Ácidos Nucléicos

MO401 - Biologia Computacional

Felipe R. da Silva

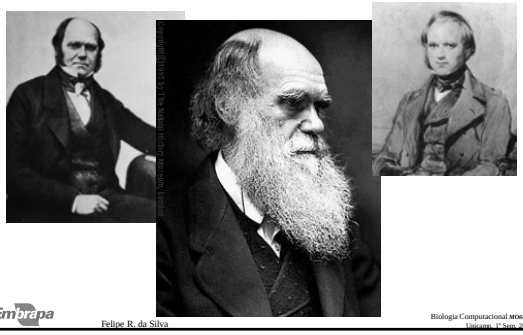
Embrapa Informática Agropecuária

Fases da História da Genética

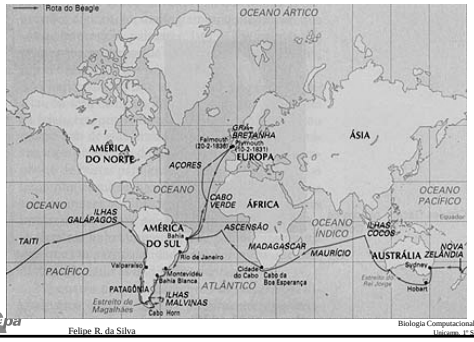
- Mendeliana
- DNA (identidade)
- Dogma Central (DNA - RNA - Proteína)
- Regulação da expressão gênica
- DNA recombinante
- Totalidade da informação genética
- Previsão do desenvolvimento

Watson, JD (1993). Gene 135: 309-315

1859: Charles Darwin
A Origem das Espécies

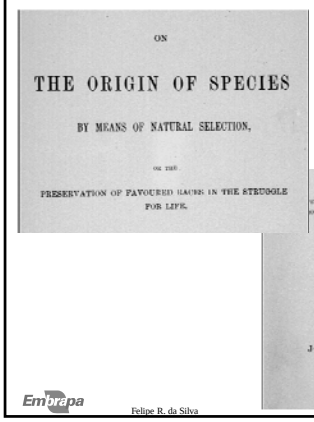


1831-1836: Viagem do Beagle



1838: lê **Ensaio sobre o princípio da população**, de Thomas Malthus (1798)

1857: artigo de Alfred Russel Wallace?


ON

THE ORIGIN OF SPECIES

BY MEANS OF NATURAL SELECTION,

OR THE

PRESERVATION OF FAVOURED RACES IN THE STRUGGLE FOR LIFE.

By CHARLES DARWIN, M.A.,

LONDON:

JOHN MURRAY, ALBEMARLE STREET.

1859.

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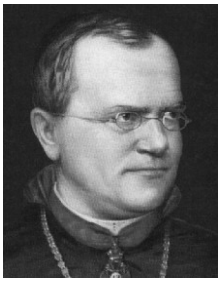
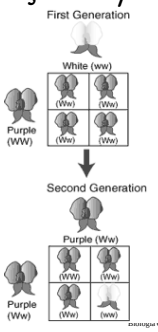
1866: Gregor Mendel

Experimentos em hibridação de plantas





Redescoberto em 1900

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Verhandlungen

des

naturforschenden Vereines

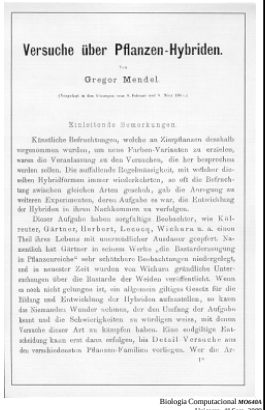
in Brünn.

IV. Band

1865.

Brünn, 1866.

Im Verlage des Vereines.


Versuche über Pflanzen-Hybriden.

von

Gregor Mendel.

Einleitende Bemerkungen.

Künstliche Befruchtungen, welche an Ziergewächsen deshalb vorgenommen wurden, um neue Farben-Varianten zu erzielen, waren die Veranlassung zu den Versuchen, die hier besprochen werden sollen. Die auffallende Regelmässigkeit, mit welcher die-selben Hybridformen immer wiederkehrten, so oft die Befruch-tung zwischen gleichen Arten geschah, gab die Anregung zu weiteren Experimenten, deren Aufgabe es war, die Entwickelung der Hybriden in ihren Nachkommen zu verfolgen.

Dieser Aufgabe haben sorgfältige Beobachter, wie Köl-reuter, Gärtner, Herbert, Lecoq, Wichura u. a. einen Theil ihres Lebens mit unermüdlicher Ausdauer geopfert. Na-mentlich hat Gärtner in seinem Werke „die Bastarderzeugung in Pflanzenreiche" sehr schätzbare Beobachtungen niedergelegt, und in neuester Zeit wurden von Wichura gründliche Unter-suchungen über die Bastarde der Weiden veröffentlicht. Wenn es noch nicht gelungen ist, ein allgemein gültiges Gesetz für die Bildung und Entwickelung der Hybriden aufzustellen, so kann das Niemanden Wunder nehmen, der den Umfang der Aufgabe kennt und die Schwierigkeiten zu würdigen weiss, mit denen Versuche dieser Art zu kämpfen haben. Eine endgiltige Ent-scheidung kann erst dann erfolgen, bis Detail-Versuche aus den verschiedensten Pflanzen-Familien vorliegen. Wer die Ar-

1*

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1869: Johann Friedrich Miescher

descoberta da "nucleína"

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1909: Wilhelm Johannsen

criação dos termos gene, fenótipo e genótipo

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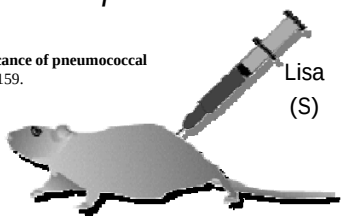
1928: Frederick Griffith

princípio transformante

Griffith, F. (1928) **Significance of pneumococcal types**. *J. Hygiene* **27**:113-159.



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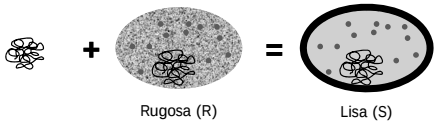
princípio transformante

- Lisa → MATA!
- Rugosa → NÃO mata
- Lisa *fervida* → NÃO mata
- Lisa *fervida* + Rugosa → MATA!??!

1944: Oswald T. Avery
DNA é o "princípio transformante"

Avery, O.T., MacLeod, C.M. & McCarty, M. (1944). **Studies on the chemical nature of the substance inducing transformation of Pneumococcal types**. *J. Exp. Med*. **79**, 137-159 (1944)

princípio transformante



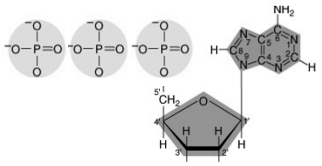
Rugosa (R) Lisa (S)

- proteínas
- capsula
- DNA

Nucleotídeo

Unidade básica formadora dos ácidos nucléicos

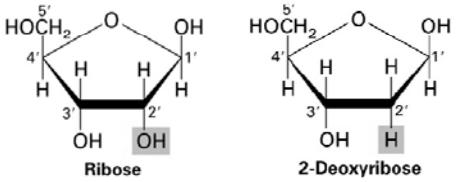
- **Açúcar** ***(pentose)***
- **Base Nitrogenada**
- **Grupo Fosfato**



Monômero

Os Açúcares

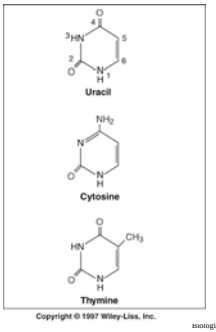
- Pentose
  - Ribose e Desoxirribose



Ribose 2-Deoxyribose

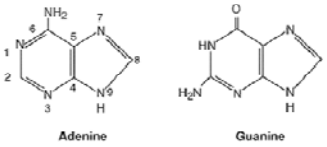
Bases Nitrogenadas

- Pirimidinas



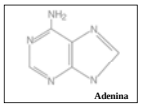
Bases Nitrogenadas

- Purinas

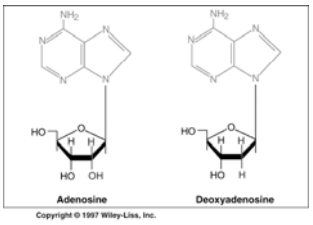


Nucleosídeos

Base Nitrogenada

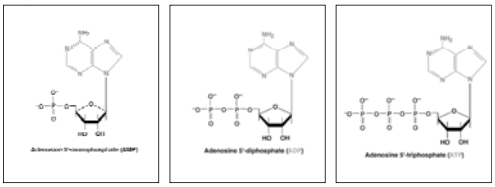


Base Nitrogenada + Açúcar = **Nucleosídeo**



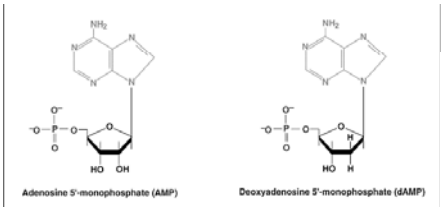
Nucleotídeos

Base Nitrogenada + Açúcar + Grupo Fosfato = **Nucleotídeo**



Nucleotídeos e Desoxirribonucleotídeos

Adenina + Açúcar + Grupo Fosfato = **Nucleotídeo**



1950: Erwin Chargaff
%A = %T e %G = %C

Conteúdo de bases *em diferentes espécies*

Conclusões de Chargaff

- A quantidade de nucleotídeos pirimidínicos (T+C) é sempre igual a quantidade total de nucleotídeos purínicos (A+G)
- A Quantidade de T = A; C = G
- A Quantidade de A+T é diferente de G + C
- A relação A + T / G + C é espécie específica

1953 – Rosalind Franklin e Maurice Wilkins (dama sombria)

- Resultados com difração de raio X
  - O DNA é longo e fino
  - Tem partes semelhantes e paralelas, correndo ao longo da molécula
  - É helicoidal
  - Raio de 10 Å; Ciclo de 34 Å e 3,4 Å entre "degraus"

Descobertas que ajudaram na elucidação da estrutura do DNA

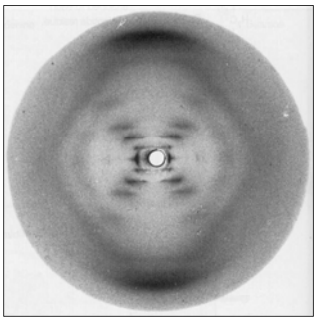
- 1953 – Rosalind Franklin e Maurice Hugh Frederick Wilkins

1916 - 2004

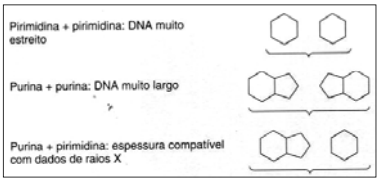
1920 - 1958

▪(dama sombria)

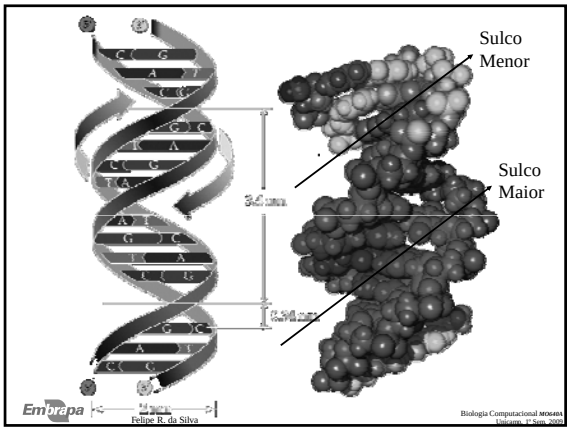
A famosa imagem 51

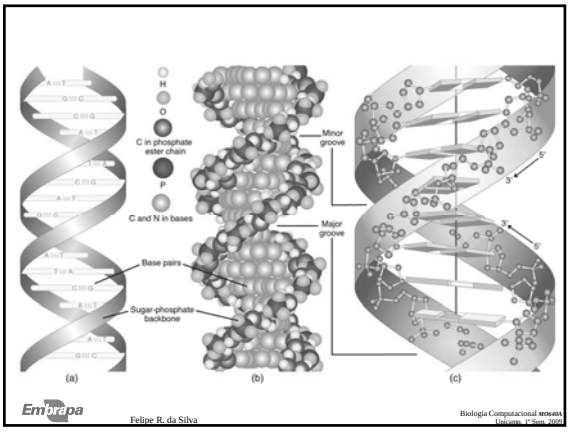


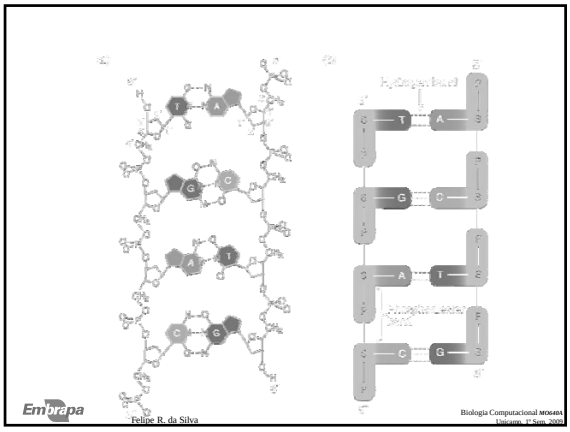
As bases e as medidas sugeridas por Rosalind



1953: Watson, J.D. & Crick, F.H.C.





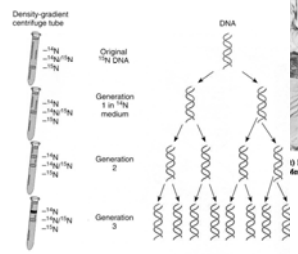


1957: Francis Crick
dogma central

DNA ⇒ proteína

RNA

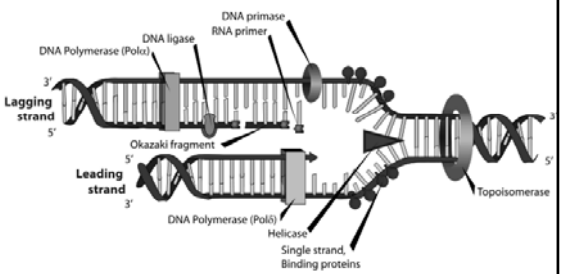
1958 - Meselson e Stahl
A natureza semiconservativa do DNA



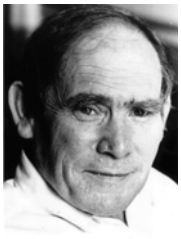
() Matthew Meselson (b. 1930). (Right) Franklin W. Stahl (b. 1929). fmeselson.]

animação

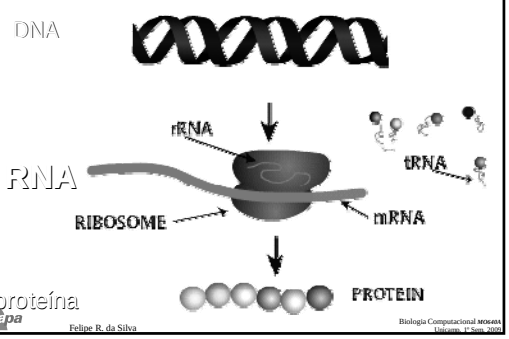
Replicação DNA



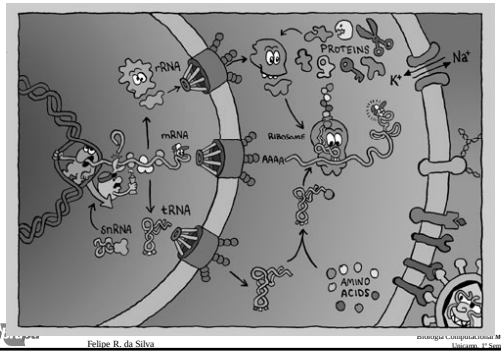
1960: Sydney Brenner, Francis Crick, François Jacob e Jacques Monod
descoberta do mRNA



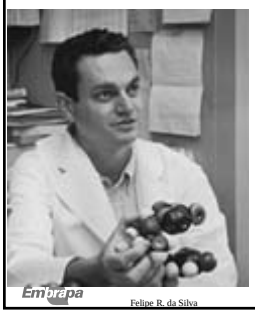
Dogma central



Dogma central



1961: Marshall Nirenberg
quebra o código genético



Nobel 1968
"pela interpretação do código genético e sua função na síntese protéica"

Nirenberg, M. W. and Matthaei, J. H. (1961)

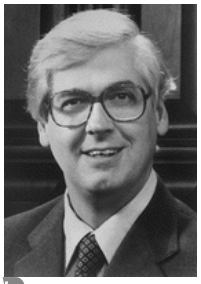
The dependence of cell-free protein synthesis in E. coli upon naturally occurring or synthetic polyribonucleotides.

Proc. Natl. Acad. Sci. USA **47**, 1588-1602

Código Genético

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

1970: Hamilton O. Smith
primeira enzima de restrição



Nobel 1978
"pela descoberta das enzimas de restrição e sua aplicação nos problemas de genética molecular"

Hamilton O. Smith and K. W. Wilcox (1970).

A restriction enzyme from *Haemophilus influenzae*. I. Purification and general properties.

Journal of Molecular Biology **51**, 379-391.

1972: Paul Berg
primeira molécula de DNA recombinante

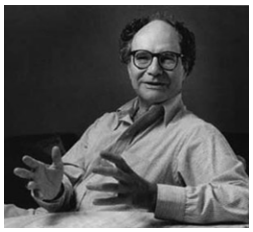
Nobel 1980
"pelos estudos da bioquímica de ácidos nucleicos, especialmente de DNA recombinante"

Jackson, DA, Symons, RH and Berg, P (1972).

A Biochemical Method for Inserting New Genetic Information into SV40 DNA: Circular SV40 DNA Molecules Containing Lambda Phage Genes and the Galactose Operon of E. coli.

Proc. Nat. Sci. USA **69**: 2904-2909.

1977: Walter Gilbert e Frederick Sanger
seqüenciamento de DNA



Nobel 1980
"pelas contribuições na determinação de seqüências de ácidos nucleicos"

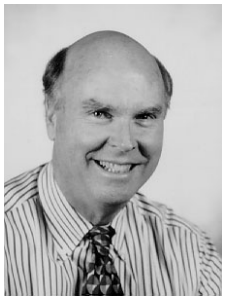
1983: Kary B. Mullis
PCR

Nobel 1980
"pela invenção da PCR"

Mullis, K.B (1983). **The unusual origin of the polymerase chain reaction**. *Sci Am*, **4**: 56-65.

Saiki R, K.; Scharf S; Faloona F; Mullis K. B; Horn G. T; Erlich H. A.; Arnheim N. (1985). **Enzymatic amplification of beta-globin genomic sequences and restriction site analysis for diagnosis of sickle cell anemia**. *Science*, **230**(4732):1350-4.

1991: J. Craig Venter
ESTs na descoberta de genes



M.D. Adams et al. (1991)

Complementary DNA sequencing: 'expressed sequence tags' and the Human Genome Project,"

Science, 252:1651-1656.

Alguns conceitos

- Fita Codificante
  - a que tem a mesma seqüência que o mRNA

Estrutura de um gene

```
tgaggaacggtgcctggaaaagggcaagaatatccggcatgggcatgagtagcttgaaactgctgaagtatgtcctgttttt
cttcaacttgccttttggatctgtgtctgctgcatttttgggctttgggatctacctgctgatccacaacacttcggagtgct
cttccataacctcccctccctcacgctgggcaatgtgtttgtcatcggggctctattatcatggtagttgcctttcctgggct
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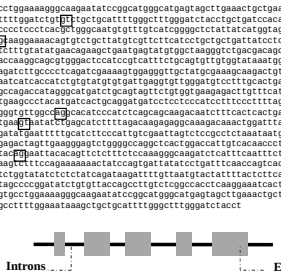
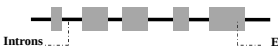
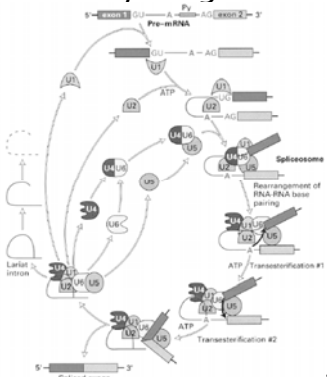
Estrutura de um gene



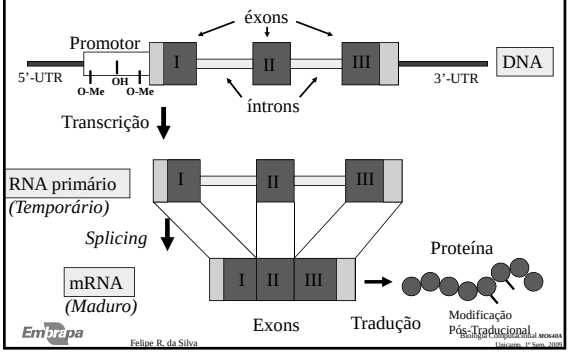
Estrutura de um gene



Splicing



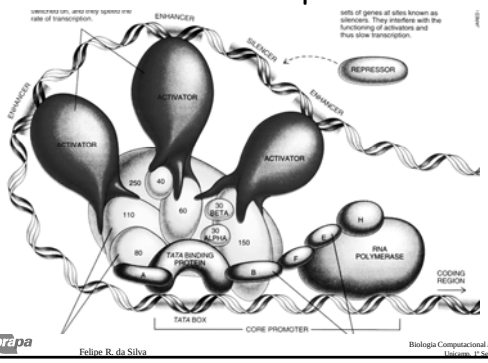
Estrutura e Expressão Gênica



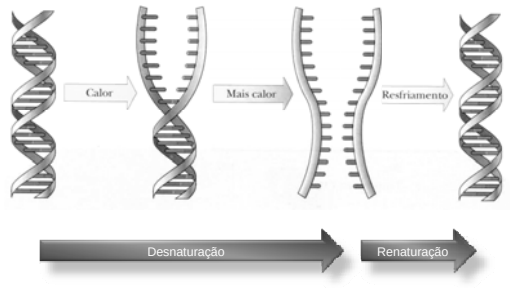
Alguns conceitos

- Fita Codificante
  - a que tem a mesma seqüência que o mRNA
- Intron x Exon
- UTR
- poliA

Estrutura de um promotor



Desnaturação e renaturação do DNA



- Garfo de replicação
- Falar dos formatos de DNA (circular, linear etc): material genético
- Splice alternativo
- Genétipo / Fenótipo.