Electric Transport in DNA

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&

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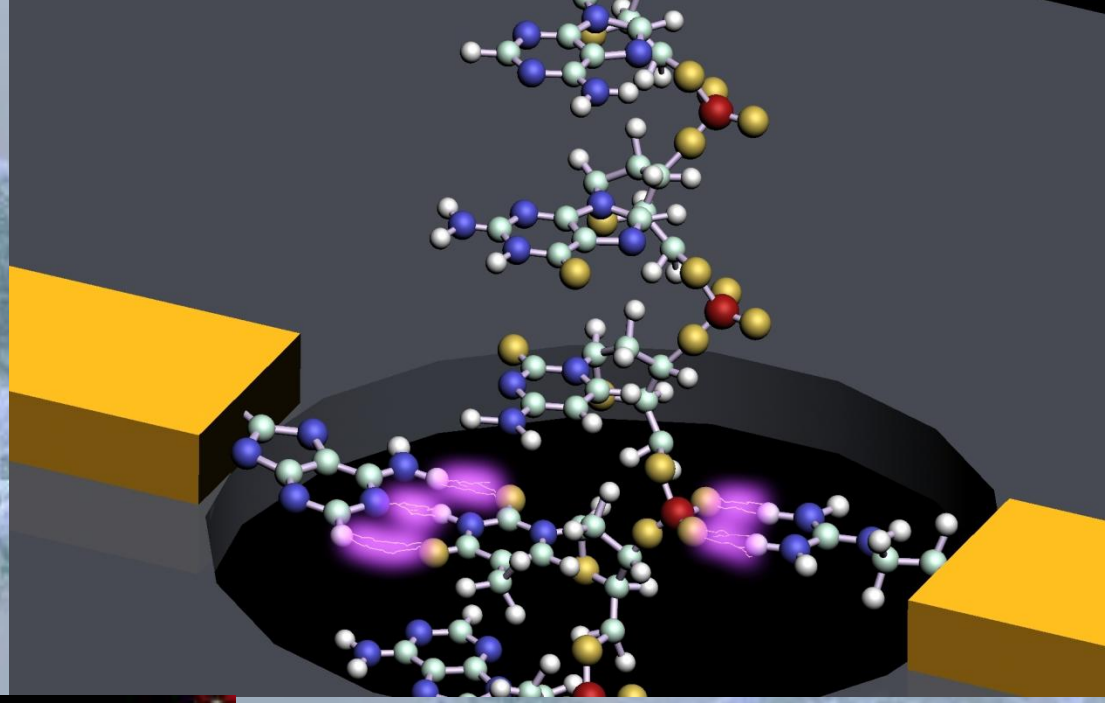
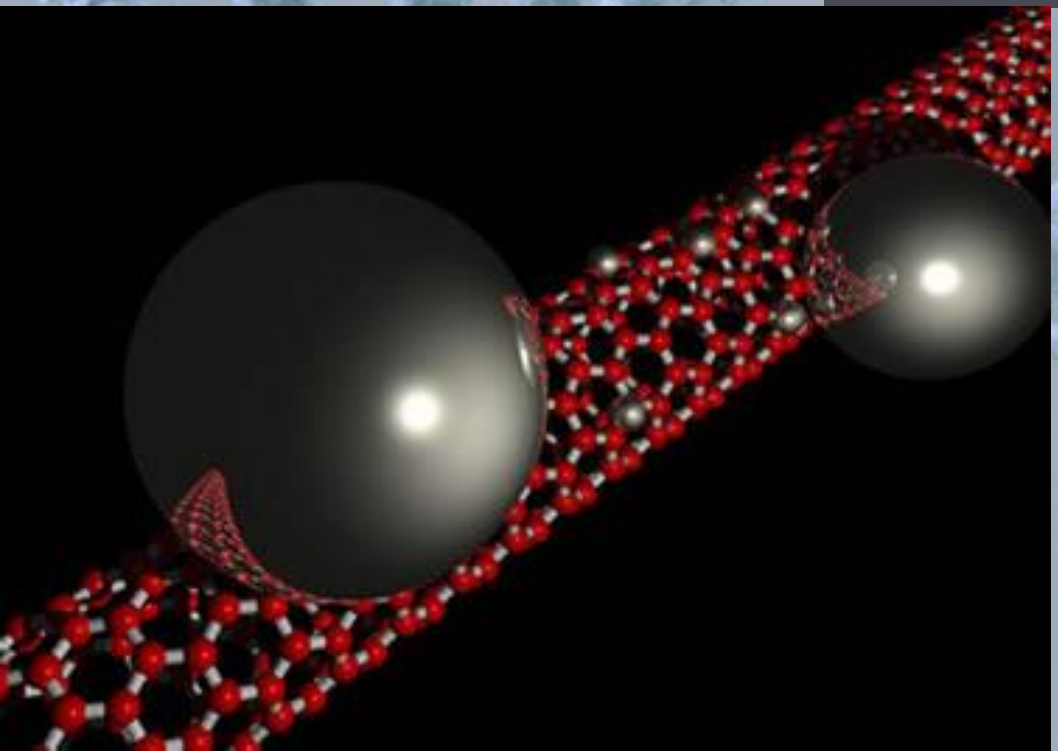
Electric Current along DNA ???





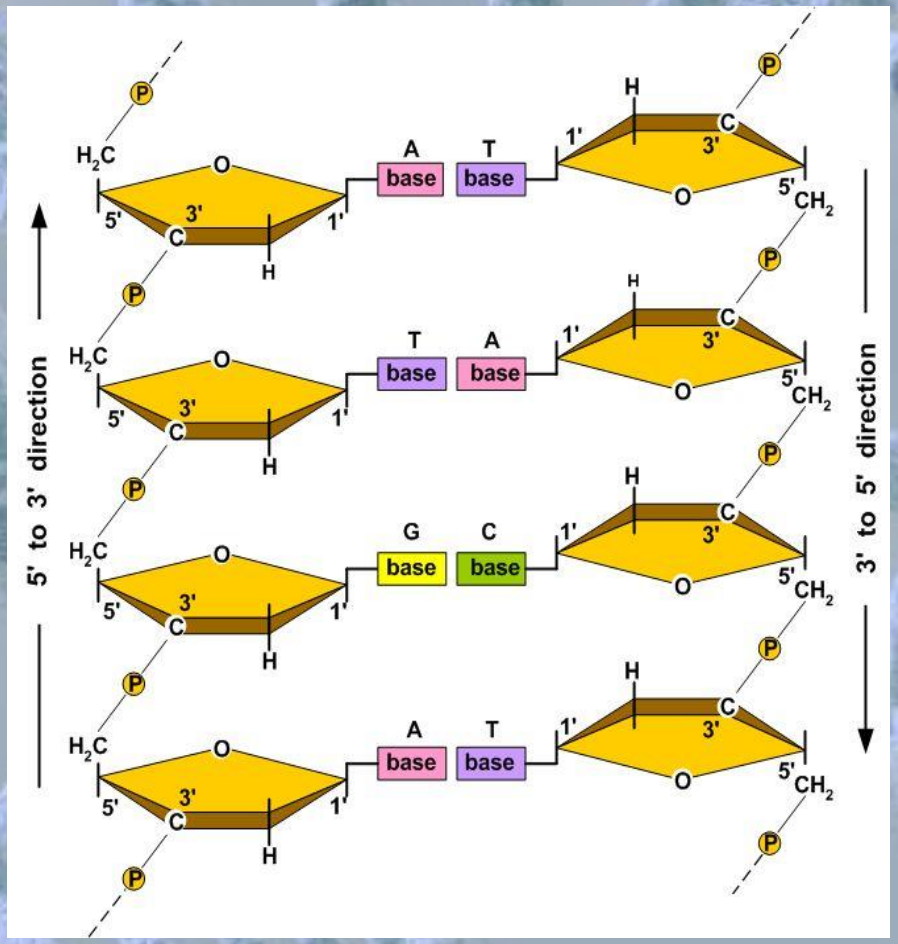
Charge Transfer along DNA ???

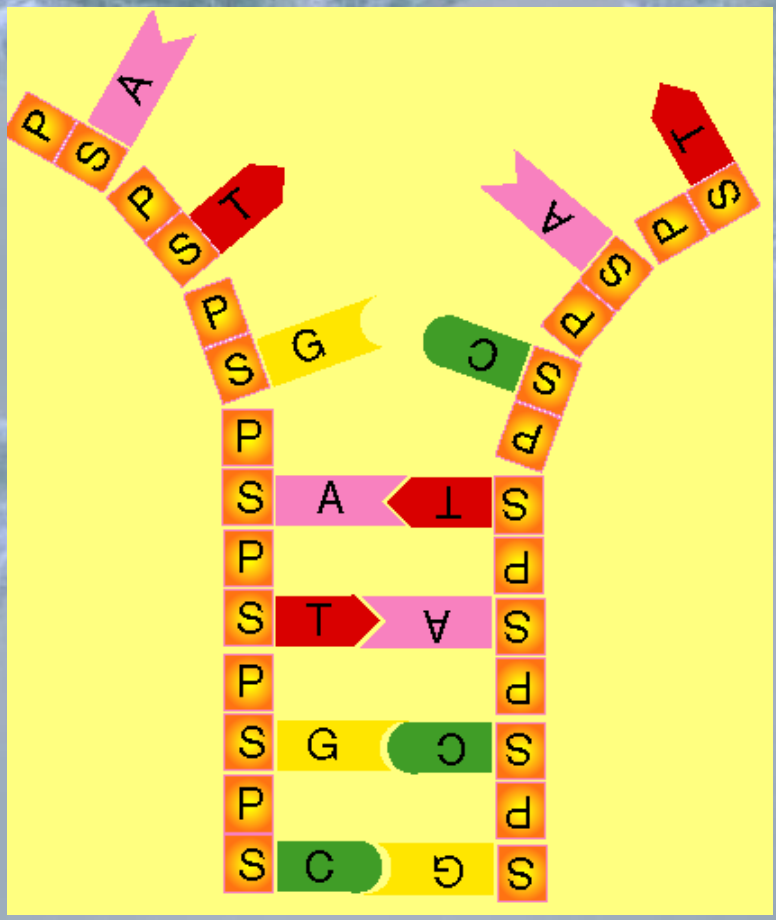
DNA Structure

- Macromolecule

- Stacks of bases: AT/TA or GC/CG connected by hydrogen bonds

- Sugar phosphate backbone





Electric Transport Models

- **Tight-Binding models**
  - 1D Model
  - 2-Channel Model
  - Fishbone Model
  - Ladder Model

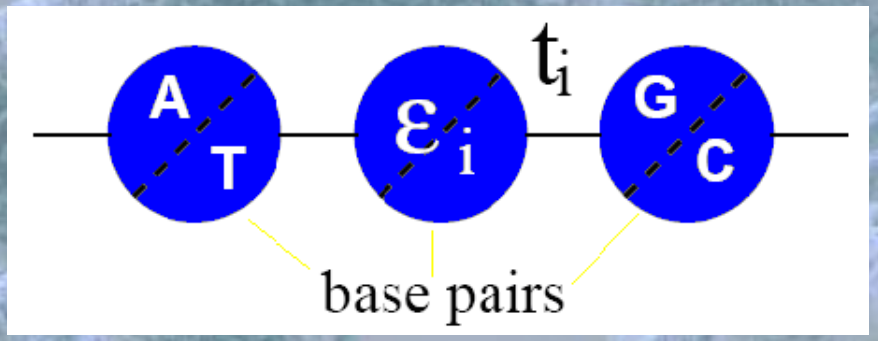
- **Tunneling & Hopping**
  - Superexchange mediated tunneling
  - Incoherent Hopping
  - Thermally Induced Charge Transition

- **Photon-Assisted Polaron-Like Hopping Model**

Tight-binding Models

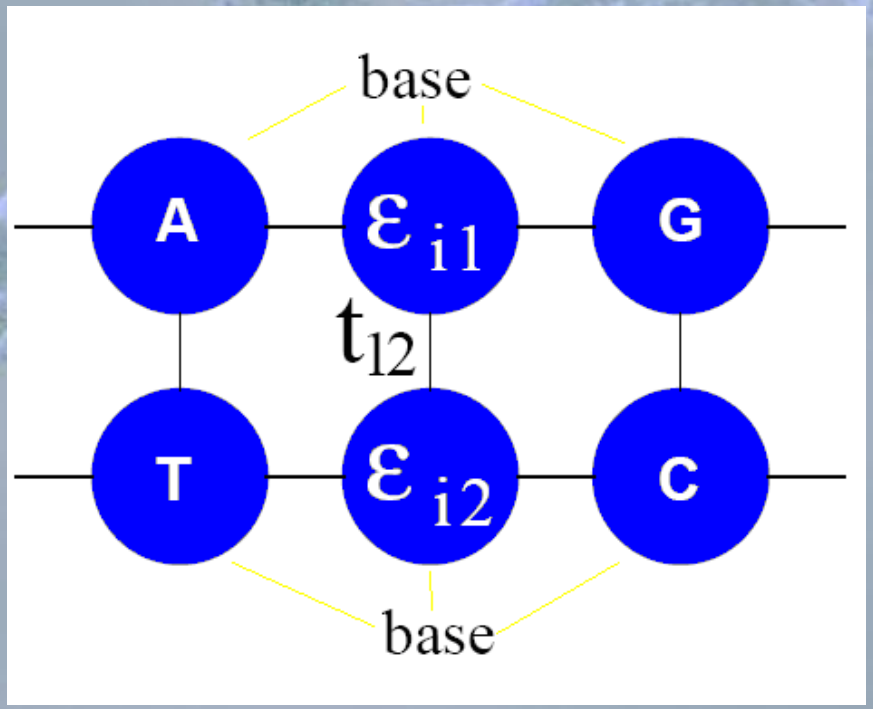
- **1D Model** →

- Oversimplification
- 1 Site = 1 Base pair
- Hopping amplitudes
- Loses polarity (GC≠CG)



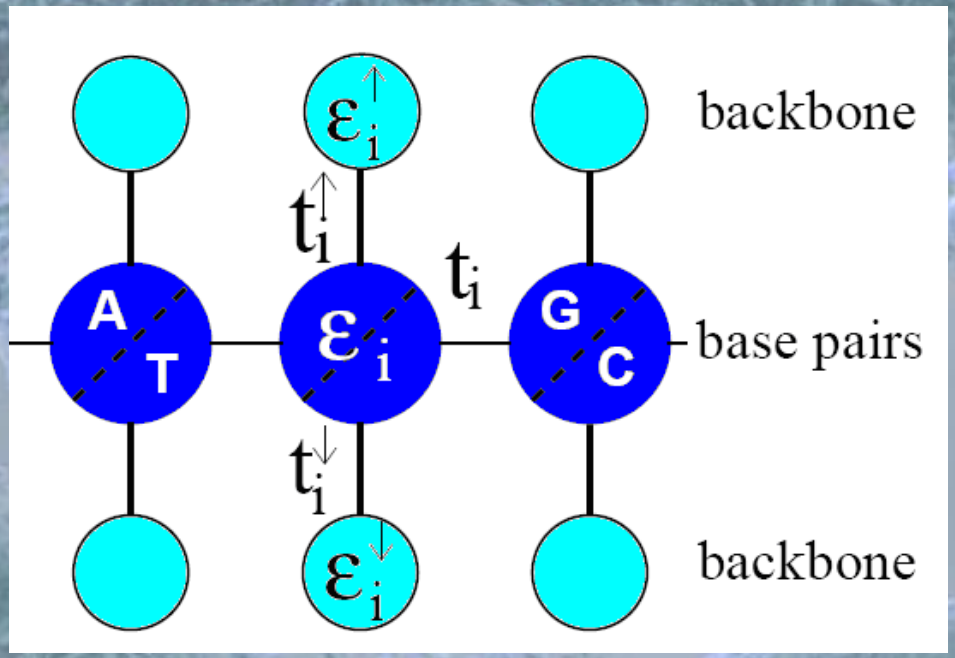
- **2-Channel Model** →

- Each base = independent site
- Hydrogen bonding = additional hopping
- Ignore backbone effects

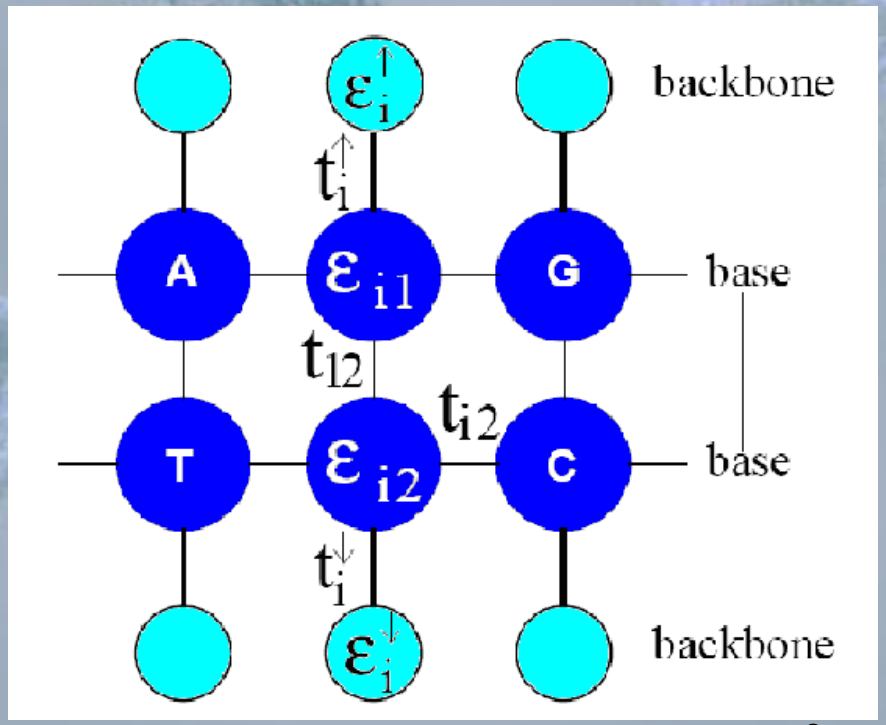


Tight-binding Models

- **Fishbone Model**



- **Ladder Model**

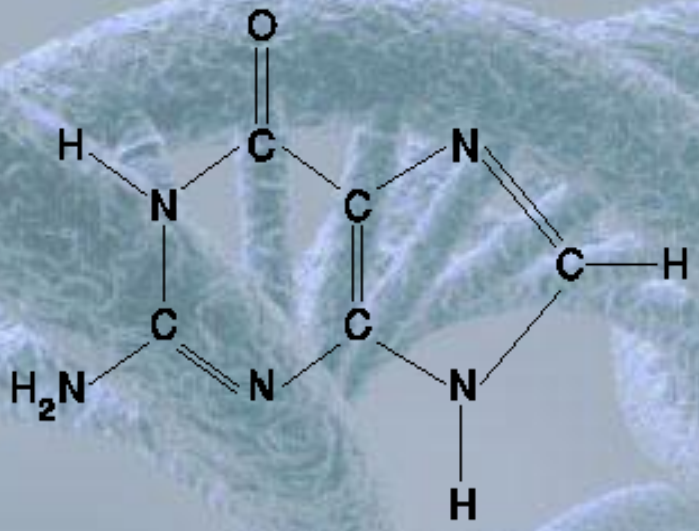


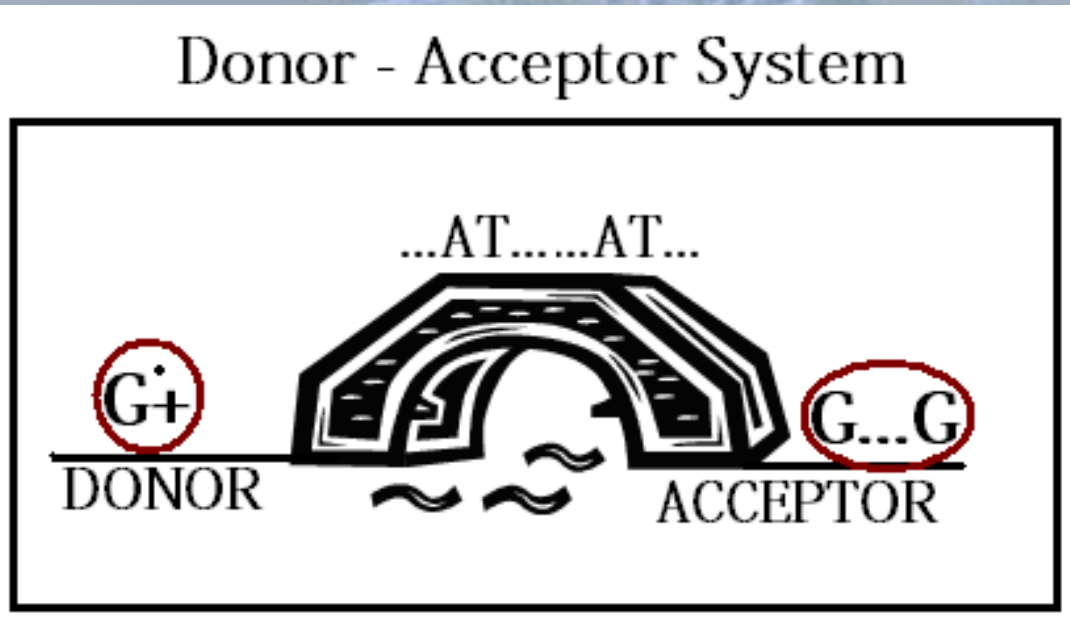
Hopping and Tunneling

- **Guanine (G) – lowest ionization energy**

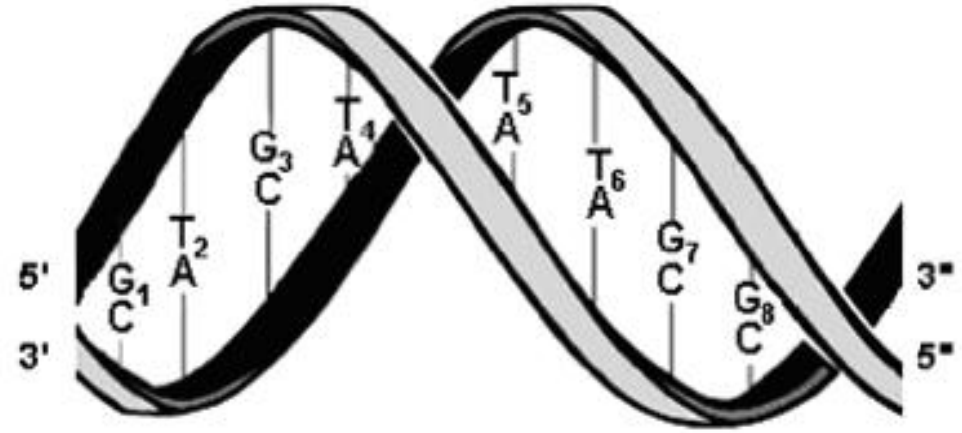
→most easily oxidized nucleobase

- **Radical hole formed!**
- **Hole travels along DNA until it reaches another guanine base**
- **Forms multiple G…G –site**
- **Ionizations energy hierarchy: G…G<G<A<C<T**

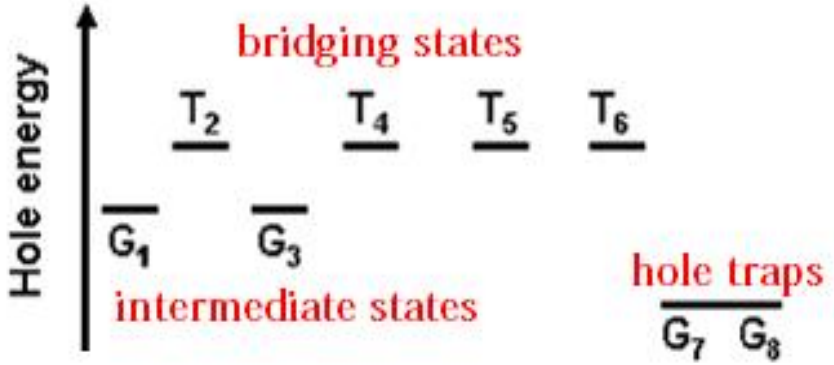




Hopping and Tunneling



- **Group 1: Hole Traps**
  - Lowest energy
  - G-agglutination into multiple G…G unit

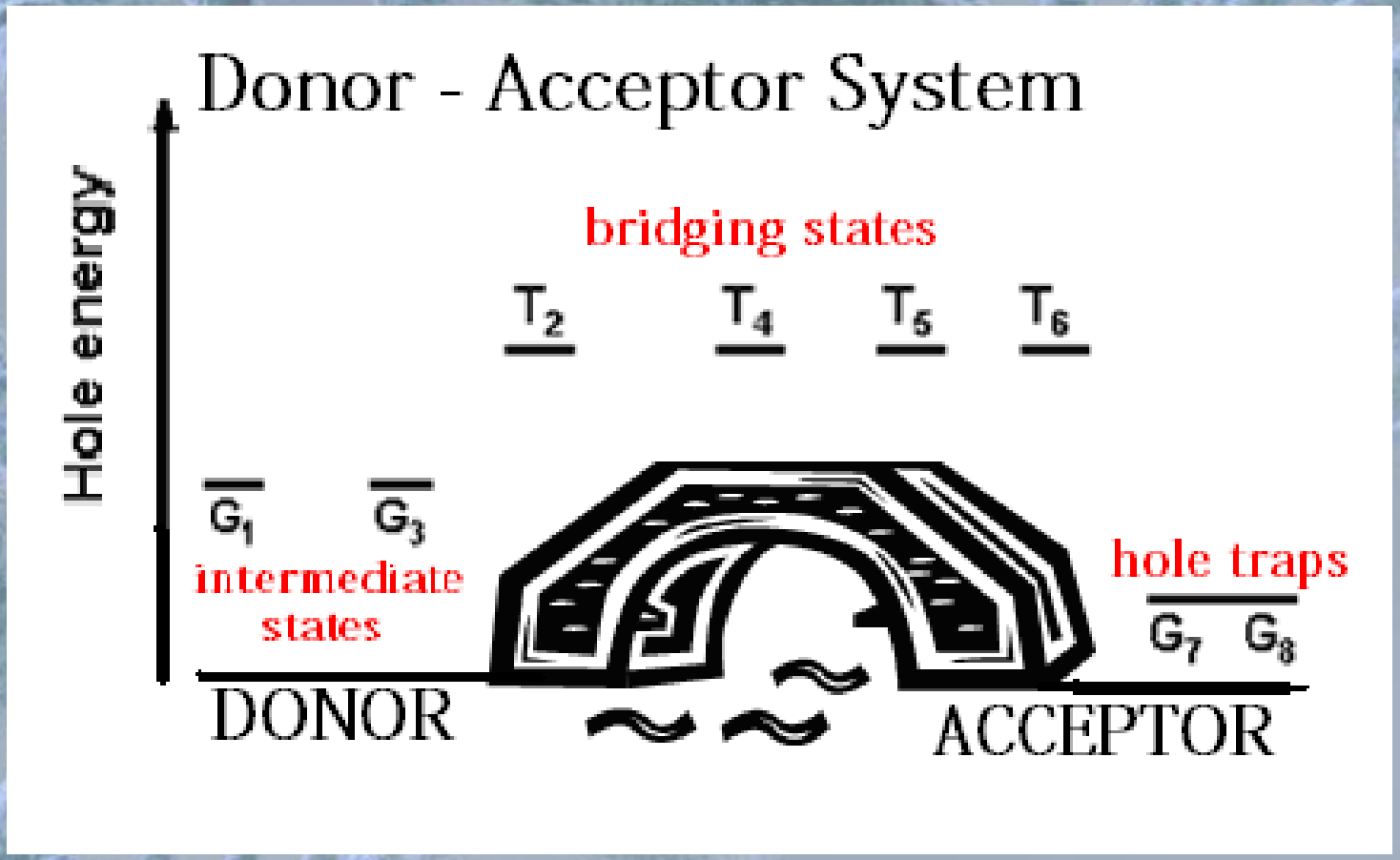


- **Group 2: Intermediate States**
  - Intermediate energy
  - Individual G bases

- **Group 3: Bridging States**
  - Highest energy
  - A, T, C - bases

Hopping and Tunneling

- **How to cross the bridge (higher energy)???**



Hopping and Tunneling

- *Big energy difference between intermediate states and donor*

➔ **Superexchange Tunneling**

- **Single step**
- **No chemical intermediates**
- **Transport rate decreases exponentially**

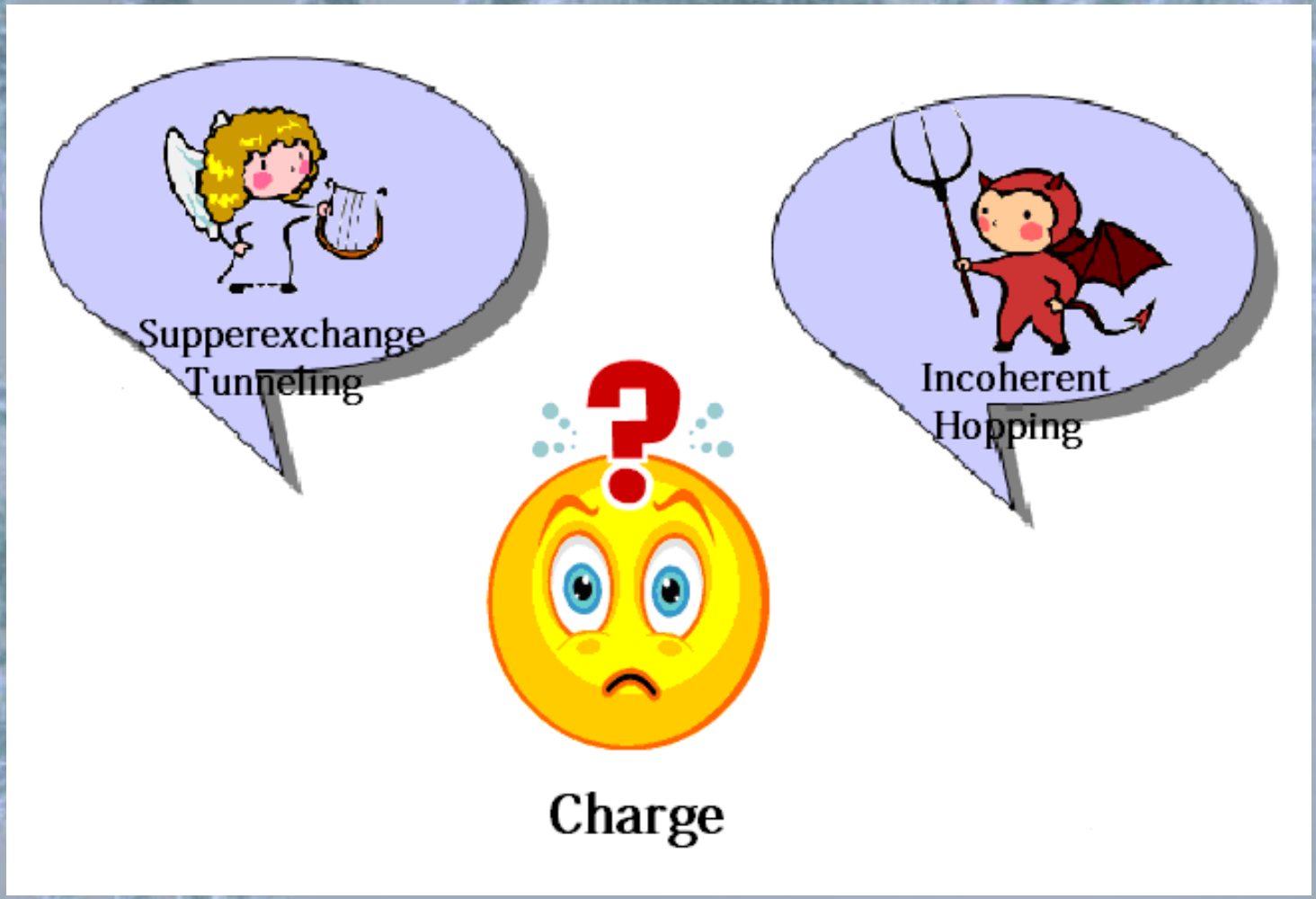
- *Small energy difference between intermediate states and donor*

➔ **Incoherent Hopping**

- **Multistep**
- **Intermediate states = Stepping stones**
- **Chemical intermediates : G+- radical**
- **Transport rate decreases linearly**

(2) Tunneling and Hopping

- Why is the charge not confused which way to go???



Tunneling and Hopping

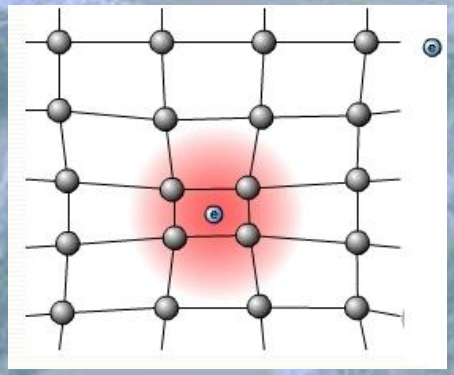
No contradiction! Processes are coupled together!

Transport Mechanism:

- *Short Steps*:
  - **Superexchange Tunneling**
- *Long Steps*:
  - **Thermally induced transition**
  - **Hopping**

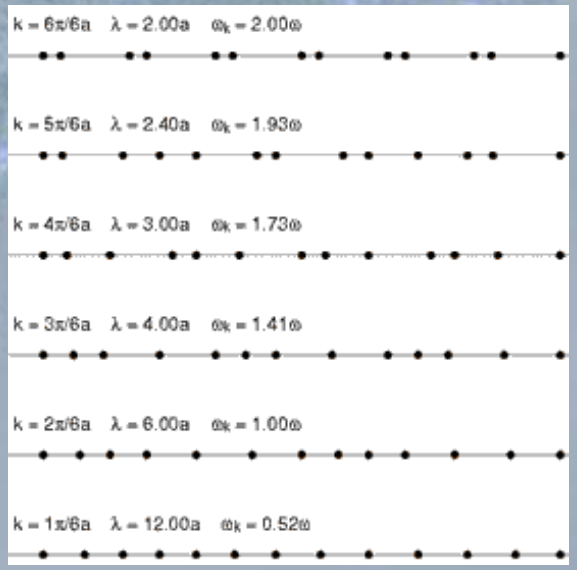
Phonon-Assisted Polaron-Like Hopping Model

- **Polaron** = "radical ion self-trapped by structural distortion of its containing medium", i.e. a part of the DNA where a base radical hole has been surrounded and therefore stabilized by structural changes



- **Electron deficiency** → **Adjustment** in the DNA structure necessary

- **Polaron-like distortion** – combination of structural changes
- Tunneling & hopping
- **Thermal motion** of the bases in/around structural disorder = reason why join/leave polaron → **Phonon-assisted hopping**



Environmental Dependence

- Environment – crucial impact on structural, chemical and therefore electrical properties

- Electrical properties demonstrate conditional dependence on:

- Temperature
- Type of DNA
- Molecular Distance
- Integrity of Intervening Base Pair Stack
- Contact Effect

HARD TO QUANTIFY!!!

Possible Applications

- Biology, Physics, Nanotechnology, Molecular Engineering…
- Correspondence between charge transport (CT) and Carcinogenesis
- Electronic sequencing
- Molecular electronics
- DNA engineering

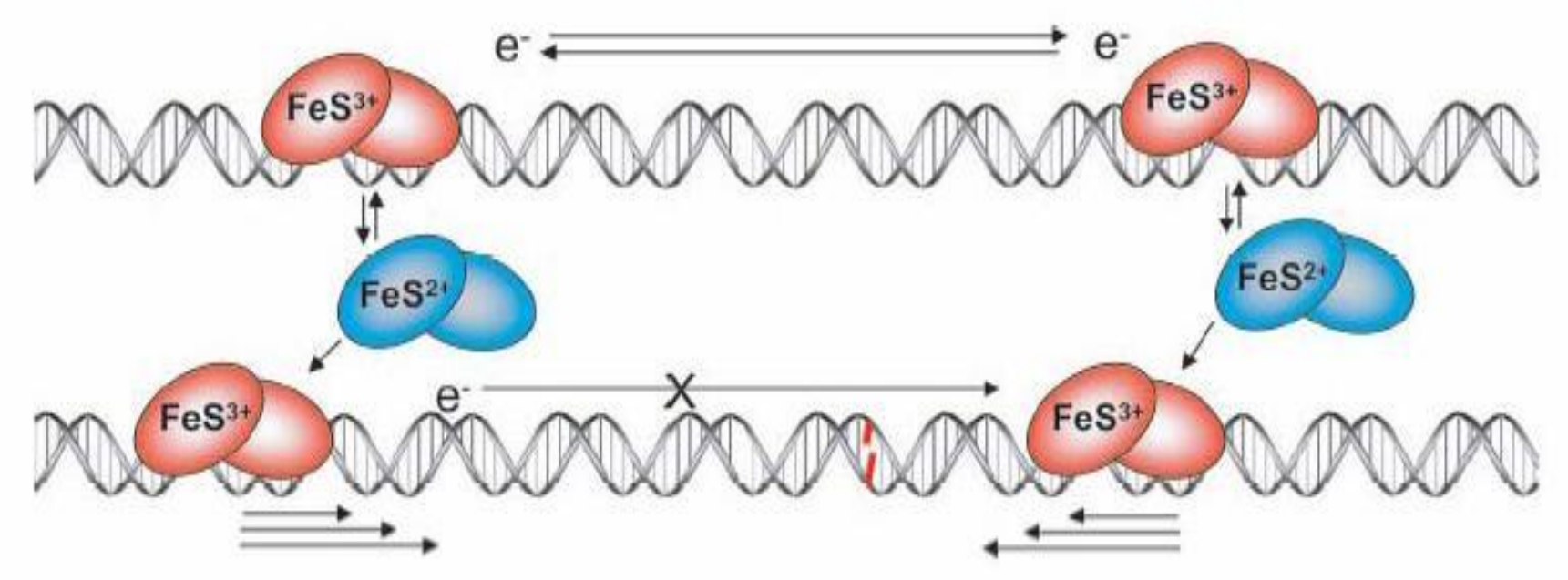
Carcinogenesis

- **CT as an indicator distinguishing between pathogenic and non-pathogenic**

Hypothesis:

- **Small CT changes → cancerous mutations**
- **Big CT changes → non-cancerous mutations**

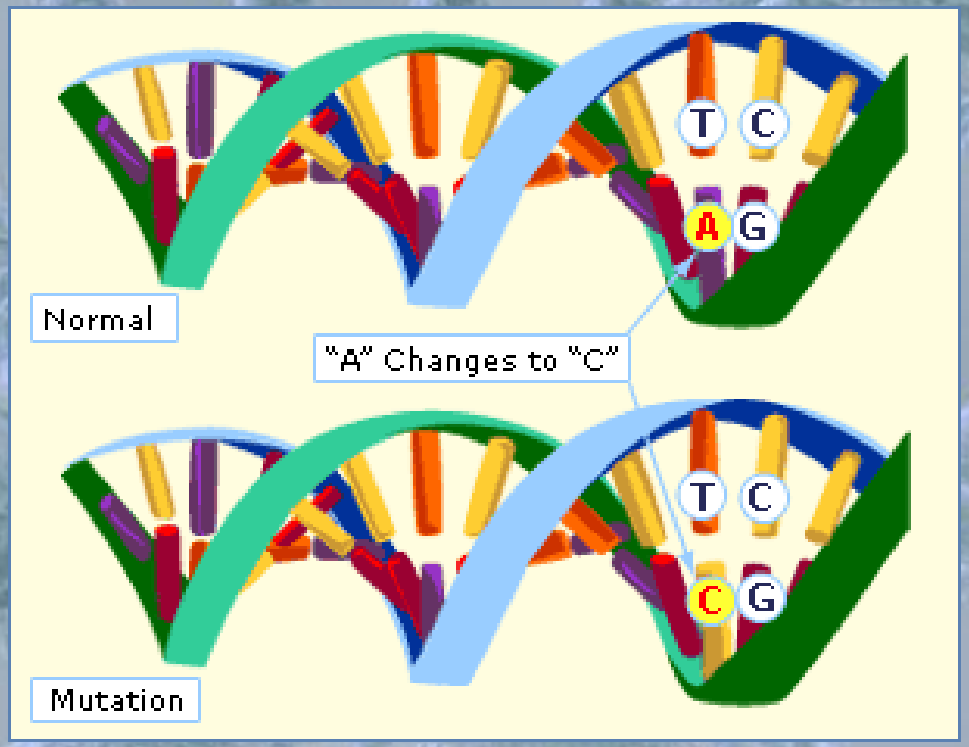
Carcinogenesis



- **BER (base excision repair) enzymes – use CT inhibition to locate lesions or mismatches**
- **Examples: Endonuclease III & MutY**
- **Small changes in CT –more likely to be missed by damage repair enzymes**

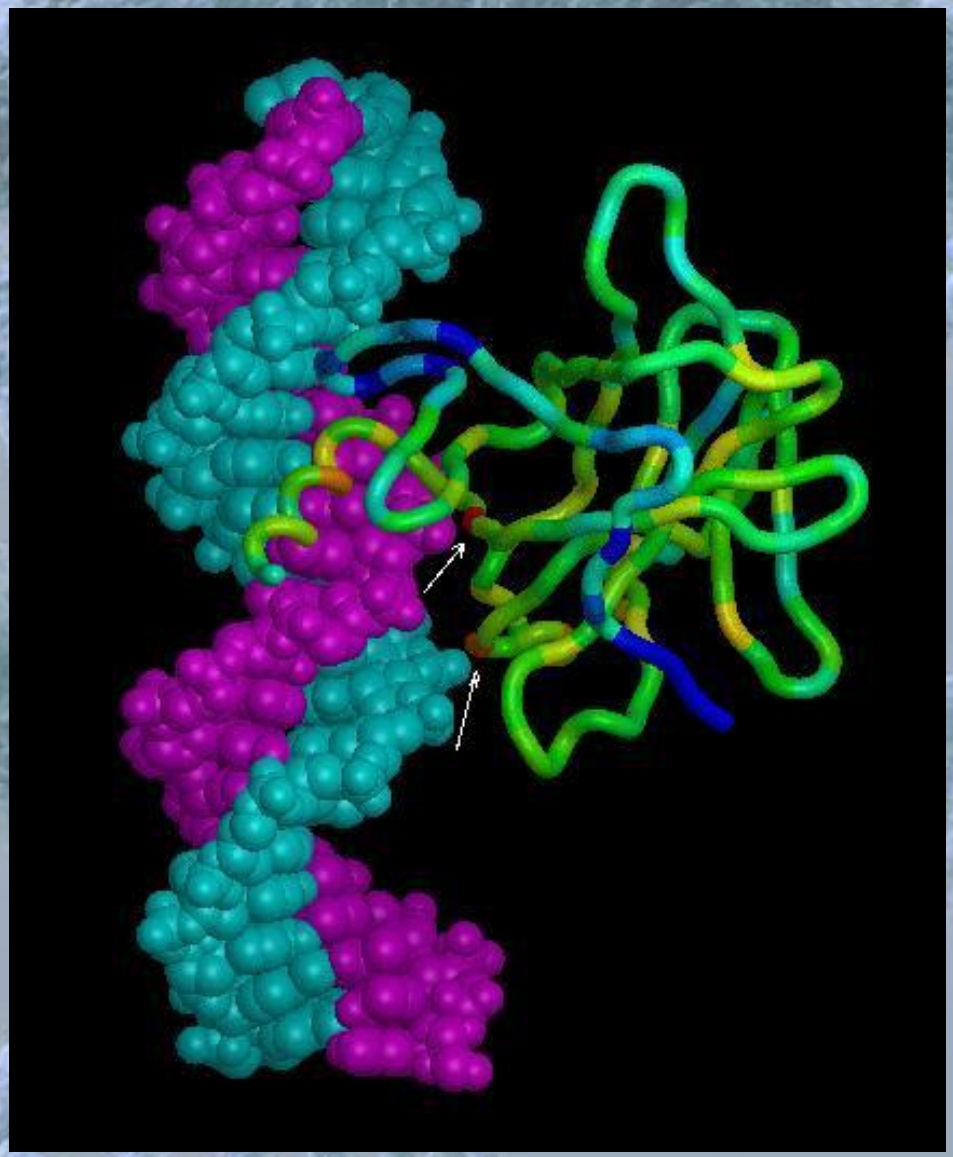
Carcinogenesis

- **Point mutation** : **one base pair substitutes another**



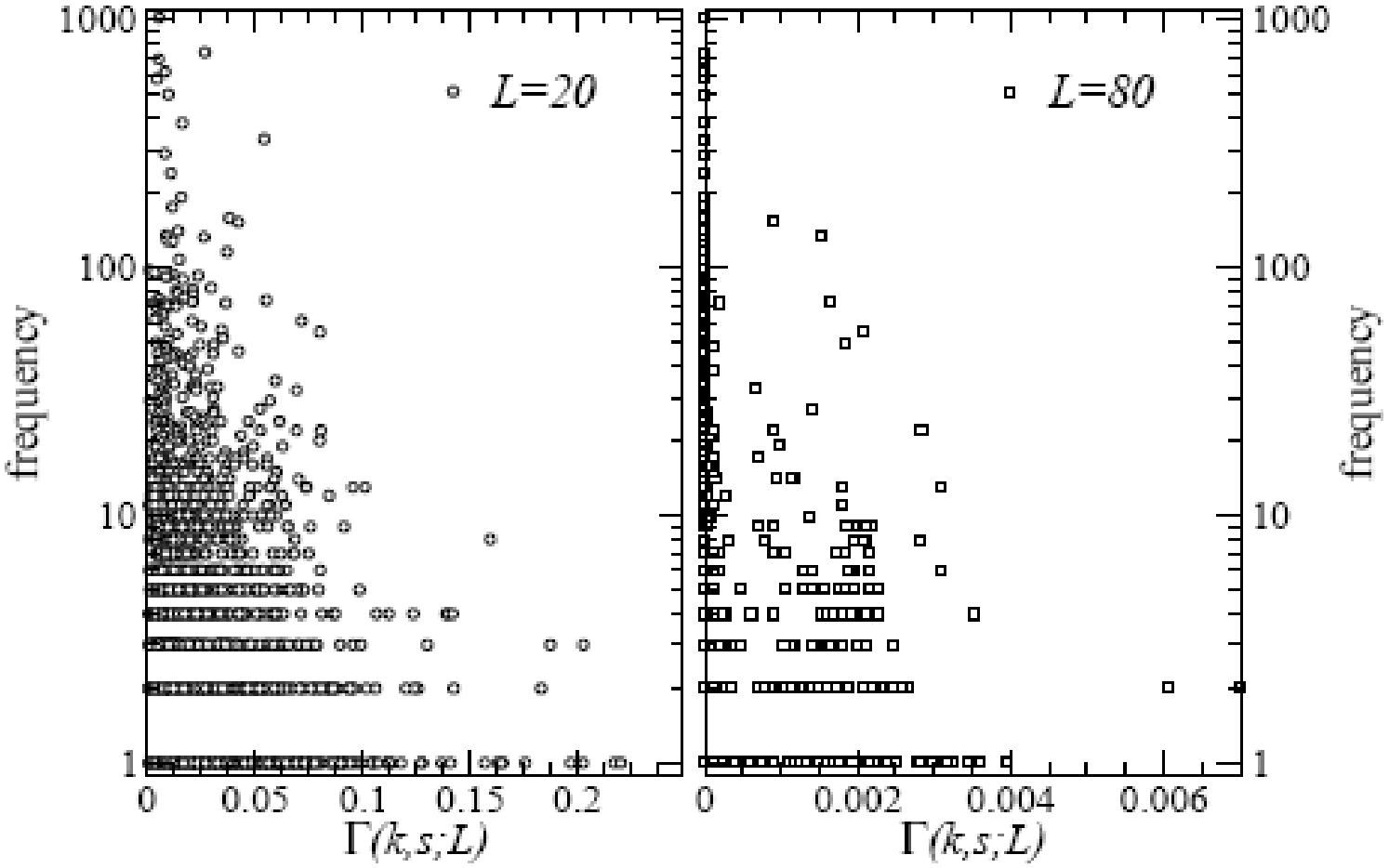
- **"Hotspots"** : **positions where mutations occur more frequently**

Carcinogenesis p53



- "Guardian of the genome"
- Related to >50% of human cancer
- Encodes TP53 protein – suppresses tumor development

Carcinogenesis



Average effect of a mutation versus occurrence frequency for 2 different values of L;

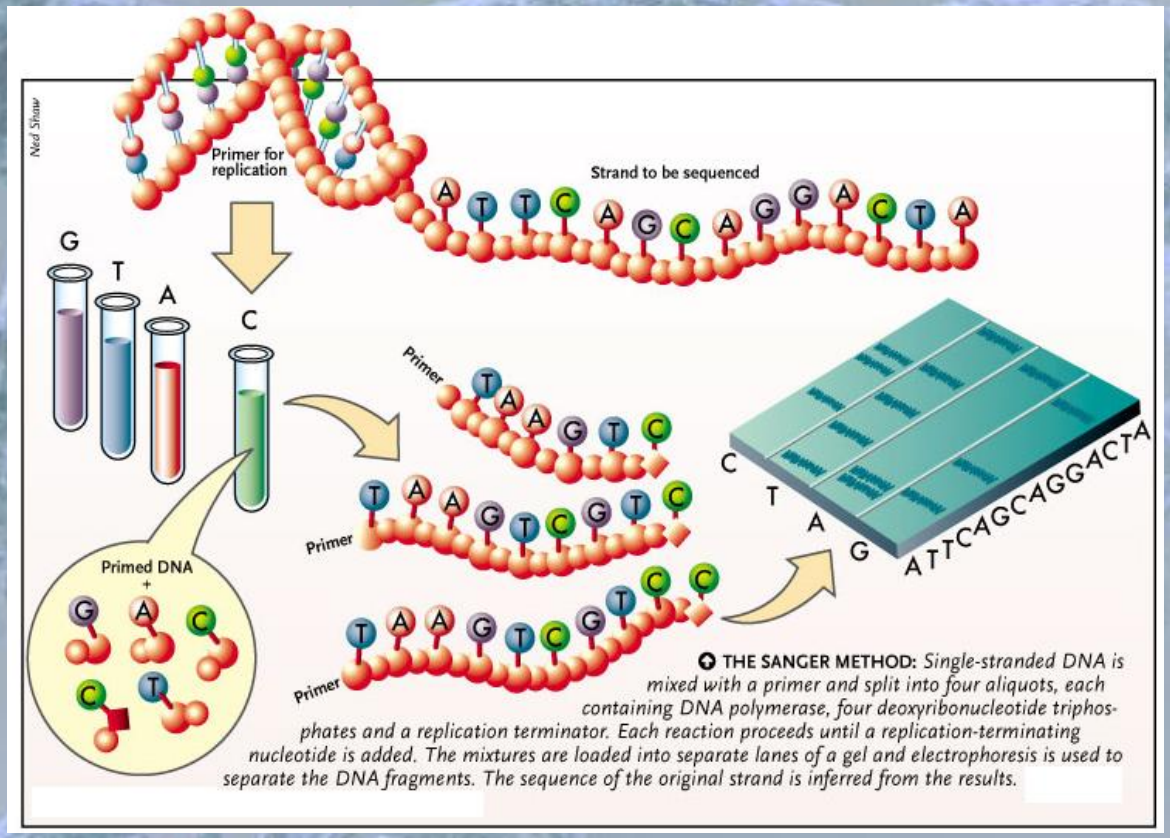
Source: "Point Mutations Effects on Charge Transport Properties of the Tumor- Suppressor Gene p53", C.T. Shih, S. Roche, R.A. Roemer, Phys. Rev. Lett. 100, 018105-4 (2008)

Electronic Sequencing

- **Sanger sequencing method →**

- **Electronic**
- **sequencing:**

- Direct
- Very quick
- Detection of unique transverse electronic signatures of DNA bases

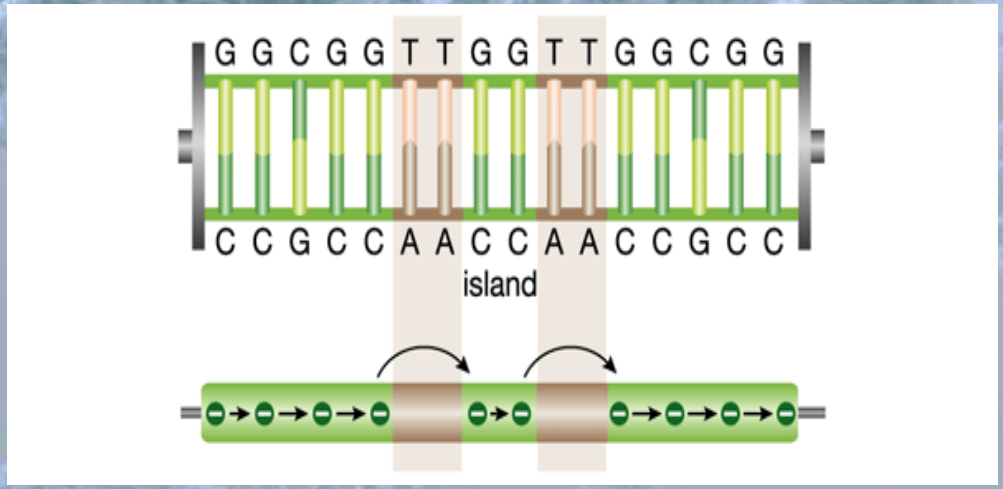


- *"Transverse Electronic Signature of DNA for Electronic Sequencing", M.Xu, R.G. Endres, Y.Arakawa*

Molecular Electronics

- **Innovative molecular devices**
- **Hybrid Technology:**

DNA-based resonant tunneling diode
("DNA electronics", V.Bhalla, R.Bajpai, L.Bharadwaj, Nature.com)

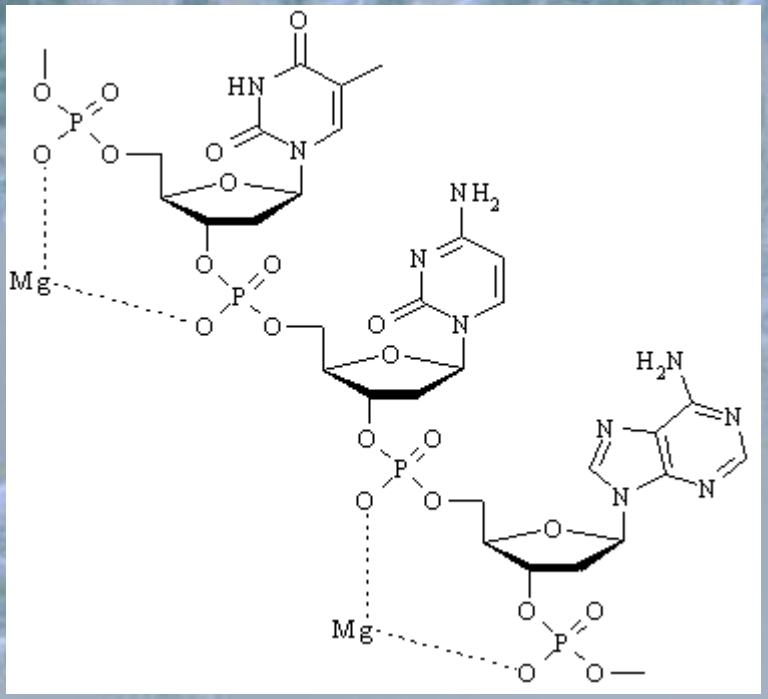


- **molecular glue**
- **Fuel for molecular engines**
- **"prototype field-effect transistor"**

- "The beauty of DNA electronics lies in the fact that it uses techniques of genetic engineering that nature has perfected under harsh conditions over billions of years"

DNA Engineering

- **Modifying** conductivity
- **Substituting** amino photon of each base pair with a **metal ion**



- **M-DNA** → Fast **electron transfer**

Conclusion

- DNA could serve as a **wire, switch, transistor** or **rectifier**

→Broad applications in **molecular electronics**

- Charge transport as a promising indicator of **carcinogenesis**

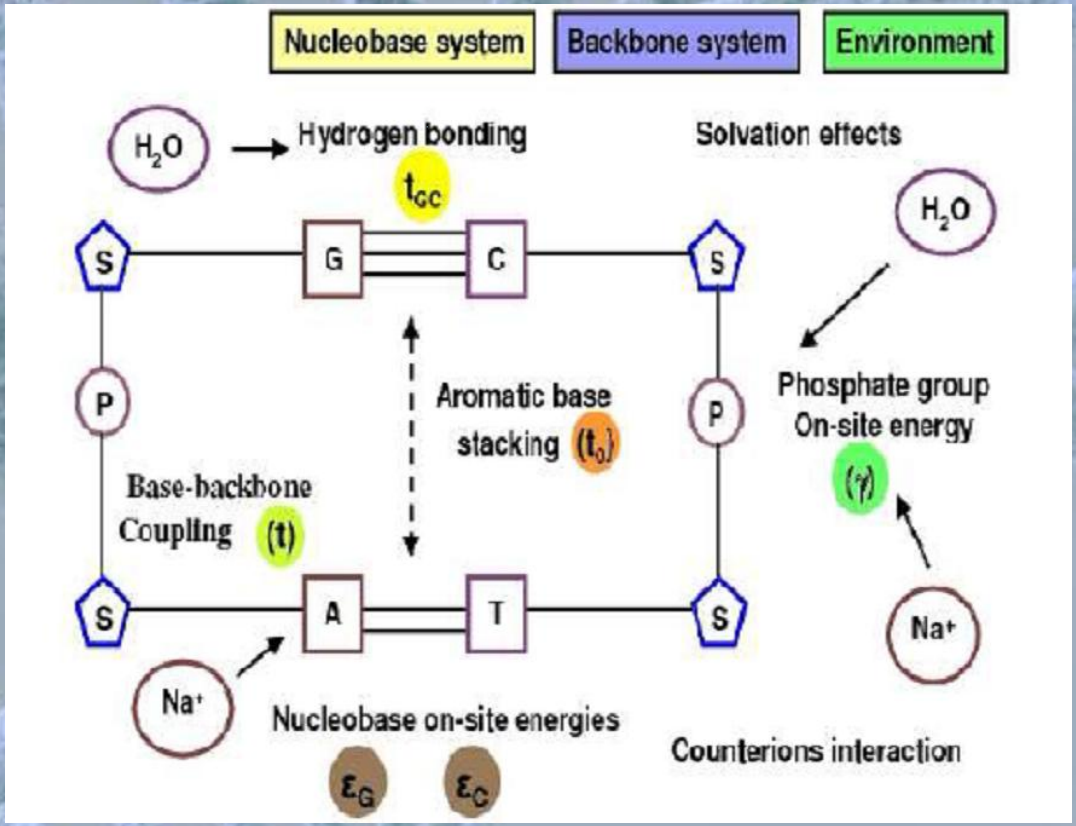
→**Practical** and **theoretical** motivation behind investigating the electrical properties of DNA

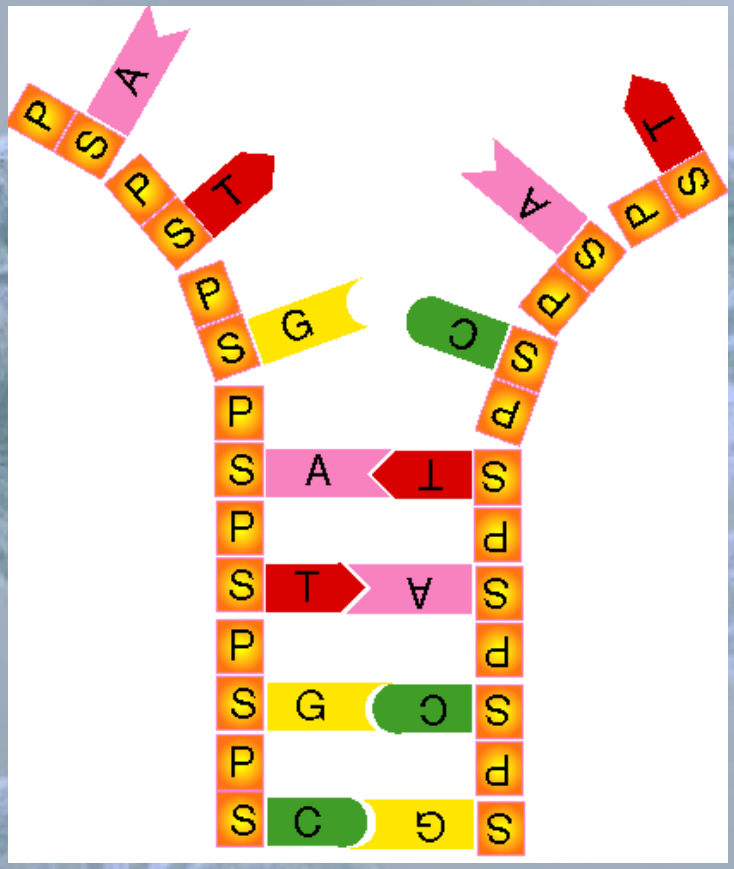
→Found the **theoretical tools**, need to outline the boundaries in terms of conditionality

→More **experimental consistency** necessary

→**Science is one!**

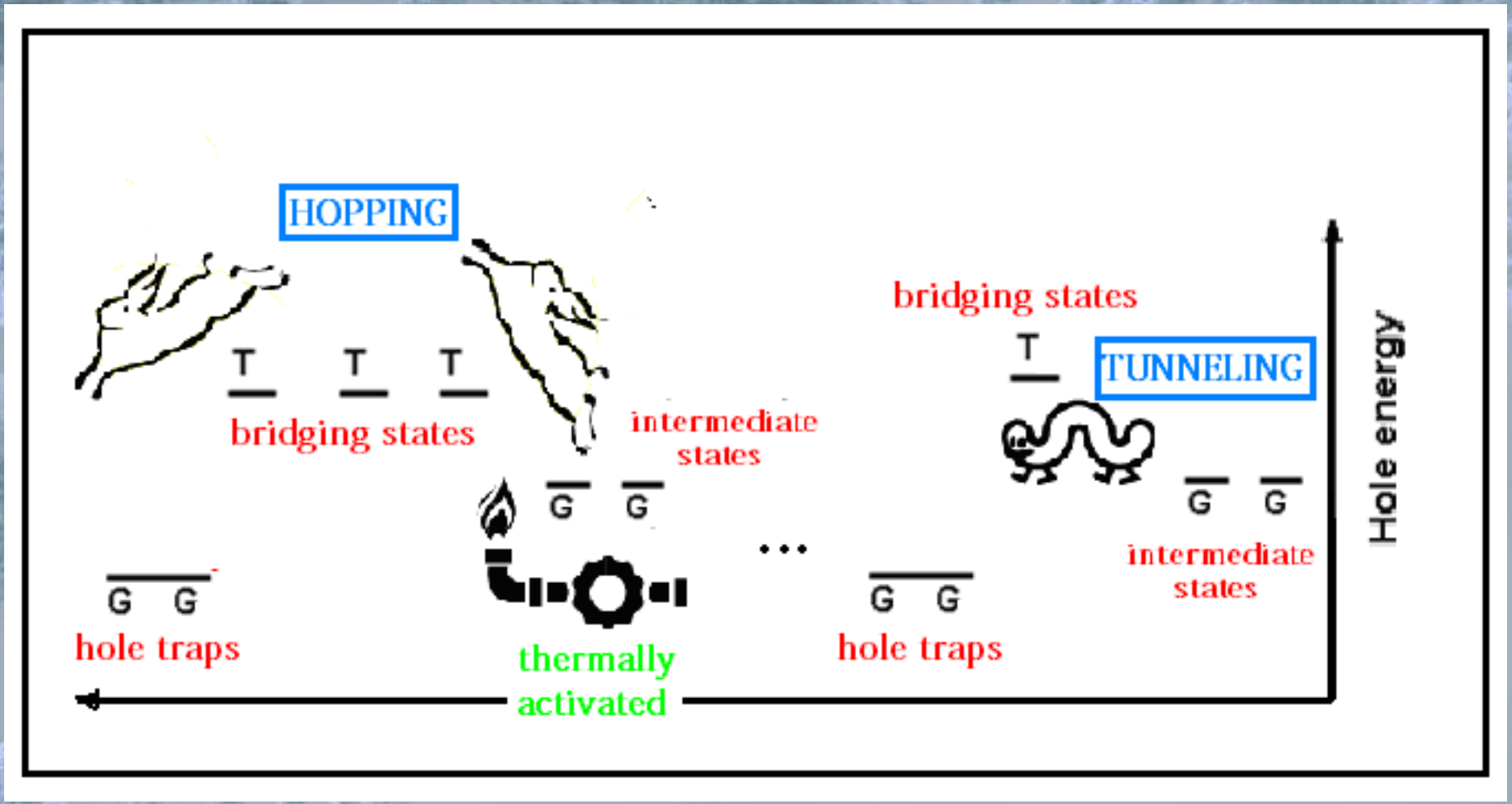
- **Electronic Energetics of DNA**



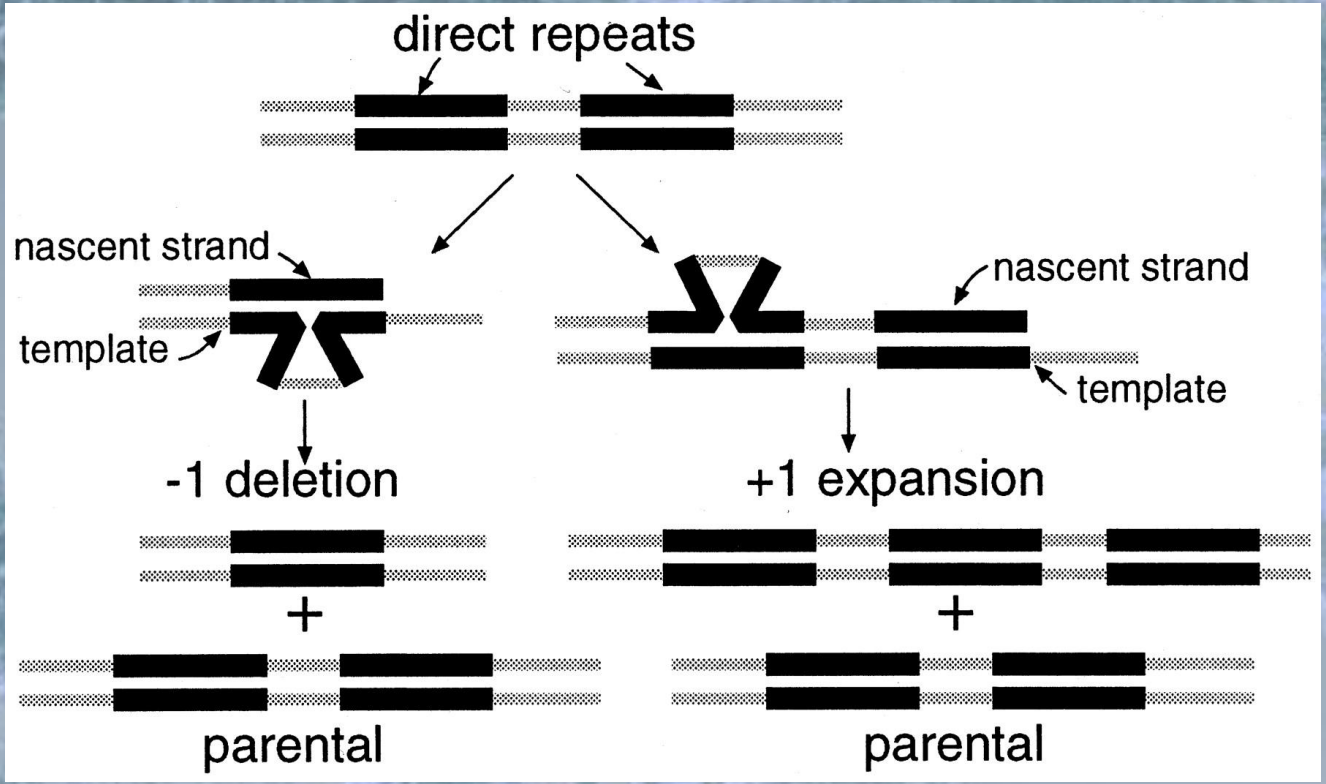


- **Recognition Process**
- **Self-Assembly**

(2) Tunneling and Hopping



Carcinogenesis



- Tumor **suppressors** & cancer associated genes responsible for **regulation** and **proliferation**
- **Disfunctioned** → abnormalities : **misalignment** and CT **inhibition**

(1) Carcinogenesis

C→G; C→A : Non – cancerous

C→T : Cancerous

s	L	1L	FB	2L	LM
$C \rightarrow A$	20	23.1	8.46	2.24	**0.43**
$C \rightarrow G$	20	37.6	**0.73**	0.83	0.57
$C \rightarrow T$	20	**5.63**	1.08	**0.34**	0.66
$C \rightarrow A$	30	15.7	54.8	96.2	1.76
$C \rightarrow G$	30	21.4	0.55	2.75	0.40
$C \rightarrow T$	30	**9.14**	**0.0006**	**0.39**	**0.15**
$C \rightarrow A$	40	1.16	30.7	31.6	17.7
$C \rightarrow G$	40	2.21	0.72	0.41	0.16
$C \rightarrow T$	40	**0.40**	**0.009**	**0.26**	**0.04**

Energy-avaraged changes in CT properties

Source: "Point Mutations Effects on Charge Transport Properties of the Tumor- Suppressor Gene p53", C.T. Shih, S. Roche, R.A. Roemer, Phys. Rev. Lett. 100, 018105-4 (2008)

Carcinogenesis

Main Points:

- Statistical significance
- Cancerous mutations → smaller CT changes
- Tendency gets stronger for highly cancerous mutations
- Different repair mechanisms based on criteria other than the CT-properties
- Intriguing correlation between the DNA hotspots structure and the DNA damage-repair process!