAG STOP | UGG Trp | G |
| C | CUU Leu | CCU Pro | CAU His | CGU Arg | U |
| | CUC Leu | CCC Pro | CAC His | CGC Arg | C |
| | CUA Leu | CCA Pro | CAA Gln | CGA Arg | A |
| | CUG Leu | CCG Pro | CAG Gln | CGG Arg | G |
| A | AUU Ile | ACU Thr | AAU Asn | AGU Ser | U |
| | AUC Ile | ACC Thr | AAC Asn | AGC Ser | C |
| | AUA Ile | ACA Thr | AAA Lys | AGA Arg | A |
| | AUG Met | ACG Thr | AAG Lys | AGG Arg | G |
| G | GUU Val | GCU Ala | GAU Asp | GGU Gly | U |
| | GUC Val | GCC Ala | GAC Asp | GGC Gly | C |
| | GUA Val | GCA Ala | GAA Glu | GGA Gly | A |
| | GUG Val | GCG Ala | GAG Glu | GGG Gly | G |

aminoacyl-tRNA syntetázy

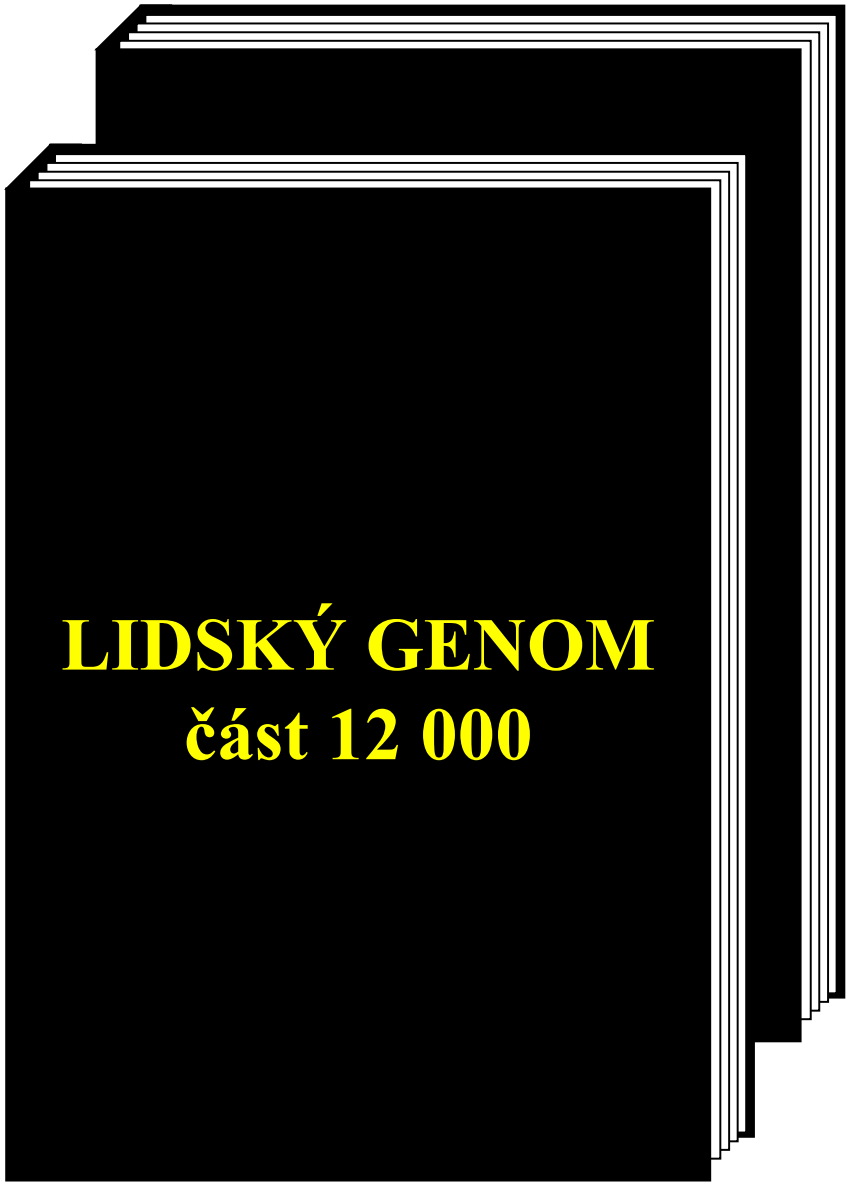





## lidský genom

jádro:
3.2 miliardy párů bází DNA
(2x)
mitochondrie:
16.5 kb kruhová DNA
(několik g/mt, stovky mt/b)
geny pro 24 RNA + 13 proteinů

1 strana 1 800 znaků




1 kniha 150 stran

270 000 znaků

tloušťka 2 cm

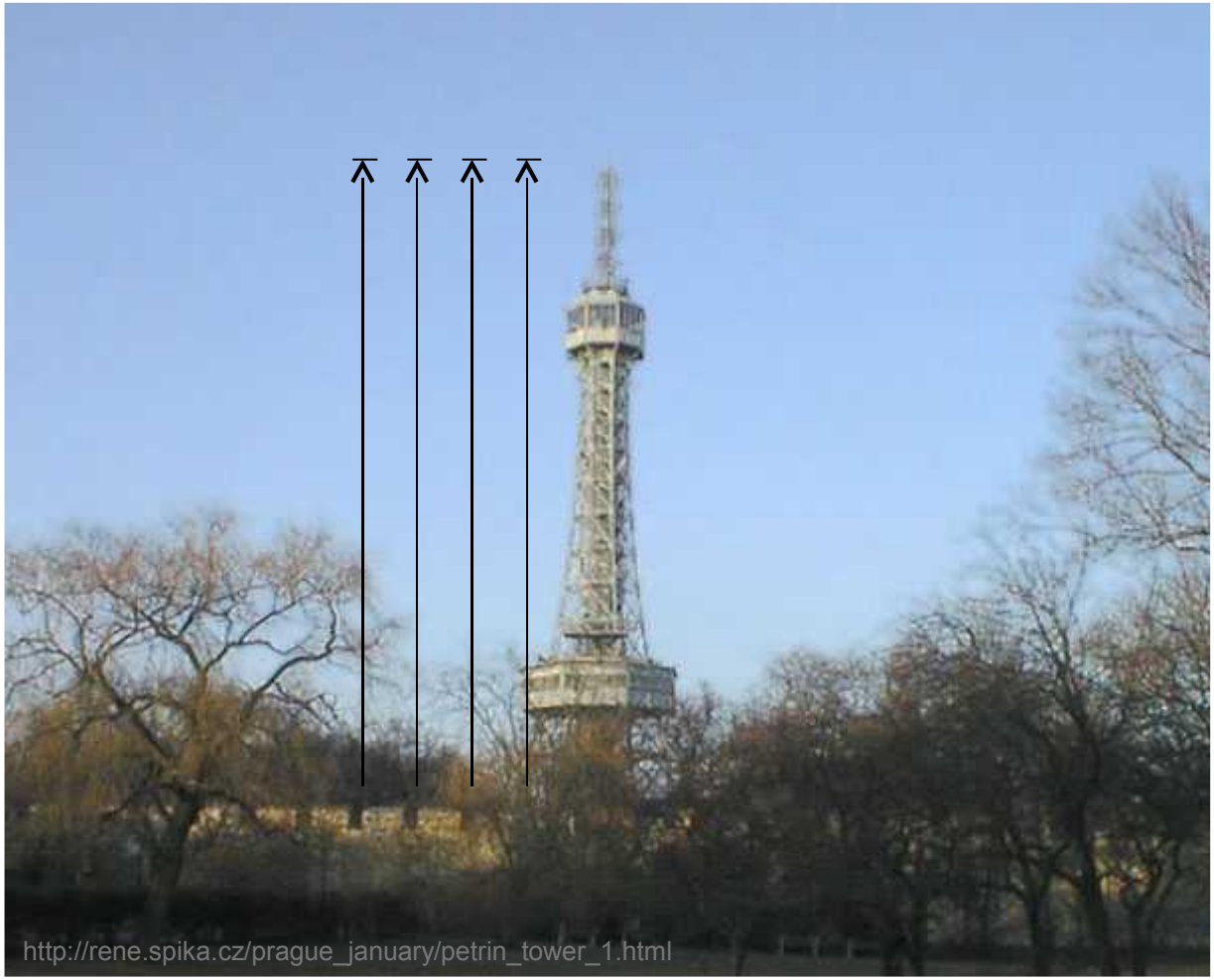
---

celý genom

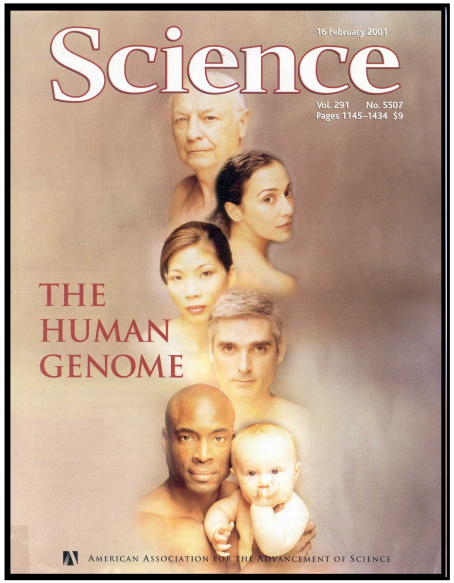
3.2 miliardy znaků

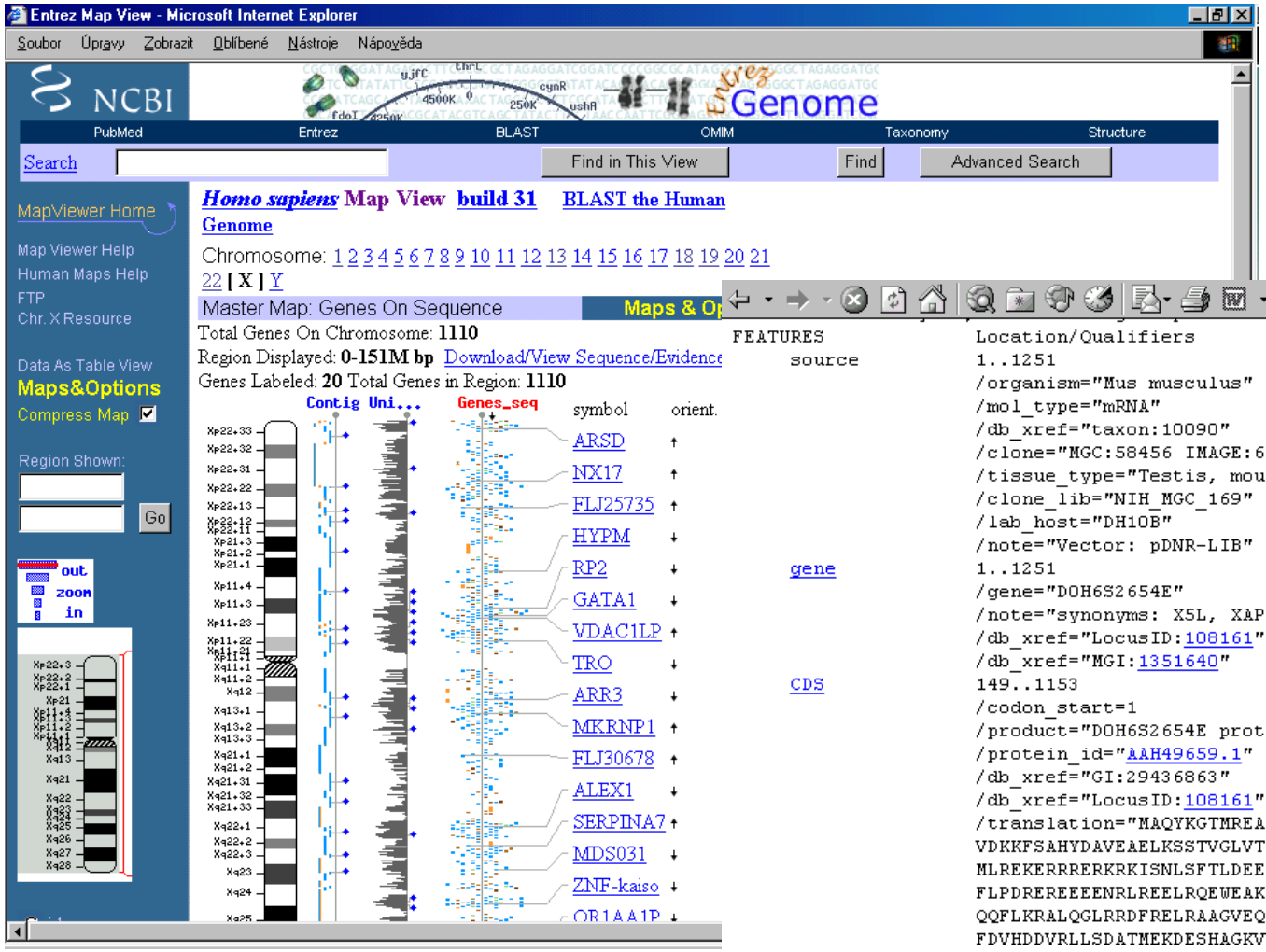
1.8 milionu stran

12 000 knih


http://rene.spika.cz/prague_january/petrin_tower_1.html

NCBI: http://www.ncbi.nlm.nih.gov/mapview/
Sanger/EBI: http://www.ensembl.org/
UCSC: http://genome.ucsc.edu



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       61 tgcagaatct gtgaactgac atcagaccca gaaggctacc agaaacaggg actgggcagg
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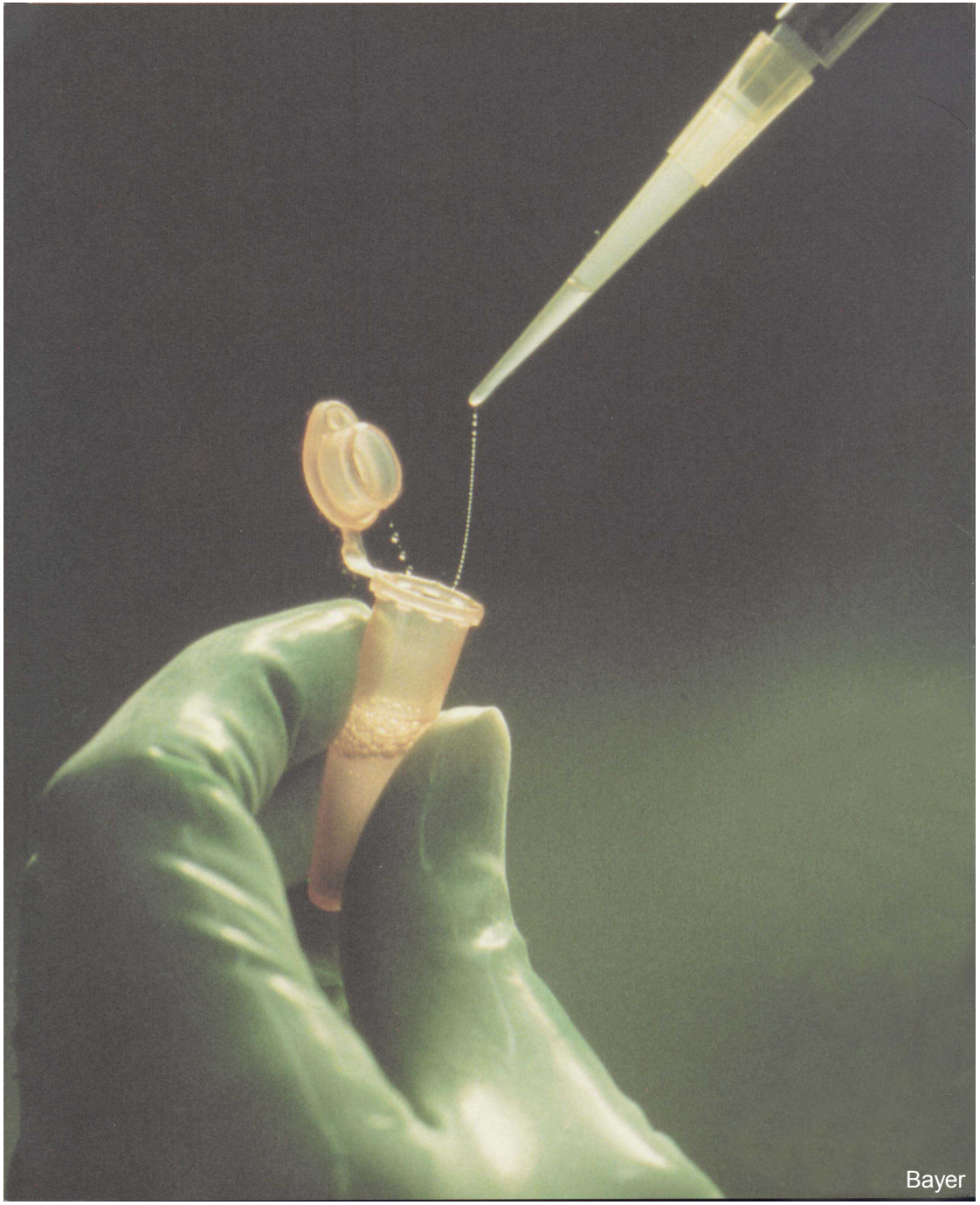
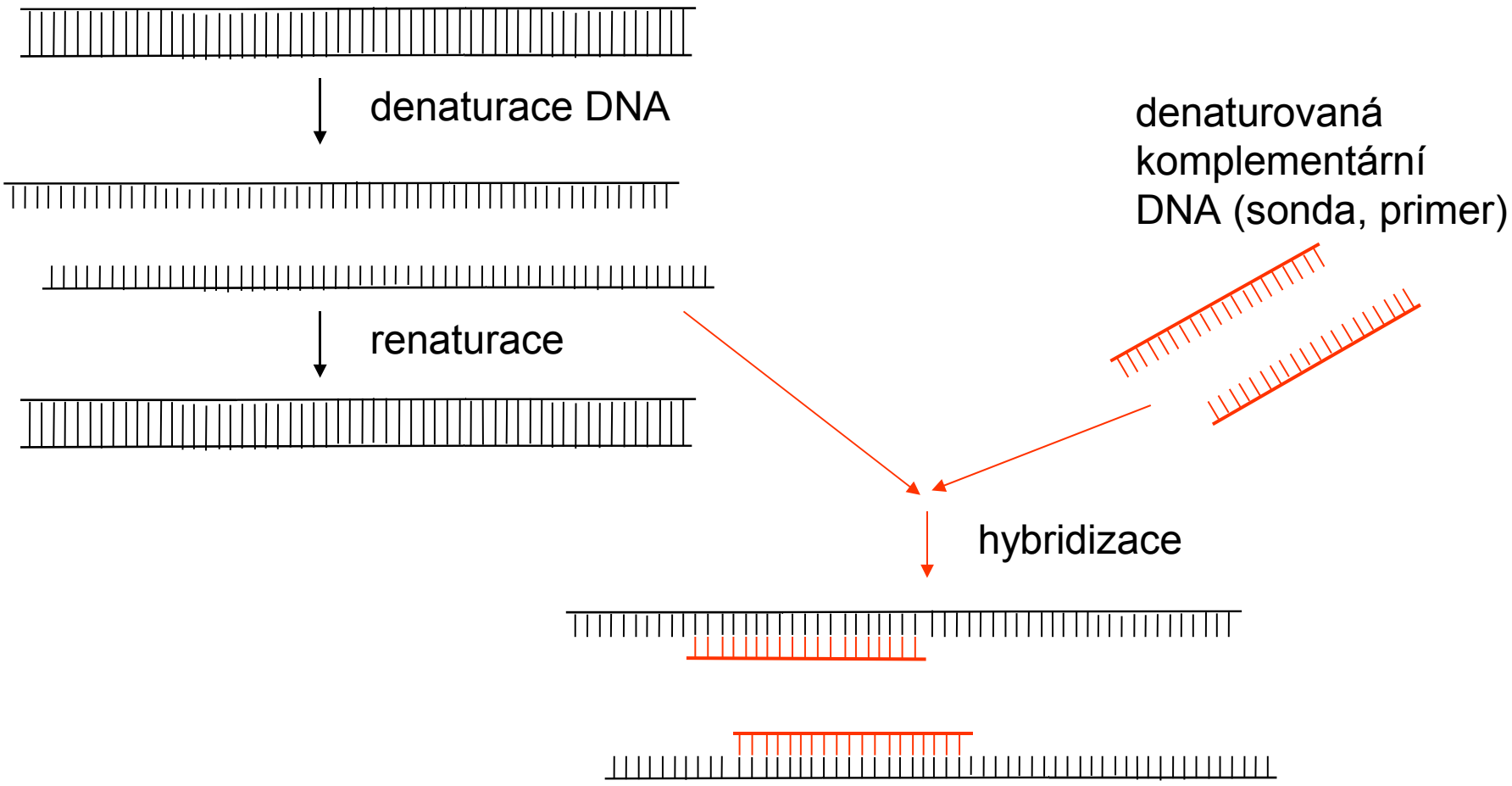
# bioinformatika

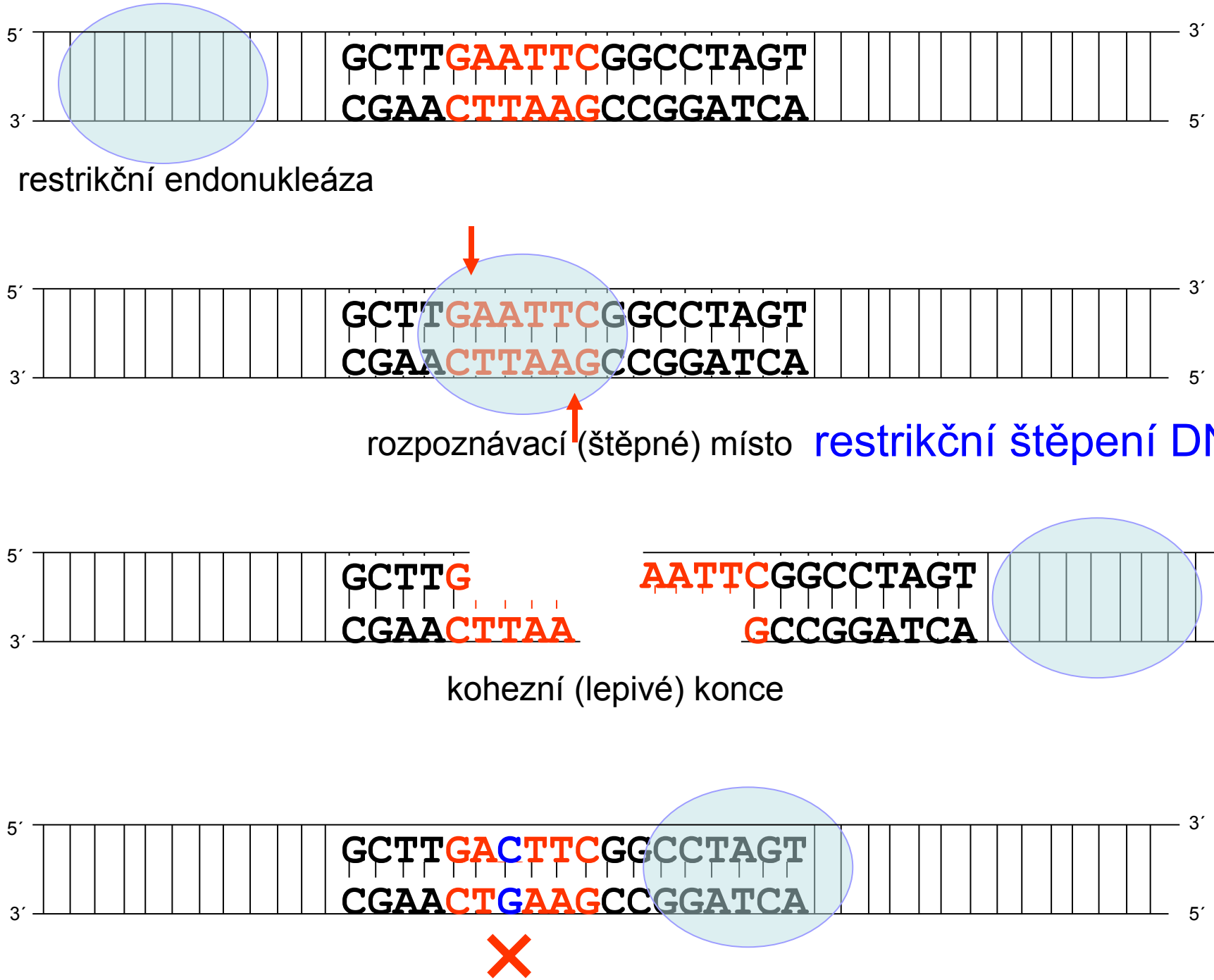
databáze a analýza

izolace
DNA



# hybridizace DNA

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3´
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CGAACTTAAGCCGGATCA
3´
5´
restrikční endonukleáza
5´
3´
GCTTGAATTCGGCCTAGT
CGAACTTAAGCCGGATCA
3´
5´
rozpoznávací (štěpné) místo
restrikční štěpení DNA
5´
3´
GCTTG
CGAACTTAA
AATTCGGCCTAGT
GCCGGATCA
3´
5´
kohezní (lepivé) konce
5´
3´
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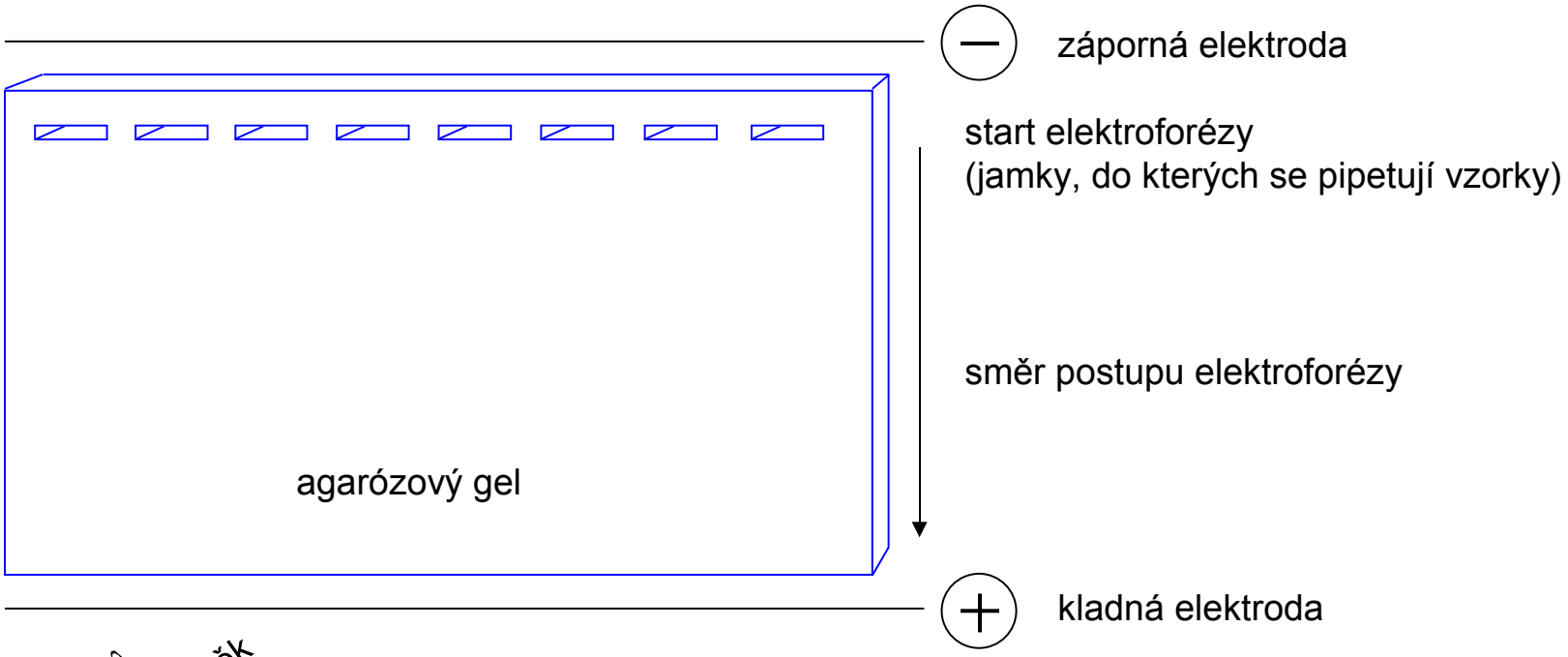
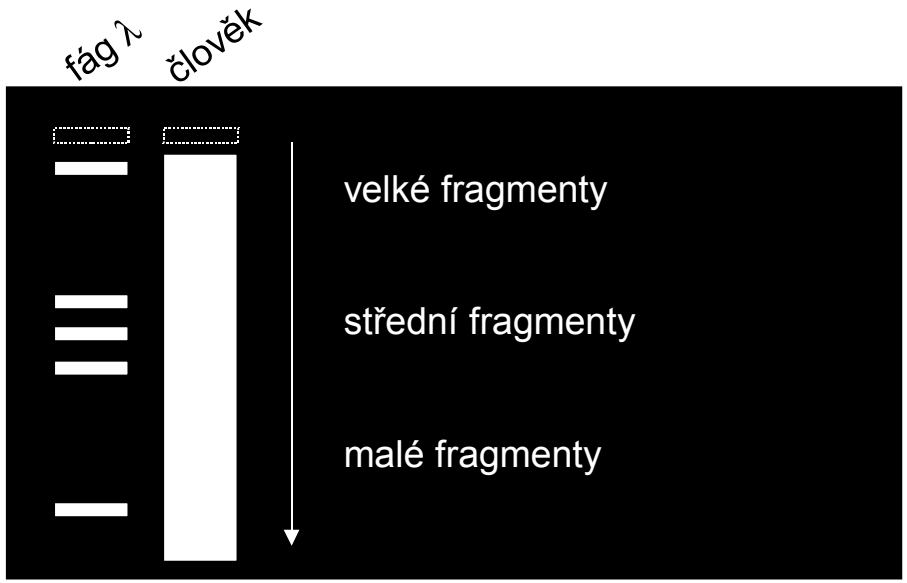
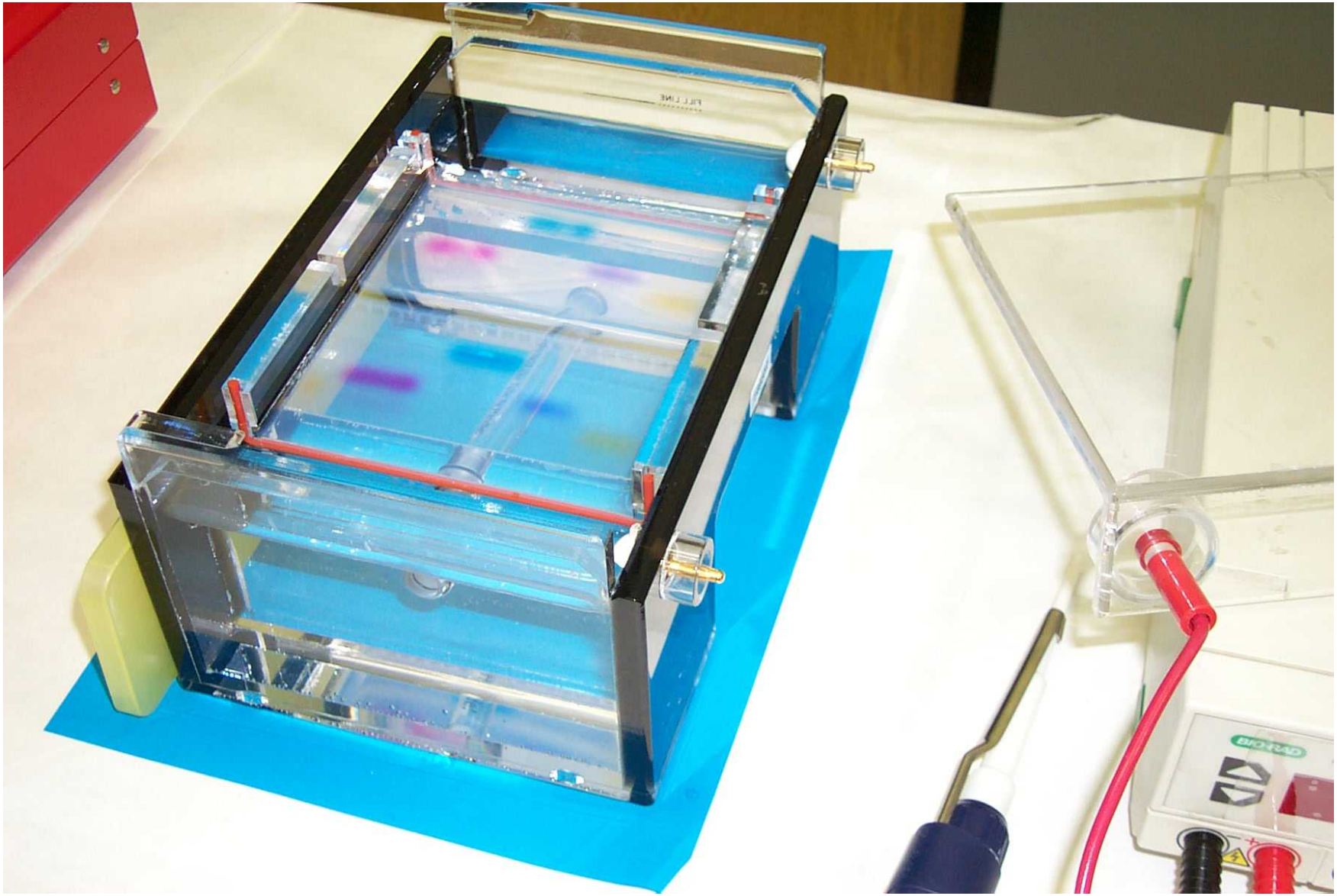
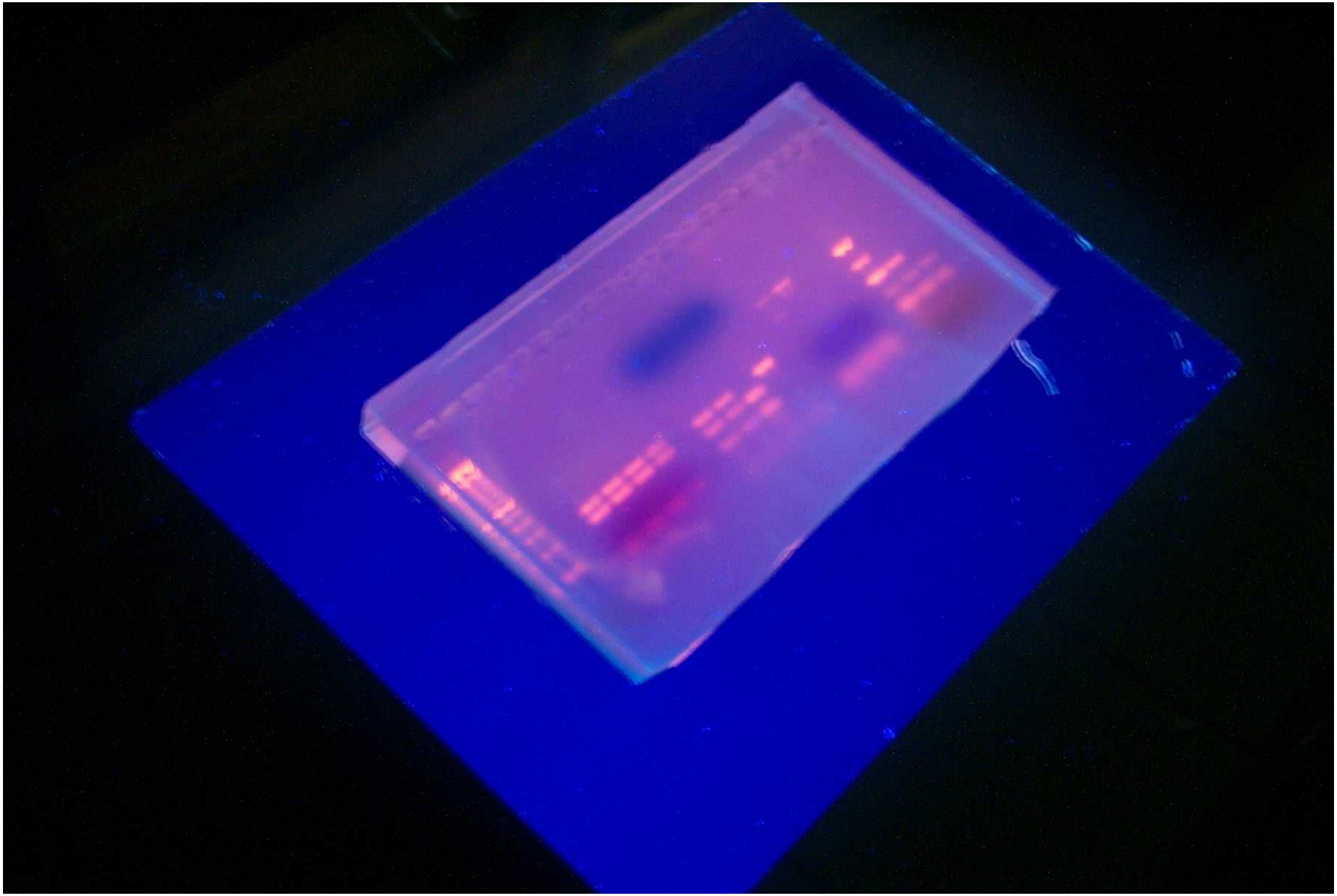
3´
5´

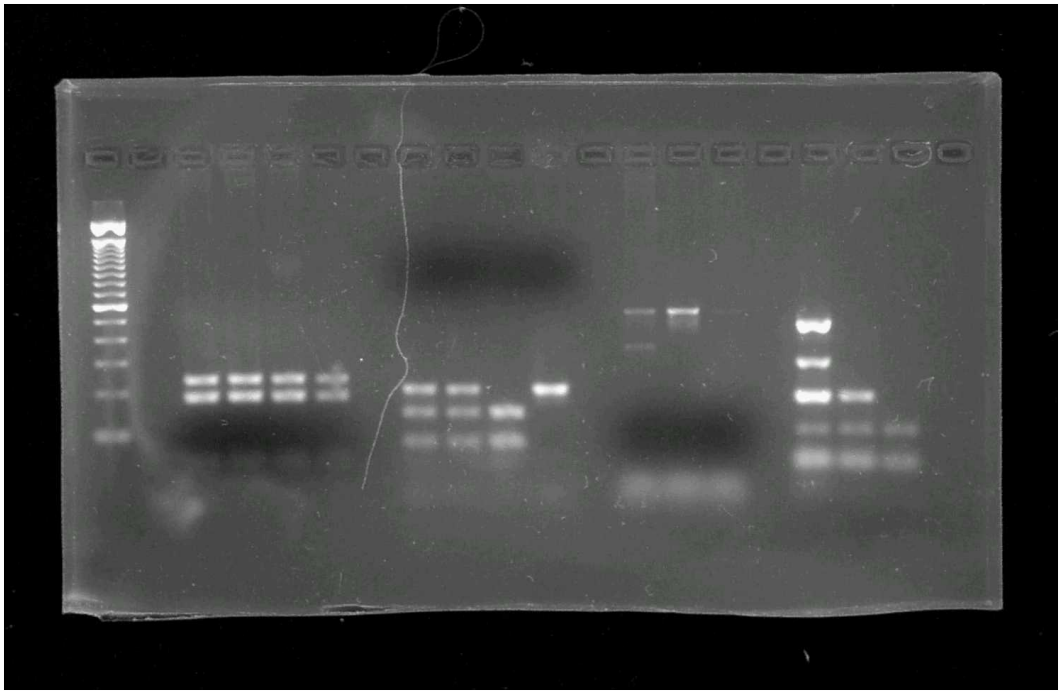
# gelová elektroforéza DNA



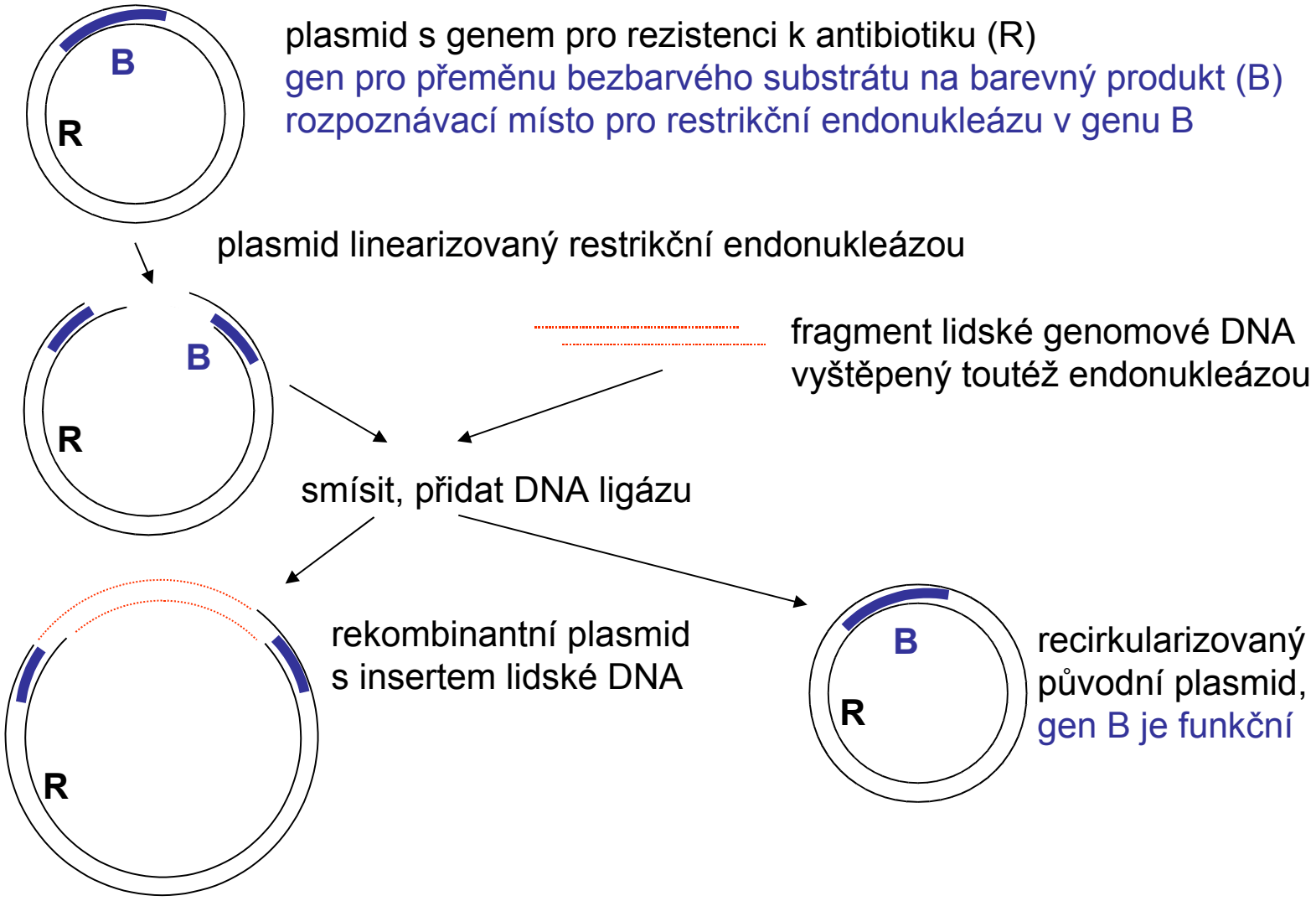





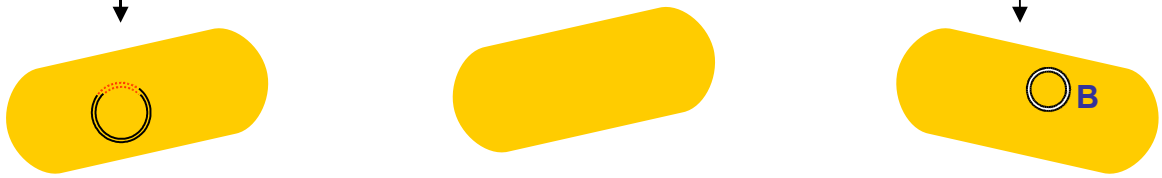




# klonování DNA



transformace hostitelských bakterií

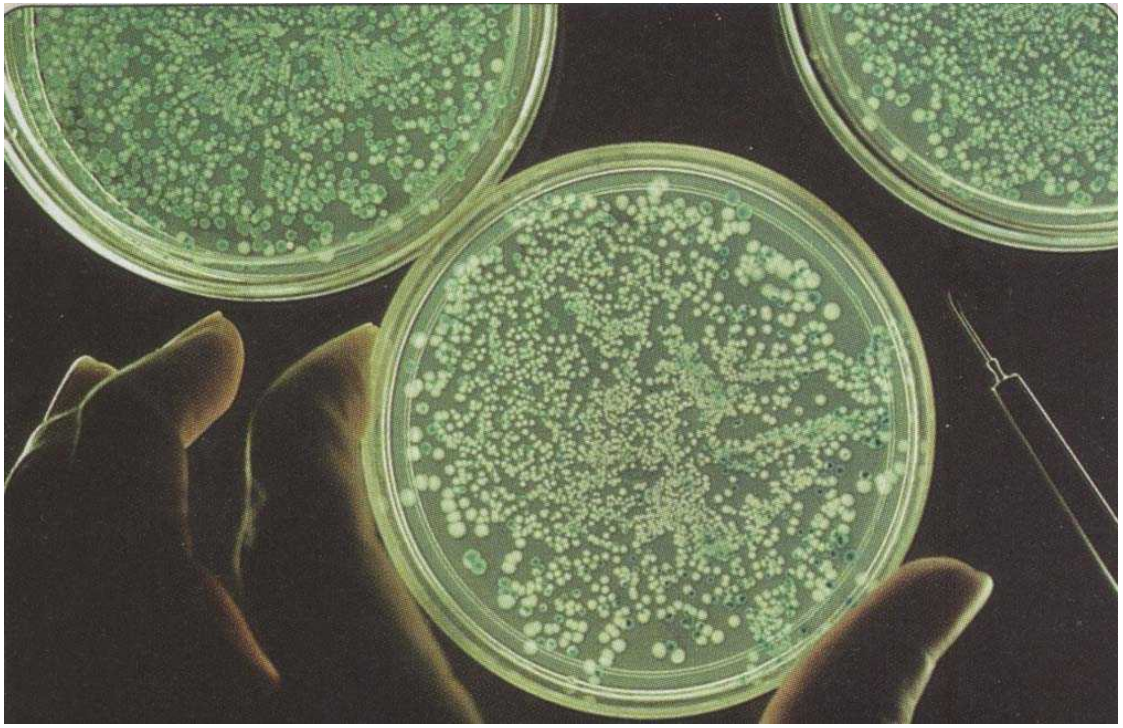


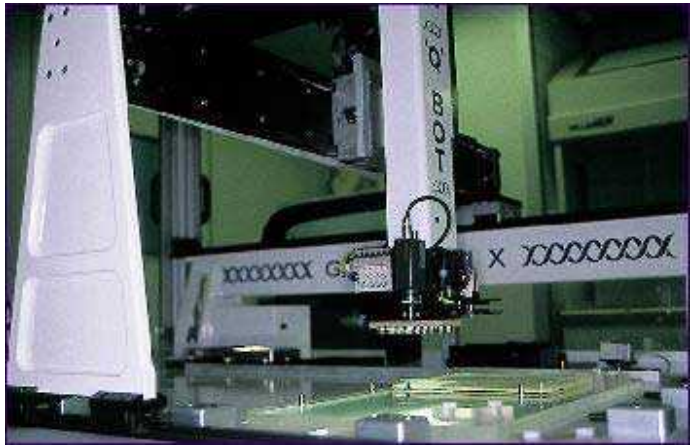

růst bakteriálních klonů na půdě
s antibiotikem a substrátem

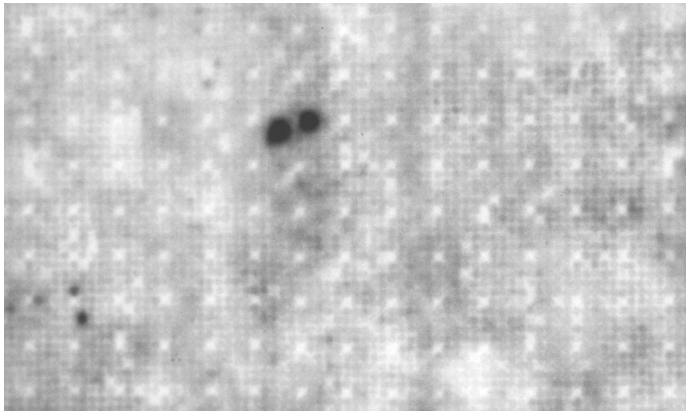
**bezbarvé kolonie**

**netransformované bakterie nevytvoří žádné kolonie**

**barevné kolonie**

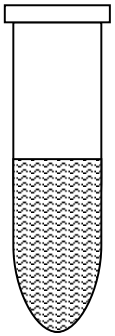




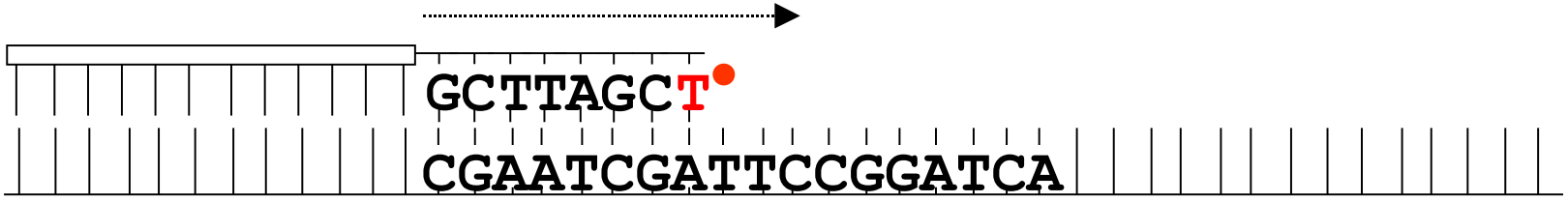


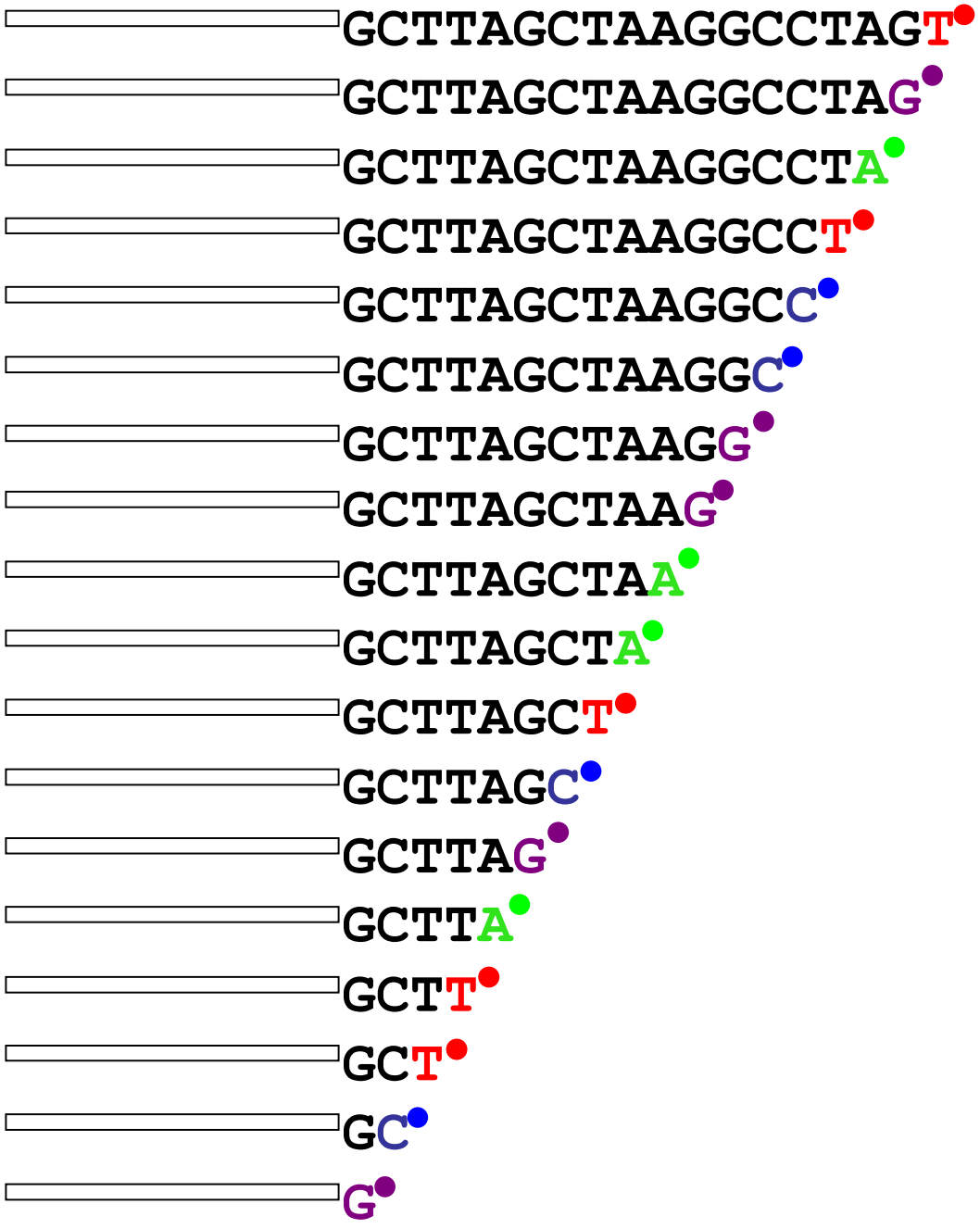
knihovny DNA

# sekvenování DNA

denaturovaná DNA
+ primer + polymeráza
+ deoxynukleotidy **G, A, T, C**
+ dideoxynukleotidy **G, A, T, C**

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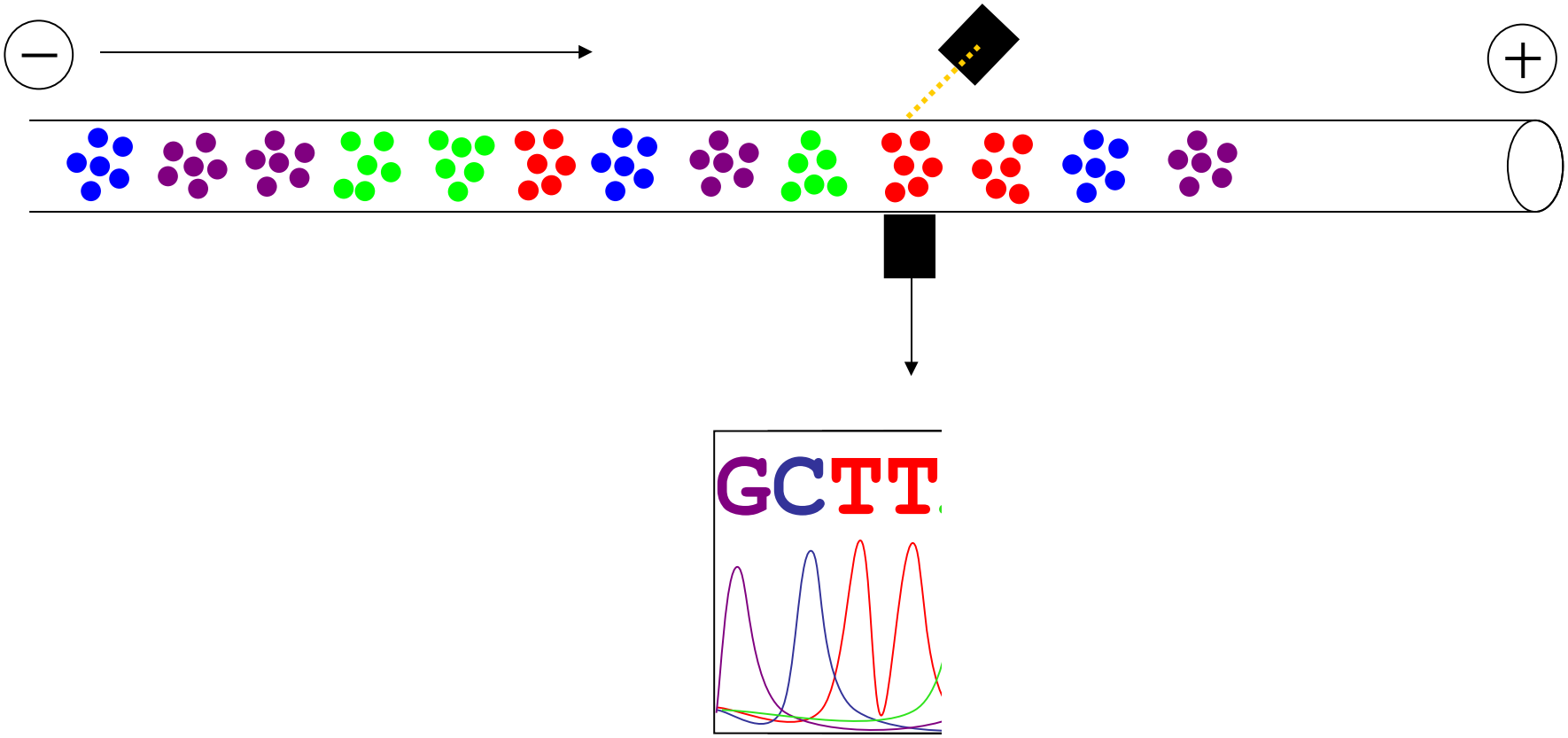
GCT
GC
G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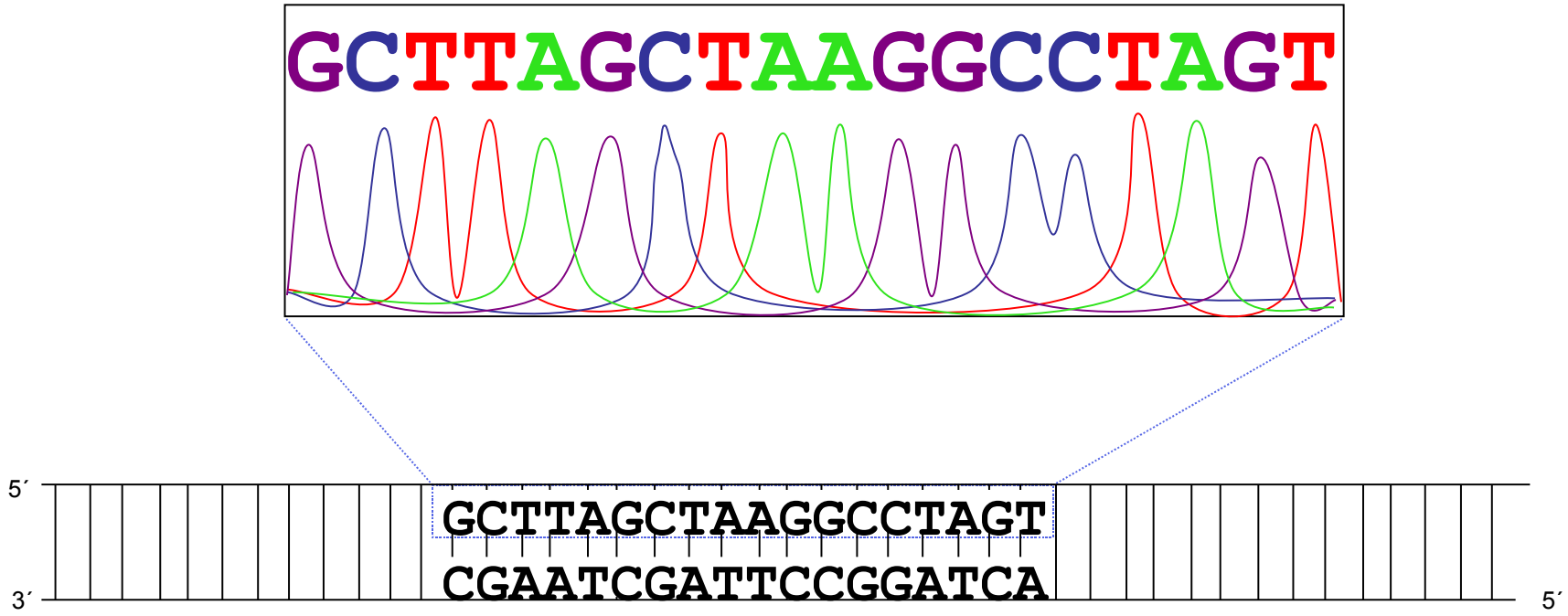
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5´
GCTTAGCTAAGGCCTAGT
CGAATCGATTCCGGATCA
3´
5´