
Symposium
MOLECULAIRE
DIAGNOSTIEK
in het Academisch Ziekenhuis Paramaribo
Zaterdag 12 november 2011 | 08.30 - 12.15u

# Nascholingscursus 'Succesvol gebruik van moleculaire diagnostiek'

7 t/m 11 november 2011

Leiden

KWALITEITSBORGING EN BEDRIJFSVOERING MOLECULAIRE DIAGNOSTIEK

IMPLEMENTATIE VAN MOLECULAIR DIAGNOSTISCHE TESTEN

ONTWIKKELING EN IMPLEMENTATIE VAN MULTIPLEX EN TESTEN TOEGESPITS OP KLINISCHE SYMPTONEN

TOEPASSINGEN IN DE MEDISCHE MICROBIOLOGIE

TOEKOMSTIGE ONTWIKKELINGEN IN DE MOLECULAIRE DIAGNOSTIEK

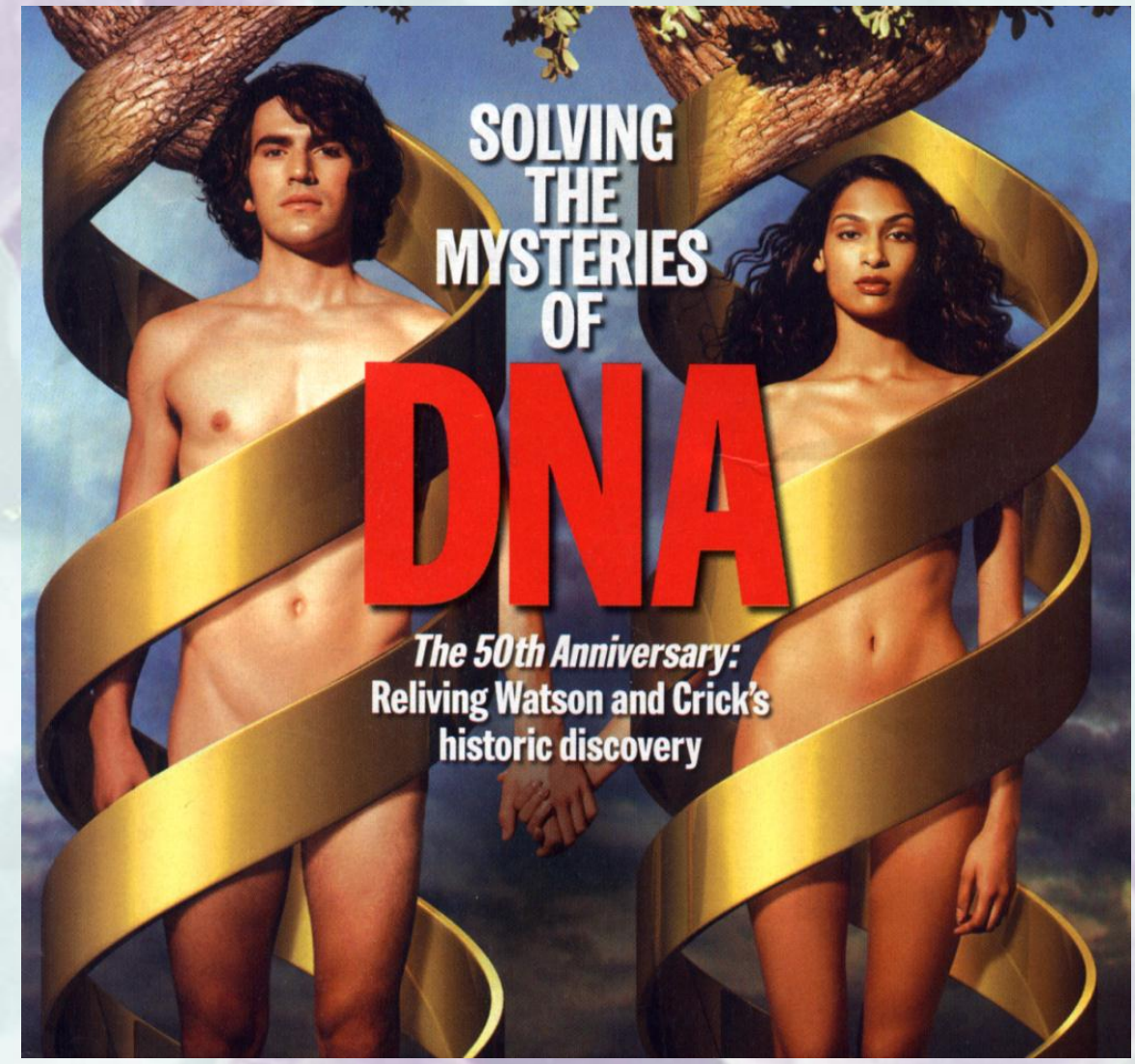
# Symposium: The future of molecular microbiology

**Multidisciplinaire samenwerking is steeds meer een begrip binnen de gezondheidszorg.**

Om die samenwerking verder uit te breiden zal er met ondersteuning van ……. op **30 november** a.s. een mini-symposium georganiseerd worden……..

**Third Scientific Meeting Molecular Diagnostics**

**Tuesday December 13th, 2011**
**Elzenveld, Antwerp.**


SOLVING
THE
MYSTERIES
OF
DNA
The 50th Anniversary:
Reliving Watson and Crick's
historic discovery

# Nature artikel 1953



equipment, and to Dr. G. E. R. Deacon and the captain and officers of R.R.S. *Discovery II* for their part in making the observations.


[1] Young, F. B., Gerard, H., and Jevons, W., *Phil. Mag.*, **40**, 149 (1930).

[2] Longair, Hughes, M. S., *Mon. Not. Roy. Astro. Soc., Geophys. Supp.*, **5**, 256 (1949).

[3] Von Arx, W. S., Woods Hole Papers in Phys. Oceanog. Meteor., **11** (1) (1950).

[4] Elsasser, W. M., *Arkiv. Mat. Astron. Fysik. (Stockholm)*, **2** (11) (1905).


## 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.

This figure is purely diagrammatic. The two ribbons symbolize the two phosphate–sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis.

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 sugar 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 acces

The structure is an open one, and i
is rather high. At lower water co
expect the bases to tilt so that th
become more compact.

The novel feature of the structur
in which the two chains are held
purine and pyrimidine bases. The pl
are perpendicular to the fibre axis.
together in pairs, a single base from
hydrogen-bonded to a single base
chain, so that the two lie side by s
z-co-ordinates. One of the pair must
the other a pyrimidine for bonding
hydrogen bonds are made as follows
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 previously 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

> *"It has not escaped our notion that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material"*



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.


[3] Pauling, L., and Corey, R. B., *Nature*, **171**, 346 (1953); *Proc. U.S. Nat. Acad. Sci.*, **39**, 84 (1953).

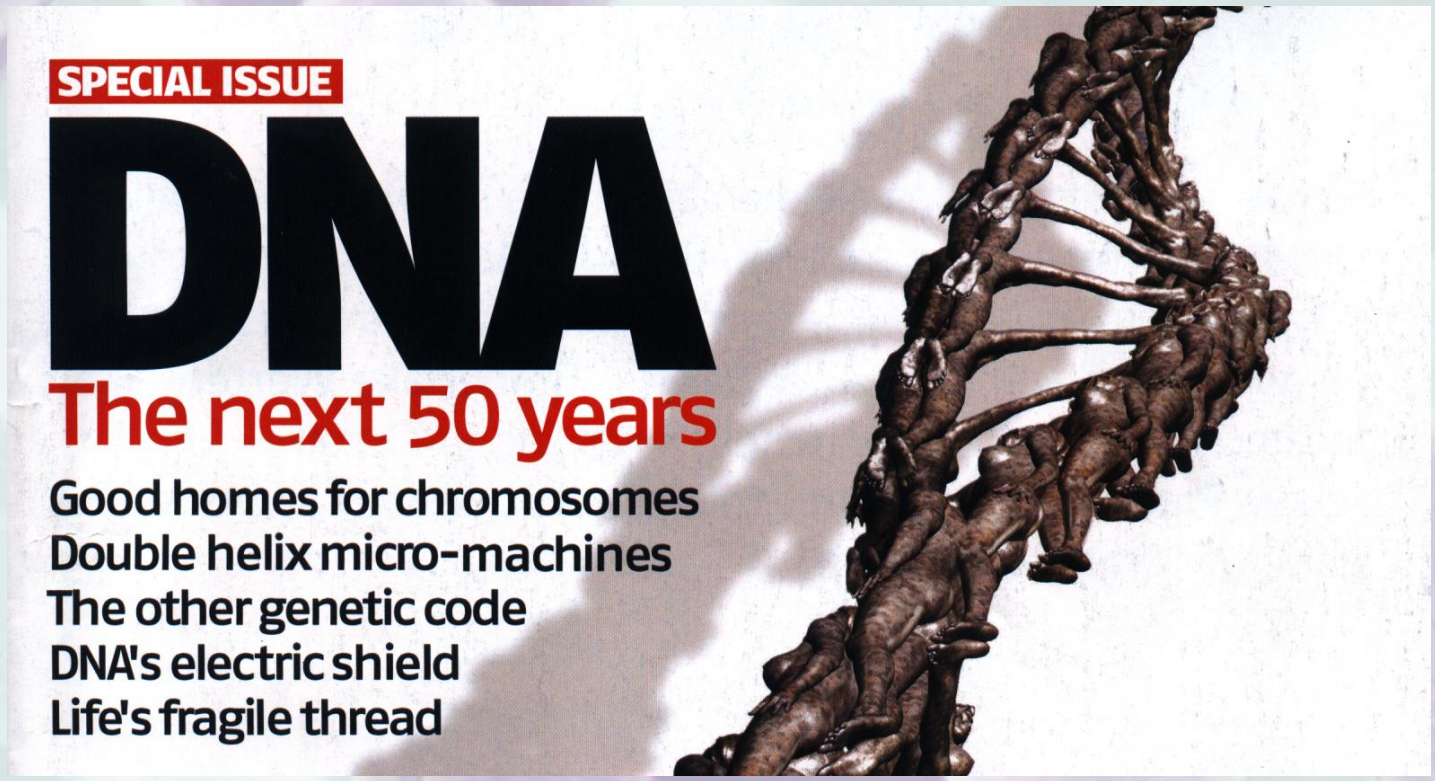
[4] Vischer, E., *Cold Spring Harbor Symp. Quant. Biol.*, **8**, 133 (1952).

[5] Chargaff, E., [illegible] Zamenhof, S., Brawerman, G., and Chargaff, R., *Biochim. et Biophys. Acta*, **9**, 402 (1952).

[6] Wyatt, G. R., *J. Gen. Physiol.*, **36**, 201 (1952).

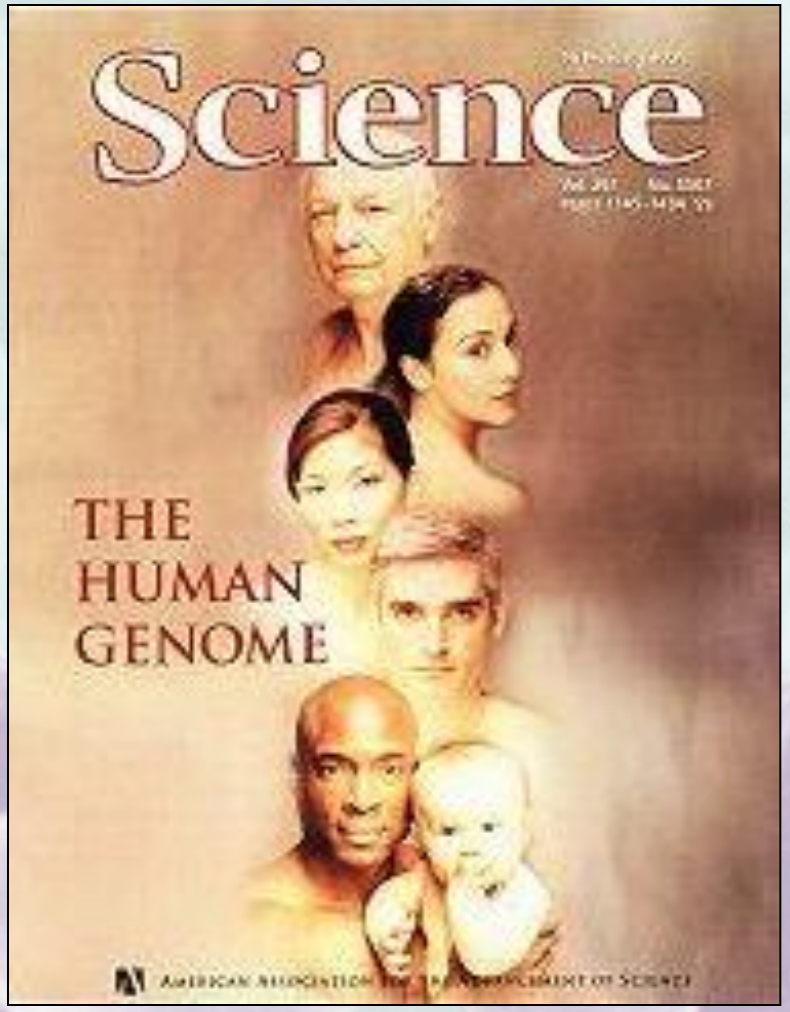
[7] Astbury, W. T., *Symp. Soc. Exp. Biol.* 1, Nucleic Acid, 66 (Camb. Univ. Press, 1947).

[8] Wilkins, M. H. F., and Randall, J. T., *Biochim. et Biophys. Acta*, **10**, (in the press).


NewScientist
The global science and technology weekly | 15 March 2003
SPECIAL ISSUE
DNA
The next 50 years
Good homes for chromosomes
Double helix micro-machines
The other genetic code
DNA's electric shield
Life's fragile thread

# Toekomst!!!

- Leeftijd: >>100
- Genomics/proteomics
- Pharmacogenomics
- Synthetische micro-organismen
- Epigenetica
- Moleculaire Diagnostiek



# *En niet-wetenschappelijke publikaties*

"Human genetic code mapped, humans could live forever"

# Wat is Diagnostiek?

*Egyptisch kleitablet uit de periode 1403 – 1365 v. Chr. (Collectie Glyptotheek Kopenhagen)*

# Klassieke Diagnostiek

**“bedside testing”**

- symptomen, omgeving, etc.

***Treat now,***

***ask questions later!!!!***

# Ontwikkelingen in de Diagnostiek

**Klassieke Diagnostiek**

↓

**Klinische Diagnostiek**

↓

**Voorspellende Diagnostiek**

# Wat is moleculaire diagnostiek?

**De term "moleculaire diagnostiek" is een verzamelnaam voor een aantal laboratoriumtechnieken die gebruik maken van nucleïnezuren (DNA en RNA).**

**GENOTYPE**

genoom

**DNA**

**expressie** **replicatie** **organisatie** **onderhoud**

*transcriptie*

**mRNA**

*translatie*

**eiwit**

celkern
chromosomen
toegankelijkheid

mutaties
reparatie
recombinatie

**FENOTYPE**

# Soorten DNA/RNA sequenties

- genen
- ‘junk’ DNA
- repeterende sequenties
  - (CA)n
  - ALU (± 300 bp, soort specifiek)
  - VNTRs (Variable Number of Tandem Repeats)
  - Poly-[T]
  - Satelieten
  - Telomeren
- pseudogenen en fragmenten

- Transcriptie (RNA)

## In het klinisch laboratorium van een ziekenhuis worden moleculaire technieken toegepast:

- bij het opsporen en identificeren van micro-organismen,
- klinische chemie (factor V)
- bij het opsporen van aangeboren aandoeningen,
- bij de diagnose, follow-up en therapie van maligniteiten,

# Methoden en Technieken in de diagnostiek

1 Microscopische detectie

2 Chemische detectie

3 Immunologische detectie

4 Moleculaire detectie

5 Combinaties van 1 t/m 4

# Analyse technieken

- DNA/RNA/Eiwit isolatie
- electroforese
- fingerprinting & RFLP
- hybridisatie
- amplificatie
- sequentie analyse
- Genomics
- Proteomics
- Nano-technologie

# Infectieziekten

- AIDS
- baarmoederhalskanker - bilharzia - bof - borreliose - botulisme - brucellose
- Chagas' - cholera – coli - chlamydia
- dengue - difterie - dysenterie
- ebola - Epstein Barr virus
- filariasis
- gele koorts - giardiasis - gonorrhoe - griep
- hantavirus - helicobacter - hepatitis - hersenvliesontsteking
- Japanse encephalitis
- Kala azar - kinkhoest
- lassa koorts - legionella - leishmaniasis - lepra - leptospirose - lintworm
- maagzweer - malaria - mazelen - melaatsheid - meningitis
- onchocerciasis
- pest - pokken - polio
- rabies - rivierblindheid - roodvonk - rubella
- SARS - schistosomiasis - schurft - slaapziekte - syfilis
- tetanus - toxoplasmose - tuberculose - tyfus
- verkoudheid
- waterpokken - wormen
- ziekte van Lyme - ziekte van Weil