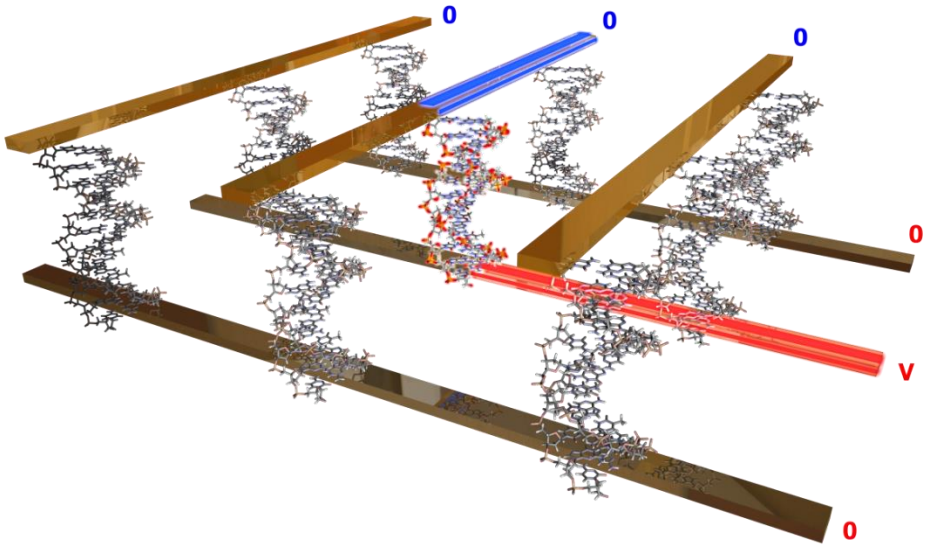
Keldysh Institute of Applied Mathematics

of Russian Academy of Sciences

DNA based nanobioinformatics and nanobioelectronics

V.D. LAKHNO



INFORMATICS

Informatics is the study of computational systems, especially those for data storage and retrieval.

synonymous – computer science, information science, information science, information technologies etc.

(Wikipedia)

Bioinformatics

Bioinformatics – is the field that develops methods and software tools for understanding biological data.

Includes:

- Sequence analysis
- Gene and protein expression
- Analysis of cellular organization
- Structural bioinformatics
- Databases

New direction:

Bioinformatics as informatics on the basis of biocomputer technologies and DNA information storages and nanobioelectronics.

DNA based information technologies. Nanobioelectronics

General problem:

The amount of generated information grows with exponential rate.

Cumulative information volume generated by humanity is about several billion terabytes per year.

Contemporary state:

The density of information store by modern media (magnetic and optical devices: compact disks, hard discs, magnetic tapes) as usual does not exceed 1000 Gb/mm^2.

The low density of information storage leads to the problem storage capacity confinement

The possibility of data losing in length of time.

This request the development of new methods of information storage and handling.

Perspectives to solve the problem:

DNA – memory

DNA – calculations

DNA - computer

DNA is essential digital, L. Adelman

DNA – memory

Modern technology of DNA synthesis and sequenation opens the way to wright on DNA: setup of 64 kilobyte data which contains a book, 11 JPG pictures and Java SCRIPT program (2012), (Church G.M. et al, Science, 2012, v.337, p. 1628)

16 Gigabyte of Wikipedia (2019)

The density of DNA information density storage (billion terabyte) / gram – billion time greater then on modern media (K.Matange, Nature Communications, (2021)12:1358)

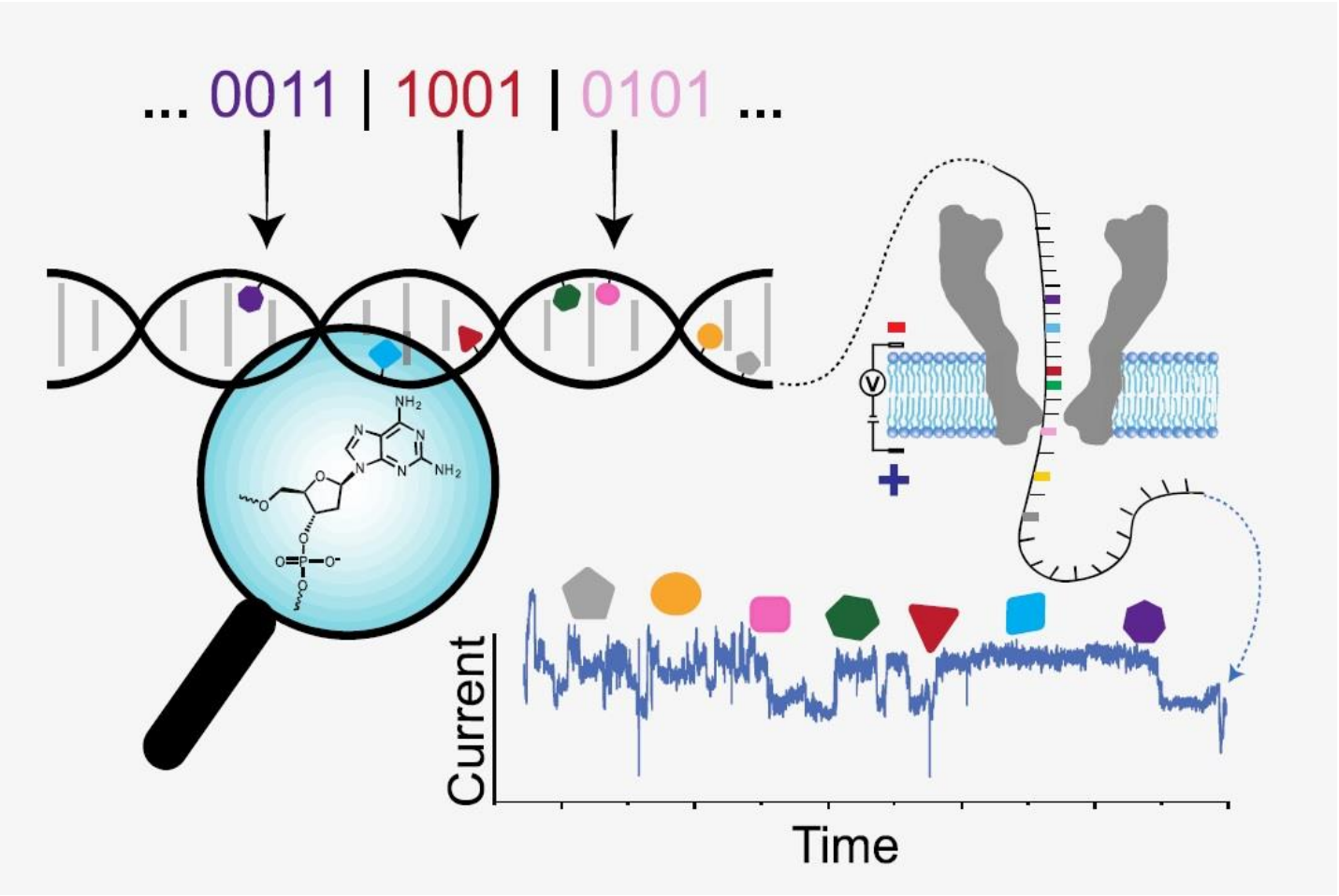
Disadvantages

The rate of information placement on DNA (e.g. the memory) can not compete with modern media. Nevertheless DNA has advantage information density and costs of storage.

(The price of coding: 1000 $ / megabyte, reading 100 $ / megabyte)

Mistakes arising in realization of DNA – memory fall, exchange, replacer, substitution, insets, tandem duplication

DNA - READING



Expanding the Molecular Alphabet of DNA-Based Data Storage Systems with Neural Network Nanopore Readout Processing
S. Kasra Tabatabaei at al, Nano Lett. 2022, 22, 1905−1914

DNA – calculations, DNA – computer

(DNA – cryptography, DNA – stenography)

DNA – computer – calculations proceed using chemical reactions between DNA fragments

Advantages

Polynomial time for solving combinatorial problems is achieved due to parallelism of calculations (a lot of semiltaneouns chemical reactions)

Disadvantages

Voyageur problem – optimal path for graph with 7 nodes (Adelman 1994)

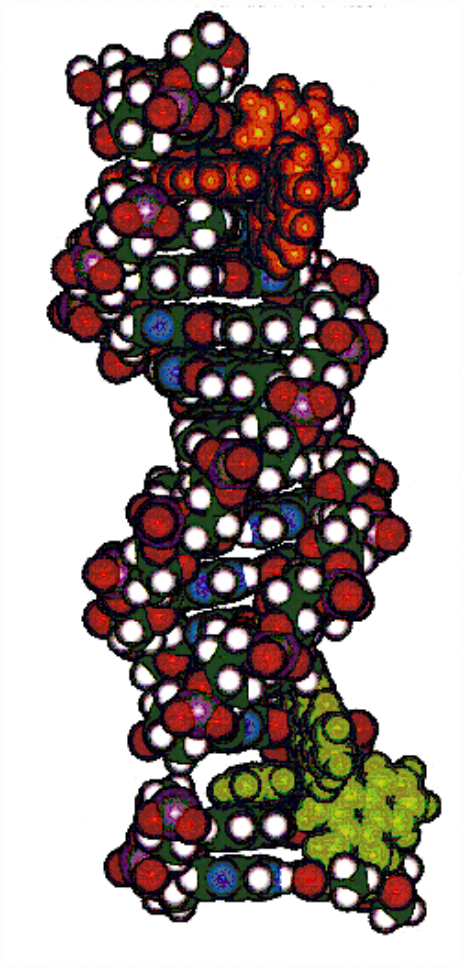
The problem with 200 nodes needs the mass of DNA which exceeds the earth mass

Potential application of DNA in nanobioelectronics

DNA nanowires
DNA nanobiochips
DNA nanomotors
DNA posistors
DNA tunneling diods
DNA transistors
DNA biosensors
DNA quantum computers

V.D. Lakhno, DNA Nanobioelectronics, Int. J. Quant. Chem., 2008;
V.Lakhno, A.Vinnikov, Molecular devices based on DNA, MBB 2021

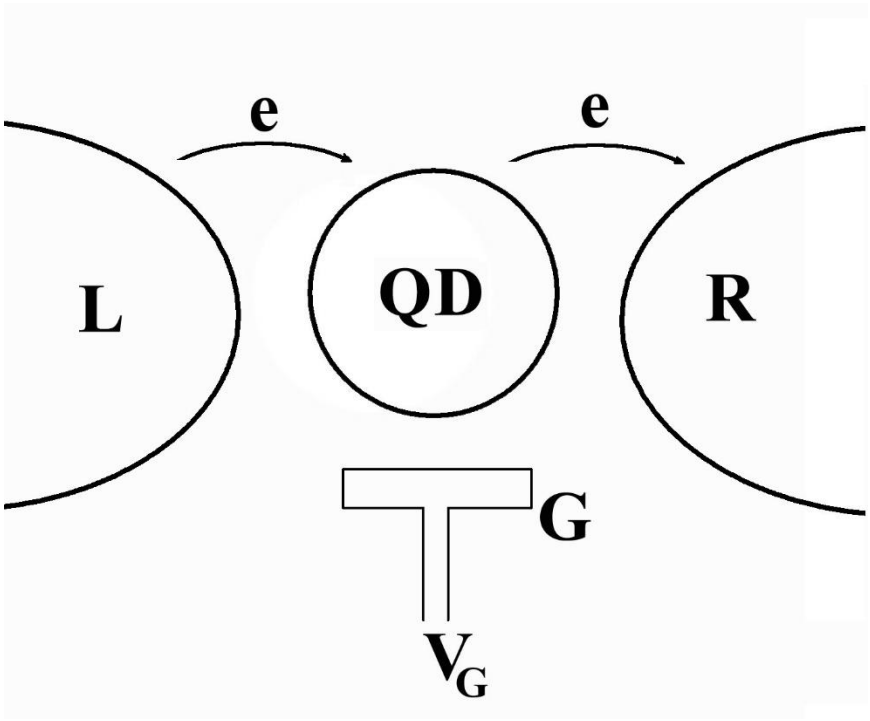
Charge transfer in oligonucleotides



Ruthenium – rhodium molecular complexes are used as donors and acceptors in experiments on electron transfer in DNA.

The donor and the acceptor are linked by a covalent bond to a DNA fragment containing 15 nucleotide pairs.

Nanotransistor

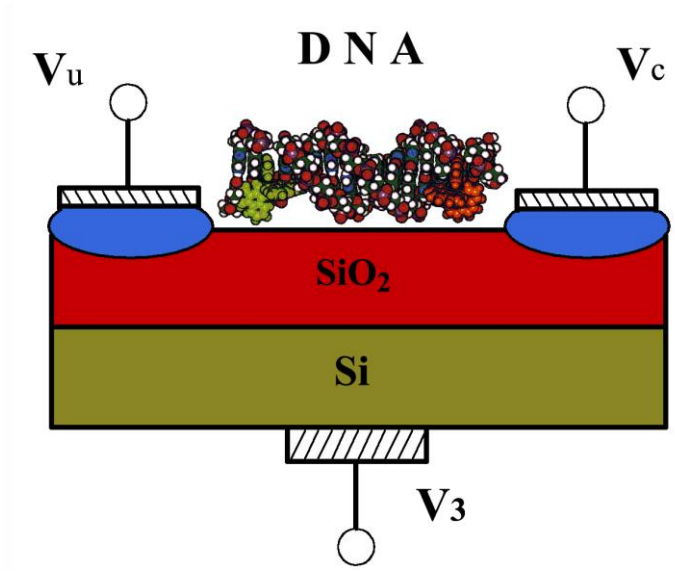


The nanotransistor scheme is shown consisting of quantum dot (QD) connected to electrodes L and R.

G – denotes the gate electrod cannected to the potential $V_{G.}$

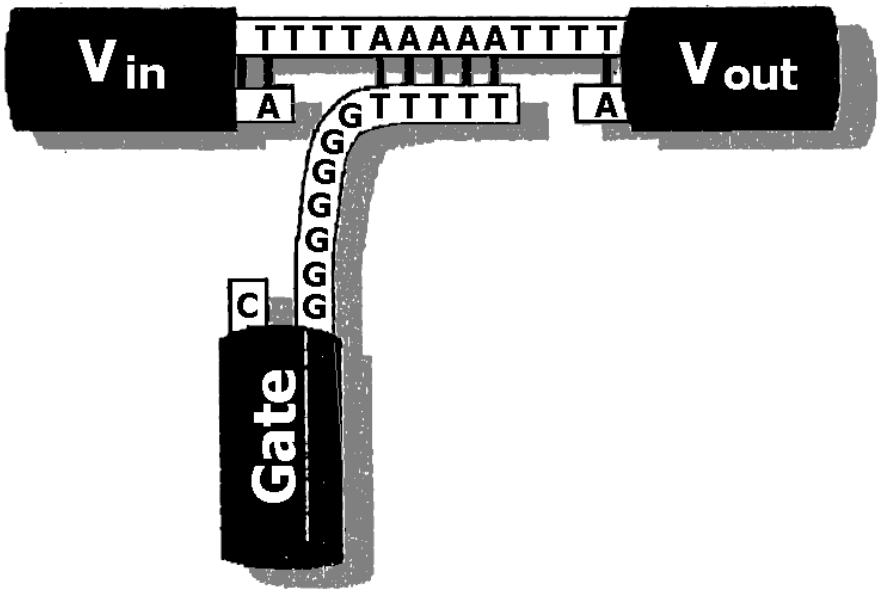
DNA FIELD TRANSISTOR

source **drain**



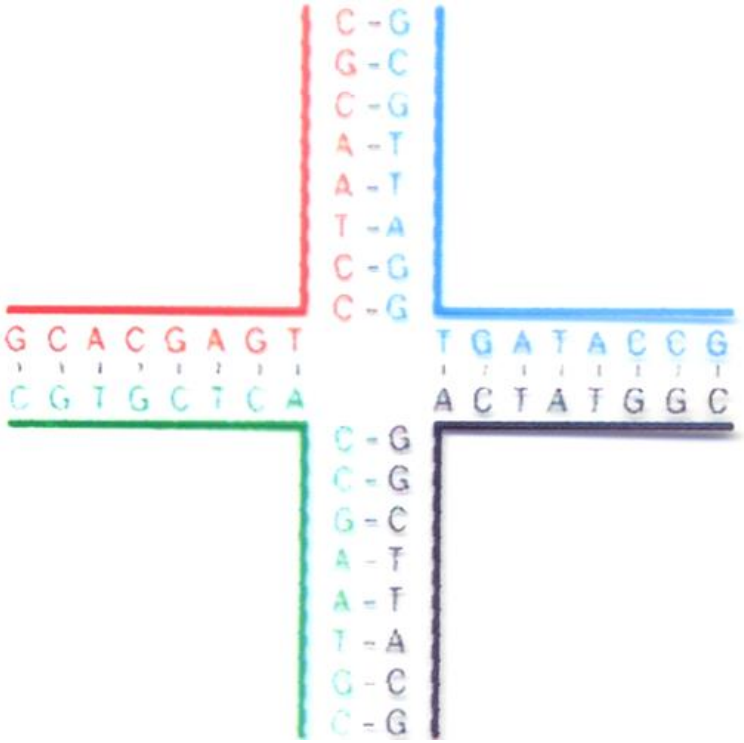
gate

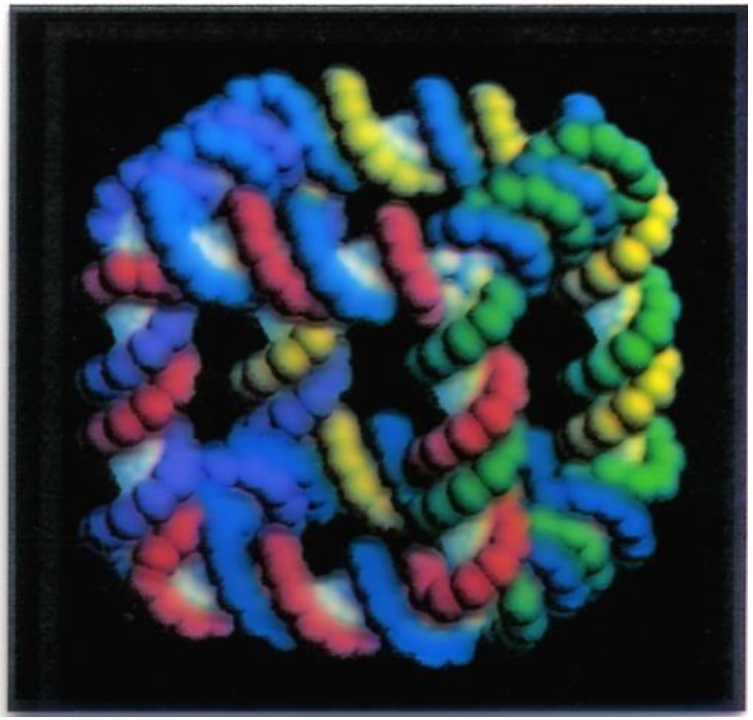
K.-H.Yoo, D.H.Ha, et al, Phys.Rev.Lett., 2001, 87, 198102



E. Ben-Jacob et al, patent, 2007

DNA nanotechnologies

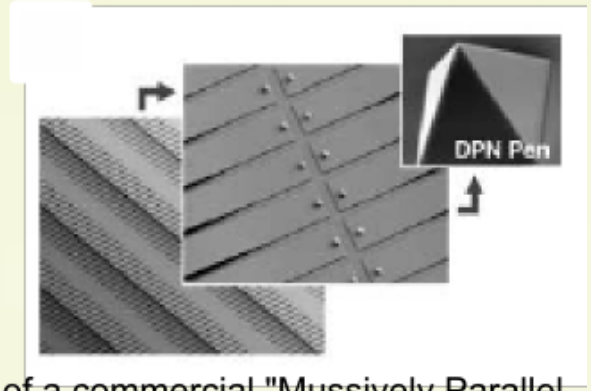




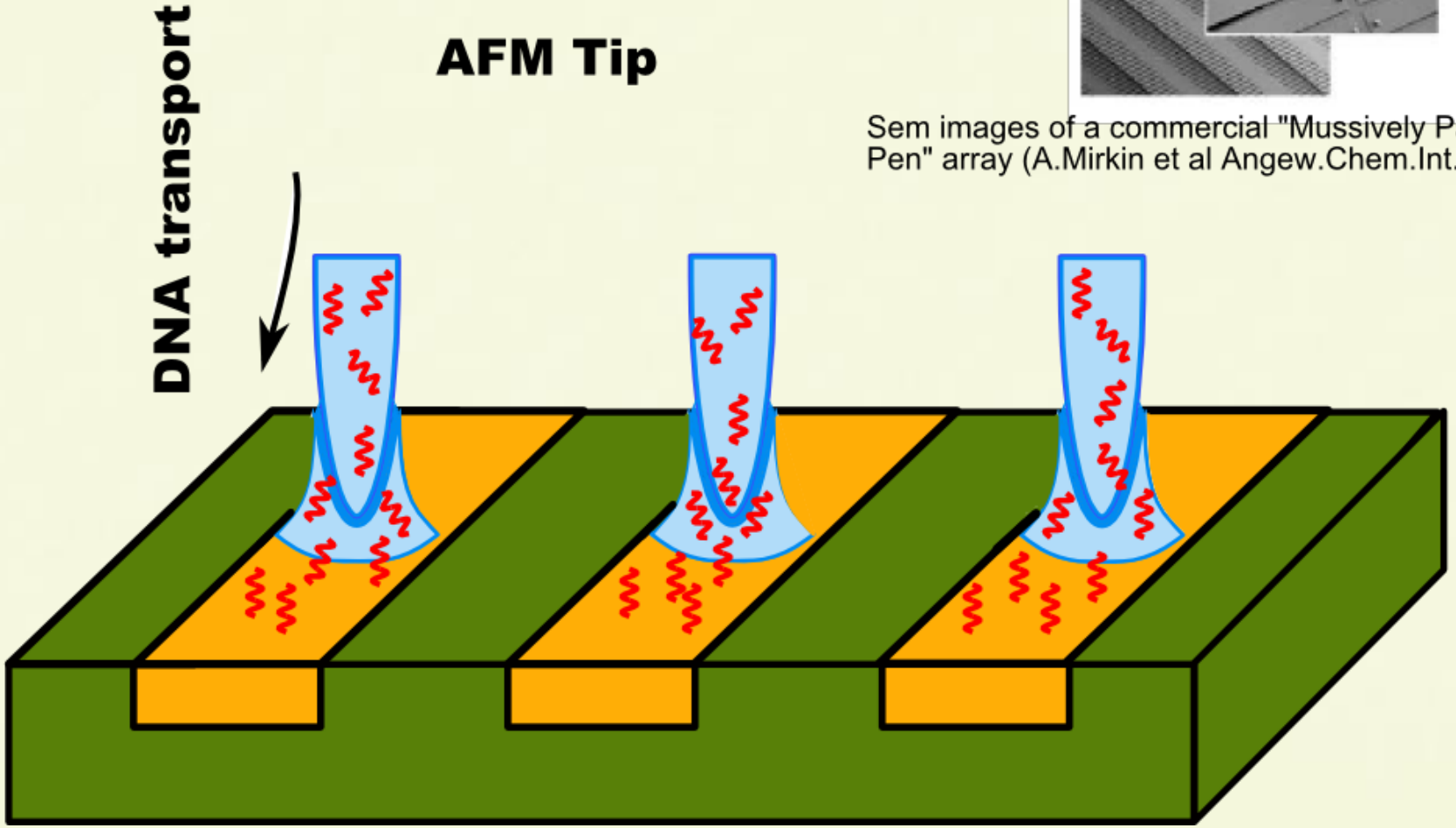
The properties of DNA selfconstruction can be used for design of different structures

(C.Dekker at al., Physics World, 2001)

Dip - Pen Nanolithography



Sem images of a commercial "Mussively Parallel Pen" array (A.Mirkin et al Angew.Chem.Int.,2004)



Single-Molecule Conductance Measurements of Single- and Double-Stranded DNA Oligonucleotides

ChemPhysChem v.7 n.1 pp.94-98

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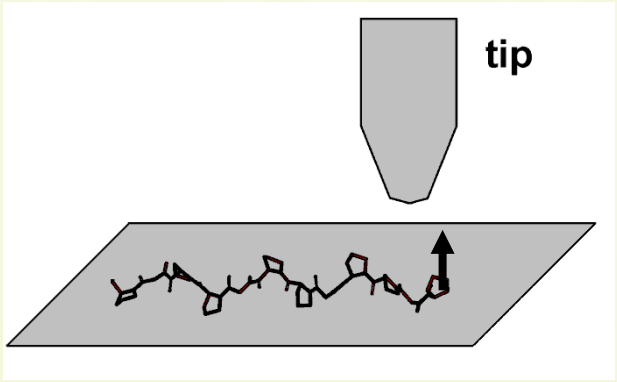
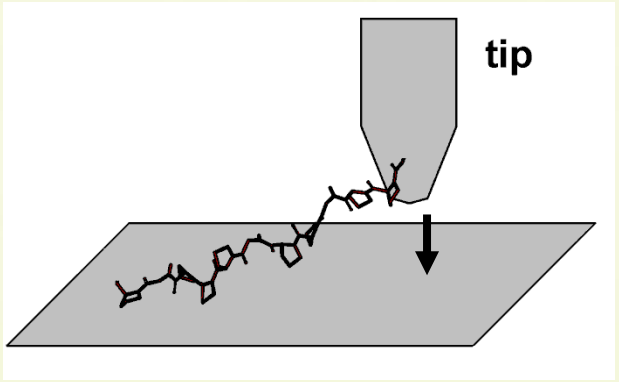
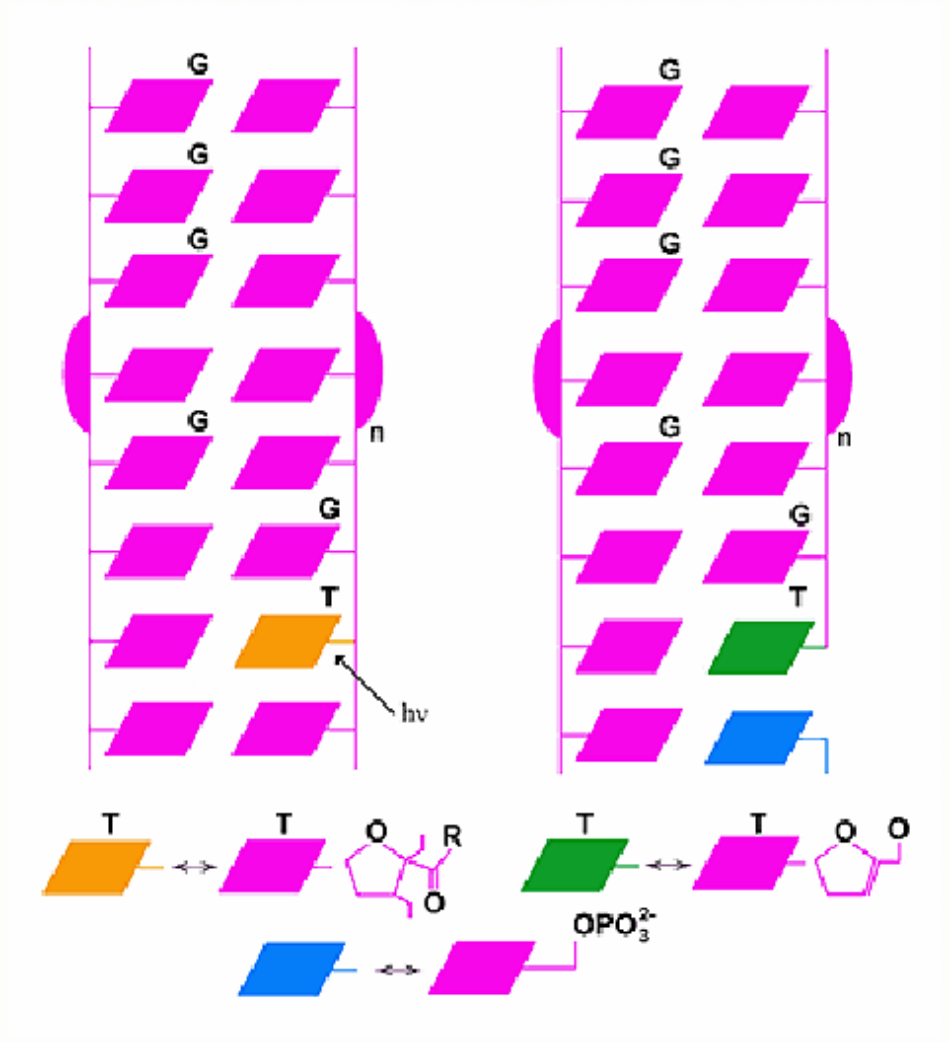


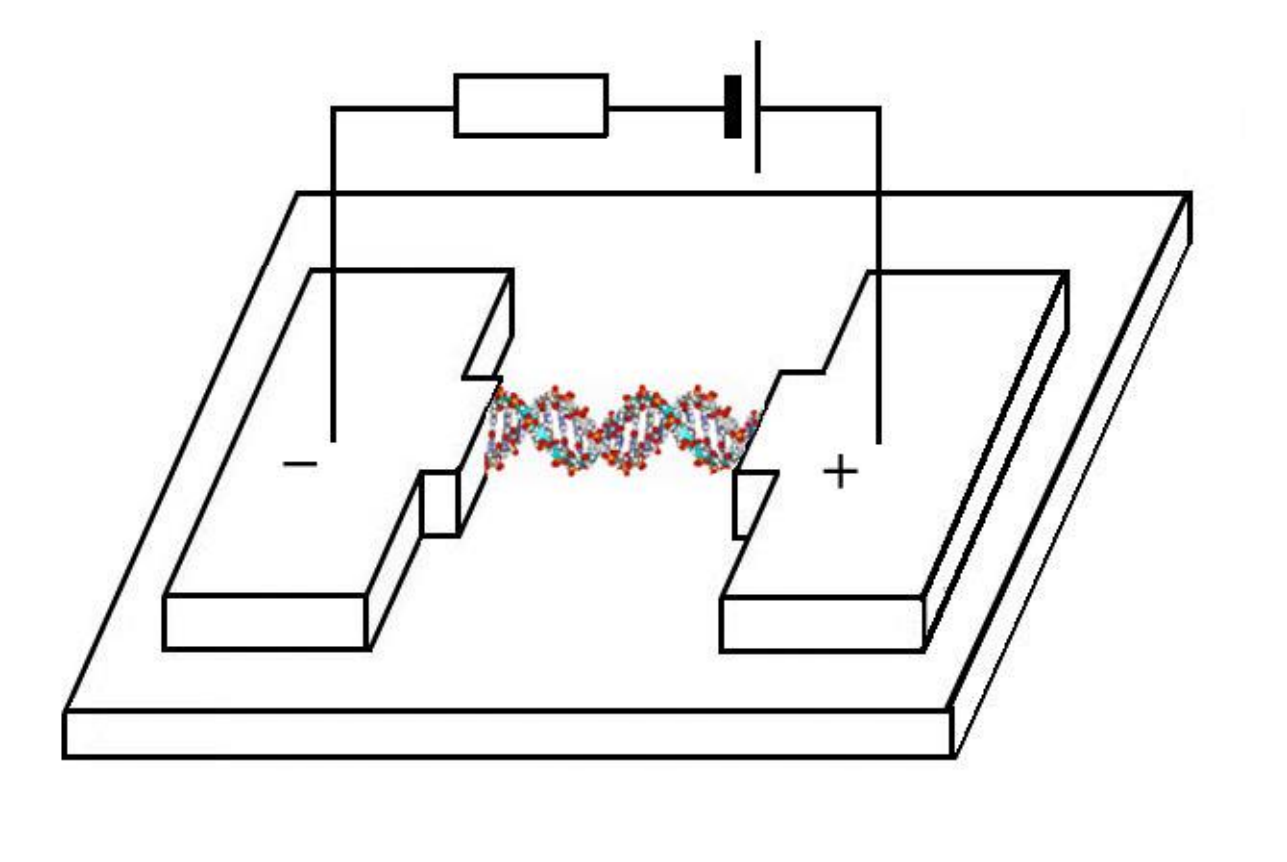


Hole injection into DNA



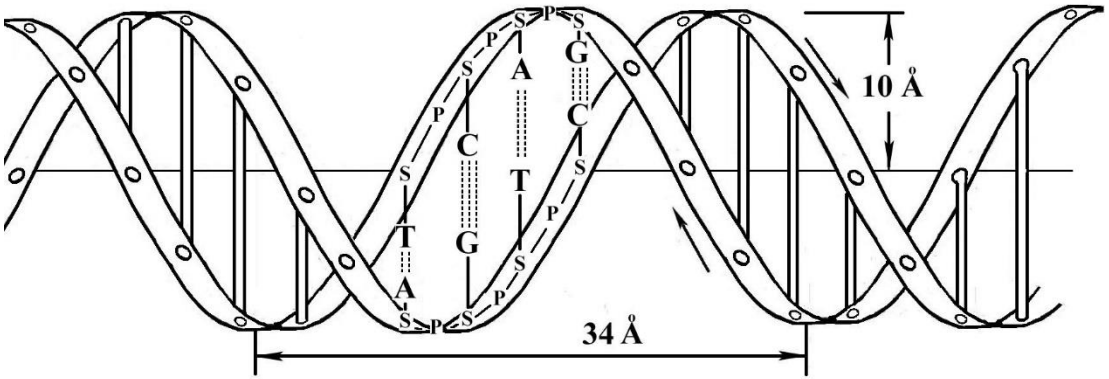
(Giese et al experiments)

Electrical transport through DNA molecules. Direct measurement.

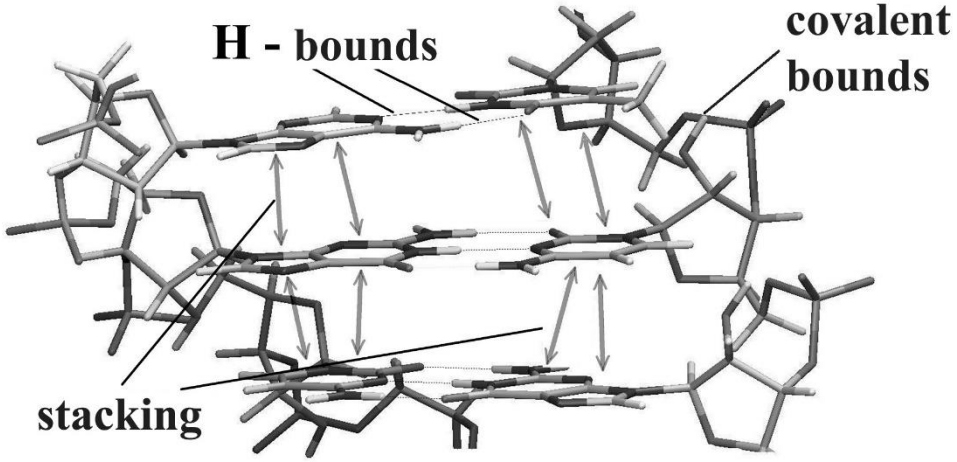


D.Porath et al, Nature, **403**, (2000), 635

Basic linear biopolymer - DNA

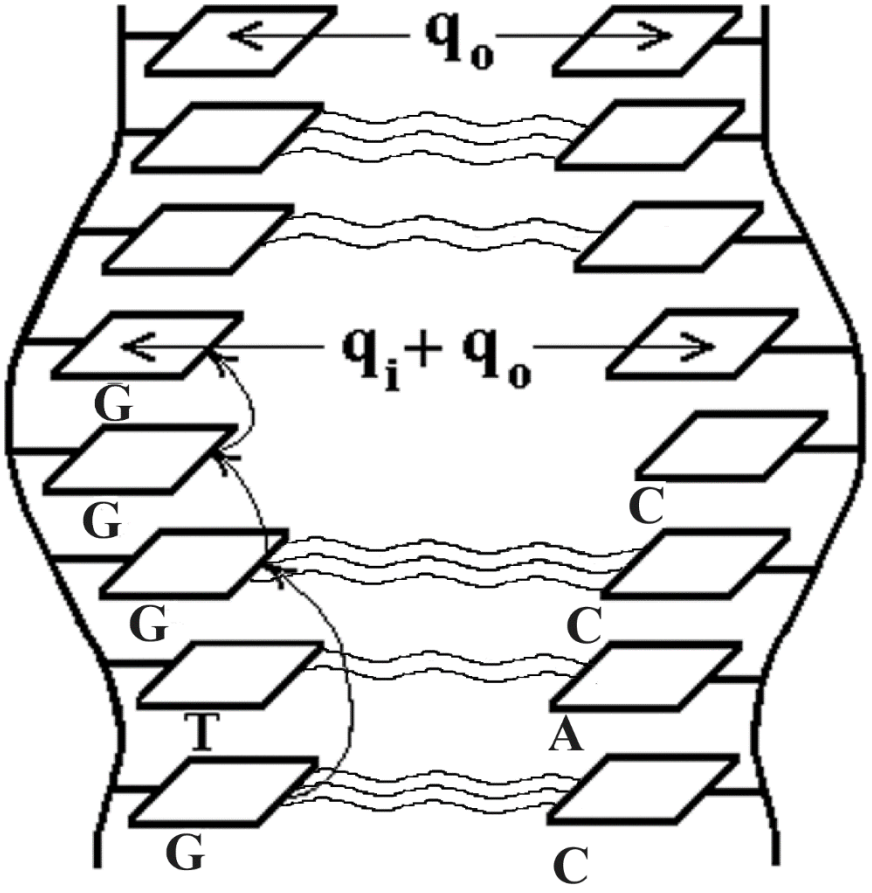


Space DNA structure



Relative space positions of H – bounds and stacking interactions in DNA

Mechanical DNA models



Covalent bound ~ 3,6 eV
Stacking interaction ~ 0,14 ÷ 0,63 eV
H-bound ~ 0,13 ÷ 0,26 eV

"Kroemer's Lemma of Proven Ignorance"

If, in discussing a semiconductor problem, you cannot draw an Energy Band Diagram, this shows that you don't know what you are talking about, with the corollary.

If you can draw one, but don't, then your audience won't know what you are talking about.

"Quasi-electric fields and band offsets: teaching electrons new tricks".

Nobel Lecture, December 8, 2000, H. Kroemer.

Electron in a rigid chain

$$\hat{H} = \sum_{n,m} \nu_{n,m} |n\rangle\langle m|$$

Homogeneous chain in the nearest neighbor approximation

$$\left(\nu_{n,n\pm1} = \nu,\ \nu_{n,m} = 0 \quad m \neq n \pm 1\right): \qquad |\Psi\rangle = \sum_n b_n |n\rangle$$

Schroedinger equation:

$$i\dot{b}_n = \nu\left(b_{n+1} + b_{n-1}\right) \qquad b_n(t) = e^{-iW_k T} R_{n,k}, \quad R_{n,k} = \frac{e^{ikn}}{\sqrt{N+1}}$$

For Poly G/Poly C chain:

$$W_k = 2\nu\cos k, \quad k = \pm\frac{2\pi l}{N}, \quad l = 0,1,2,\mathrm{K}\ \tfrac{N}{2}$$

$\Delta W = 4\nu$ - **conductivity band width.**

Regular chains

Band structure for Poly(GT)/Poly(CA)

$$n = 2j: \quad \nu_{2j,2j} = 0, \quad \nu_{2j,2j+1} = \nu_1, \quad j = 0, \pm 1, \pm 2, \Lambda$$

$$n = 2j+1: \quad \nu_{2j+1,2j+1} = \alpha_T, \quad \nu_{2j,2j-1} = \nu_2$$

Eigen value equations:

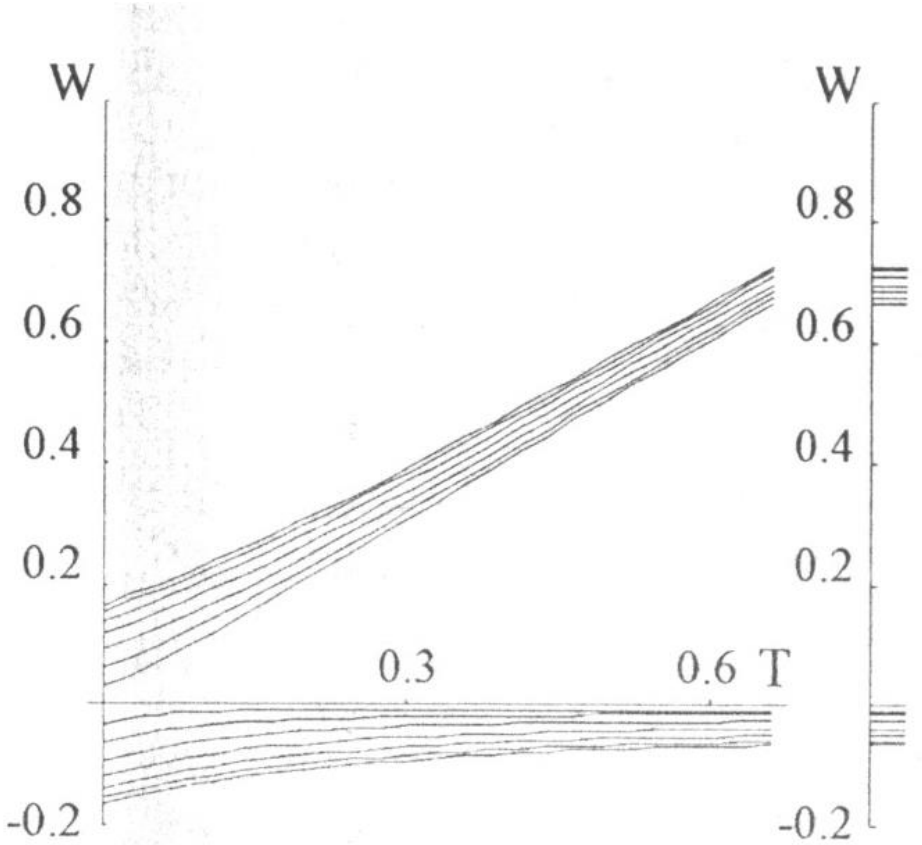
$$W_k R_{2j,k} = \nu_1 R_{2j+1,k} + \nu_2 R_{2j-1,k}$$

$$W_k R_{2j+1,k} = \alpha_T R_{2j+1,k} + \nu_2 R_{2j+2,k} + \nu_1 R_{2j,k}$$

$$R_{2j+1,k} = u_2 \exp\left[ik\left(2j+1\right)\right], \quad R_{2j,k} = u_1 \exp\left[ik\left(2j\right)\right],$$

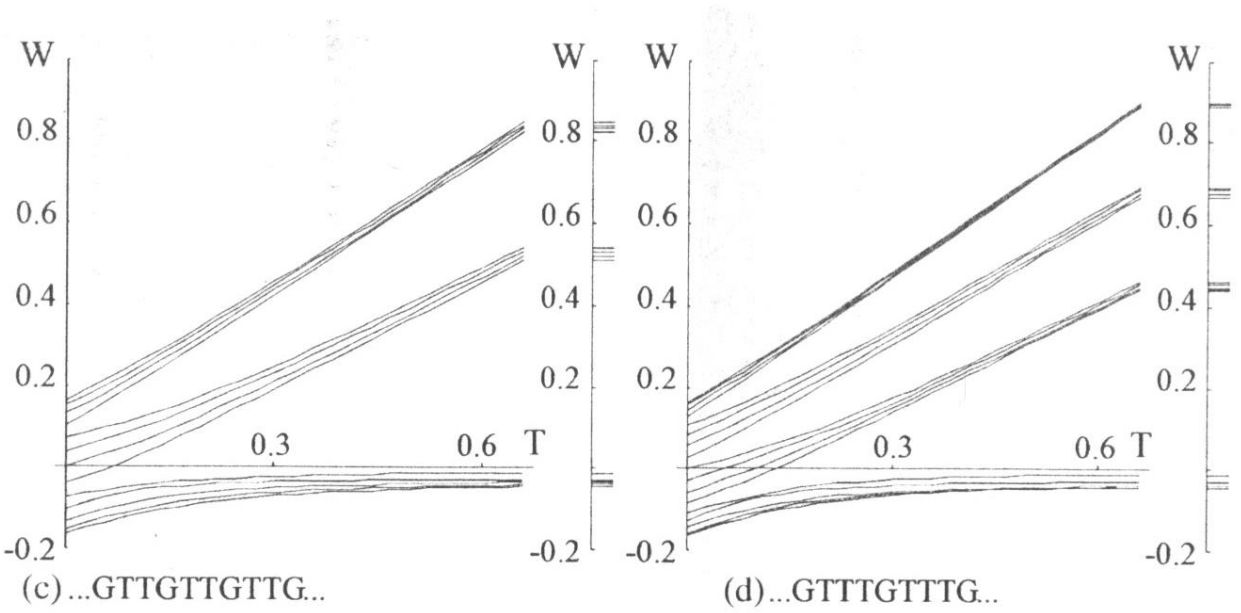
$$W_k^{\pm} = \frac{\alpha_T}{2} \pm \sqrt{\left(\alpha_T / 2\right)^2 + \left(\nu_1^2 + \nu_2^2 + 2\nu_1\nu_2 \cos 2k\right)^2}$$

Poly(GT)/Poly(CA)



(b) ...GTGTGTG...

Band structures of various regular chains



For regular chains, that contain **m** sites in an elementary cell, there are **m** different branches determining their band structure.

V.D.Lakhno in "Modern Methods for Theoretical Physical Chemistry of Biopolymers", Ed. By E.B.Staricov , J.P.Lewis, S.Tanaka, (2006), Elsevier

V.D.Lakhno, V.B.Sultanov, Theor.Math.Phys., v.176, 1194, (2013)

Conclusion

1. For regular chains, that contain m sites in an elementary cell, there are m different branches determining their band structure.

2. For finite regular chains the discrete levels can arise in the forbidden bands, which correspond to localised at the chain ends states (Tamm levels).

Formation of a soliton (polaron) state in a deformable chain

$$\hat{H} = \nu \sum_n \left(a_n^+ a_{n-1} + a_n^+ a_{n+1} \right) + \sum_n \alpha\, q_n\, a_n^+ a_n + \sum \frac{\hat{P}_n^2}{2M} + \sum \frac{k\, q_n^2}{2}$$

- Holstein model

$$\left| \Psi(t) \right\rangle = \sum_n b_n(t) a_n^+ \exp\left\{ -\tfrac{i}{\eta} \sum_j \left[\beta_i(t) \hat{P}_j - \pi_j(t) q_j \right] \right\} \left| 0 \right\rangle$$

$$\left\langle \Psi(t) \left| q_n \right| \Psi(t) \right\rangle = \beta_n(t), \quad \left\langle \Psi(t) \left| \hat{P}_n \right| \Psi(t) \right\rangle = \pi_n(t)$$

Motion equation:

$$i\eta \dot{b}_n = \alpha \beta_n b_n + \nu \left(b_{n-1} + b_{n+1} \right)$$

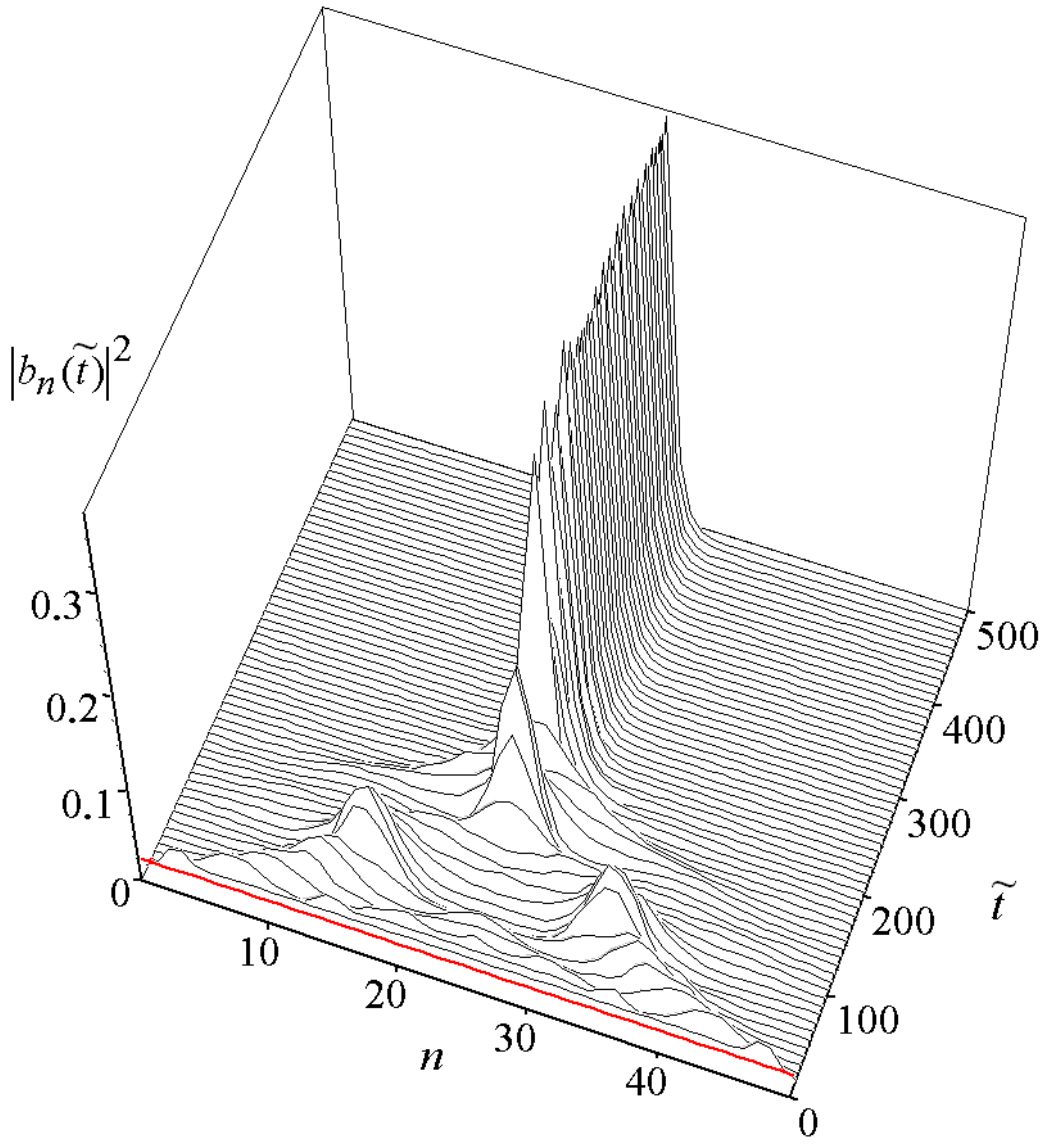
$$M \ddot{\beta}_n = -\gamma \dot{\beta}_n - k \beta_n - \alpha \left| b_n \right|^2$$

Exact solution for a rigid chain $(\alpha = 0)$

$$b_n(t) = \sum_m b_m(0) (-i)^{n-m} J_{n-m}\left(2\nu t / \eta \right)$$

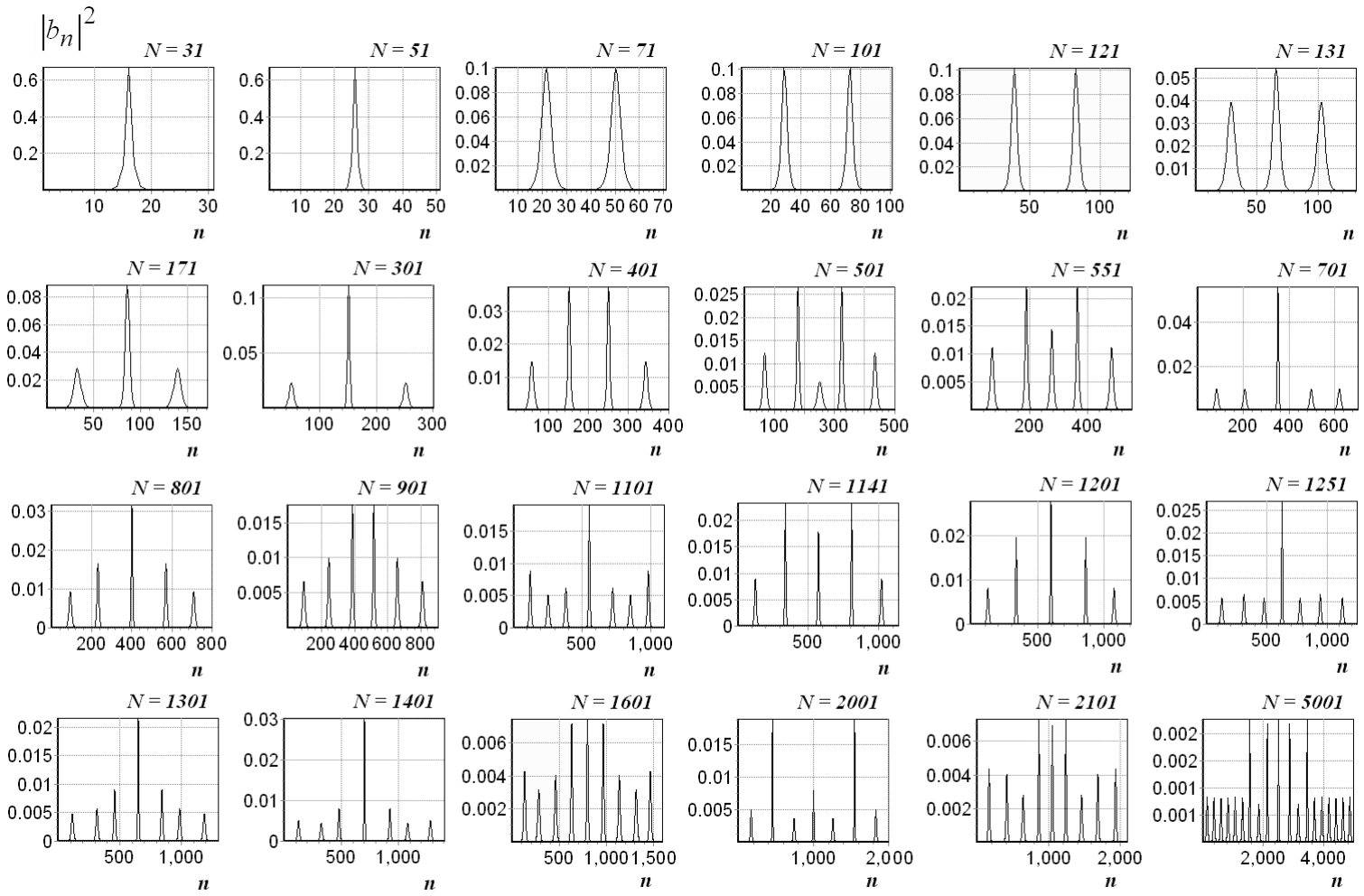
J_n **- Bessel function of the first kind, describes dynamics of the wavepackage spreading .**

Numerical solution for $(\alpha \neq 0)$



Formation of a soliton state

Formation of multisoliton states



Lakhno V.D., Korshunova A.N., Mathem. Biol. And Bioinform., v.5, (2010), p.1-29.

Results of modelling

1) A delocalized state in the chain is unstable.
2) A polaron (soliton) state is formed both in the presence and in the absence of dissipation.
3) The time for which a localized state is formed depends greatly on the wave function phase.
4) In multisoliton states objects with fractional electron charge are formed which can be found experimentally.

Electron motion in an electric field in a rigid chain $(\alpha = 0)$

Exact solution of Schroedinger equation for a rigid chain:

$$b_n(t) = \sum_{m=-\infty} b_m(0)(-i)^{n-m} e^{-i(n+m)\omega_\beta t} J_{n-m}(\zeta(t))$$

$$\zeta(t) = \frac{4\nu}{\eta\omega_B} \sin\left(\frac{\omega_B t}{2}\right), \quad \eta\omega_B = e\varepsilon a$$

$J_n(x)$ **- Bessel function of the first kind**

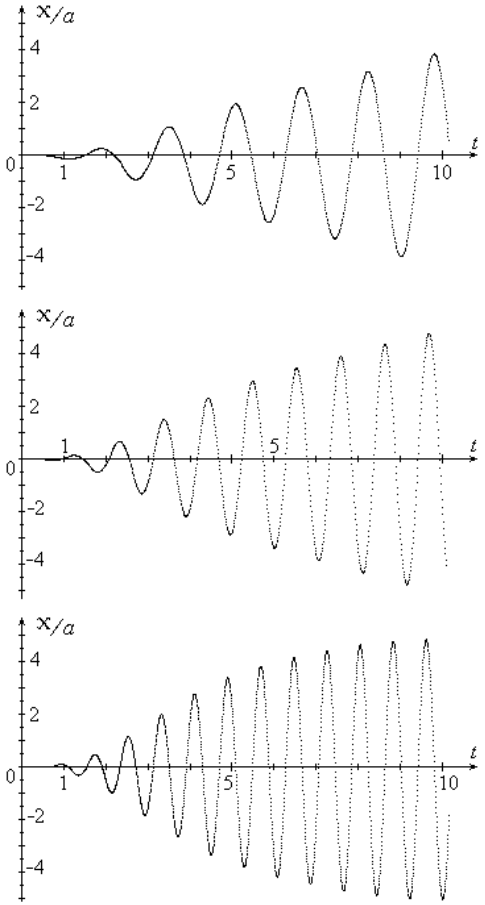
$$X(t) = \sum_n^N |b_n(t)|^2 na$$ **- displacement of the electron's mc**

$$X(t) = X(0) + \frac{2a\nu}{\eta\omega_B} |S_0| (\cos\theta_0 - \cos(\omega_B t + \theta_0))$$

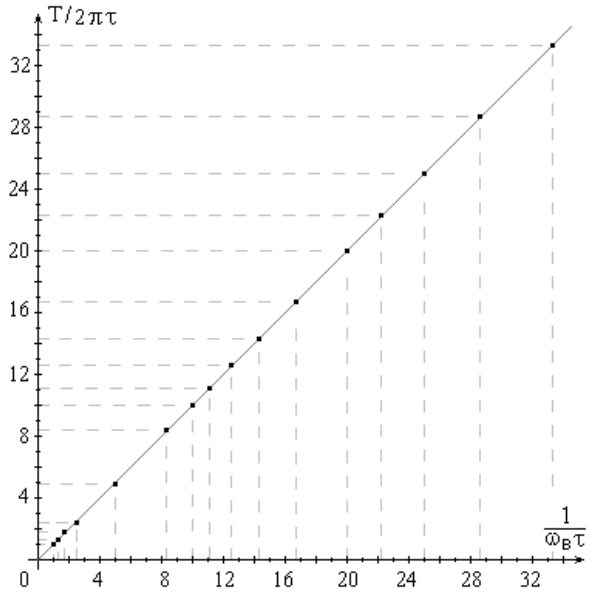
$$S_0 = \sum_{-\infty}^{\infty} b_m^*(0) b_{m-1}(0) = |S_0 e^{i\theta_0}|, \quad X(0) = a\sum_{-\infty}^{\infty} m|b_m(0)|^2$$

Oscillation amplitude $X(t) = 0$ **, if** $b_m(0) = 1$

Generation of Bloch oscillations in a deformable chain $(\alpha \neq 0)$



Time dependence of the hole's center of mass for various values of the electric field intensity (a) $\tilde{E} = 0.04$, (b) $\tilde{E} = 0.06$, (c) $\tilde{E} = 0.08$.



Solid line indicates the dependence of the Bloch oscillations period on the electric field intensity E ($T_B = 2\pi / \omega_B$ $\omega_B = eEa/\eta$ - Bloch frequency), for $\kappa = 0$. Black dots indicate calculation values for $\kappa = 4$,

$$\left(\alpha_n' \sim 1.3 \cdot 10^{-4} eV / \text{Å}^{\circ}\right)$$

V.D.Lakhno, N.S.Fialko, Pis'ma v ZhETF, v.79, (2004), p.575-578.

Bloch oscillations in a homogeneous nucleotide chain

Conclusion

1) **It is shown that at zero temperature, a hole placed in homogeneous synthetic nucleotide chain with applied electric field demonstrates Bloch oscillations.**

2) **The oscillations of the hole placed initially on one of base pairs arise in response to disruption of the initial charge distribution caused by nucleotide vibrations**

3) **The finite temperature fluctuations result in degradation of coherent oscillations. The maximum permissible temperature for DNA "Bloch oscillator" occurrence is estimated.**

Soliton in a continuum approximation

$$i\eta\frac{\partial b}{\partial t}+\frac{\eta^2}{2m}\frac{\partial b}{\partial X^2}-\chi q b=0$$

$$\frac{\partial^2 q}{\partial t^2}+\Omega_0^2 q+\frac{\chi}{M}|b|^2=0$$

Davydov: how a soliton can move in the absence of dispersion (JETP, 1980)

$$q(\xi)=-\frac{\chi}{M\Omega_0^2}\int d\xi\,\omega(\xi'-\xi)|b(\xi')|^2,$$

$$\omega(\xi)=\frac{\theta(\xi)}{\sqrt{|\varepsilon|}}\sin\frac{\xi}{\sqrt{|\varepsilon|}},\quad \varepsilon=-\frac{V^2}{a^2\Omega_0^2},$$

$$b(\xi)=\frac{1}{\sqrt{2r}}\,\mathrm{ch}^{-1}(\xi/r),$$

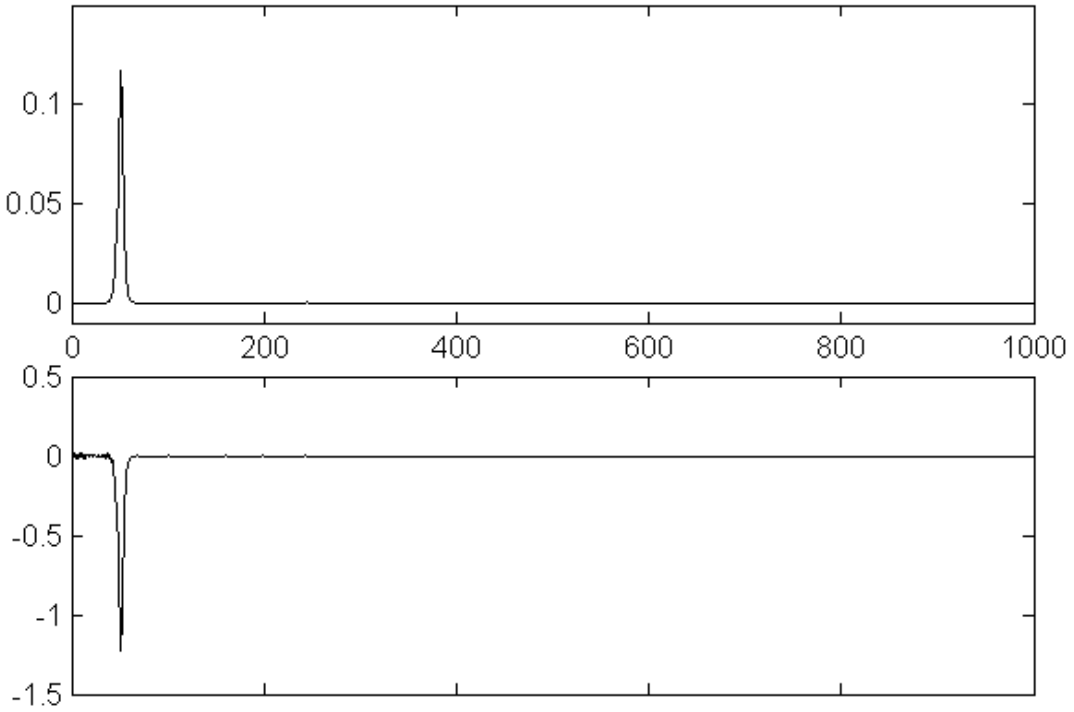
$$r=4M(\eta\Omega_0)_2/m\chi^2a^2,\quad \xi=(X-vt)/a,\quad q(\xi)=c\sin(\xi/\sqrt{|\varepsilon|})$$

V.D.Lakhno, Int. Quant. Chem.,V.110, (2010), pp.129-137

Emission of phonons by a moving soliton in a dispersionless chain.

Probability of charge's occurrence on site $|b_n|^2$

Displacements of sites u_n



$$\eta = 0.1, \quad \omega^2 = 0.1, \quad \kappa = 0.1,$$

$$(\eta = \nu\tau / \eta, \quad \omega = \Omega_0 \tau, \quad \kappa = x^2\tau^3 / M\eta)$$

Dispersion

$\xi\left(q_{n-1}+q_{n+1}\right)$ - **for a discrete model**

$\xi\, a^2\, \frac{\partial^2 q}{\partial X^2}$ - **for a continuum model**

$\Omega^2 = \Omega_0^2 - \frac{2\xi}{M}\cos k$ - **discrete**

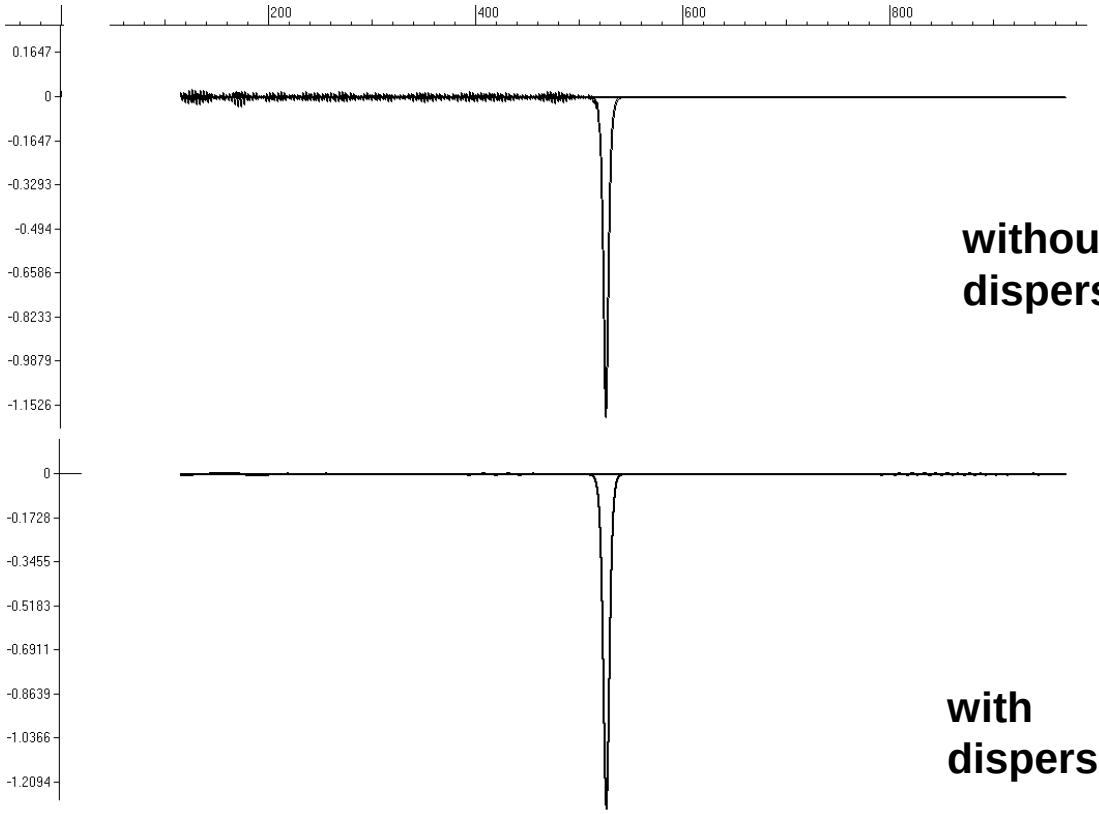
$\Omega^2 = \Omega_0^2 + V_0^2 k^2$ - **continuum**

Davydov:

for $V < V_0$ **- steady state of a soliton exists**

for $V > V_0$ **- steady state is impossible because of the emission**

Moving soliton



without dispersion

with dispersion

$$\eta = 0.1, \quad \omega^2 = 0.1, \quad \kappa = 0.1, \quad \xi = 0.001$$

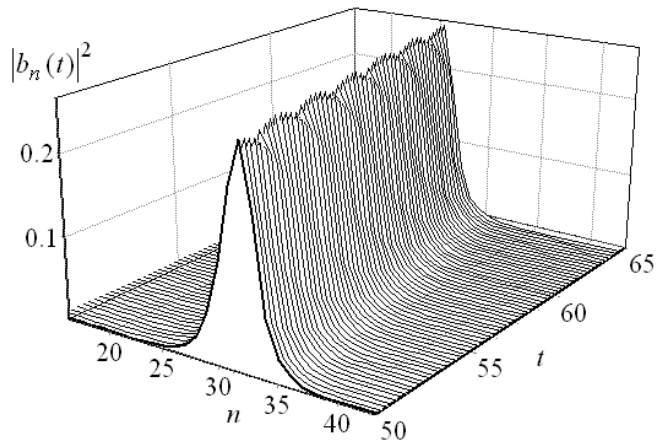
Conclusion

1) In a molecular chain with dispersionless phonons at zero temperature the stationary motion is impossible.
2) In a molecular chain with disperionless phonons at zero temperature, a “quasistationary” moving soliton state of an excess electron is possible
3) As the soliton velocity vanishes, the path length of the excess electron exponentially tends to infinity.
4) In the presence of dispersion, when the soliton initial velocity exceeds the maximum group velocity of the chain, the soliton slows down until it reaches the maximum group velocity and then moves stationary at this maximum group velocity.

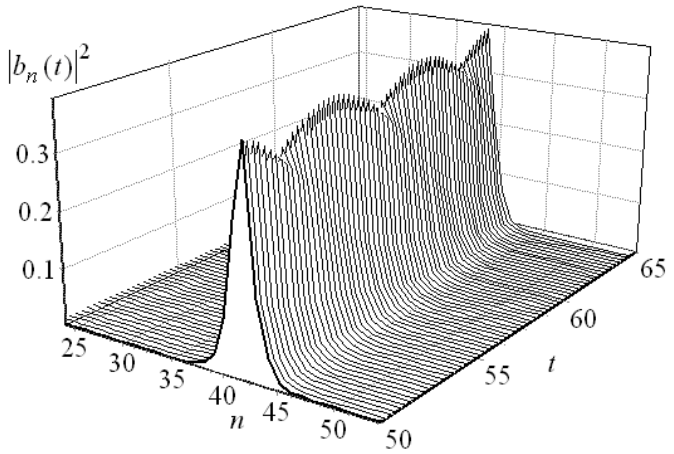
Homogeneous motion of a polaron over a chain in an electric field

$$i\eta\dot{b}_n = \nu\left(b_{n-1} + b_{n+1}\right) + \alpha'\beta_n b_n + e\varepsilon a n b_n$$

$$M\ddot{\beta}_n = -k\beta_n - \alpha'\left|b_n\right|^2$$



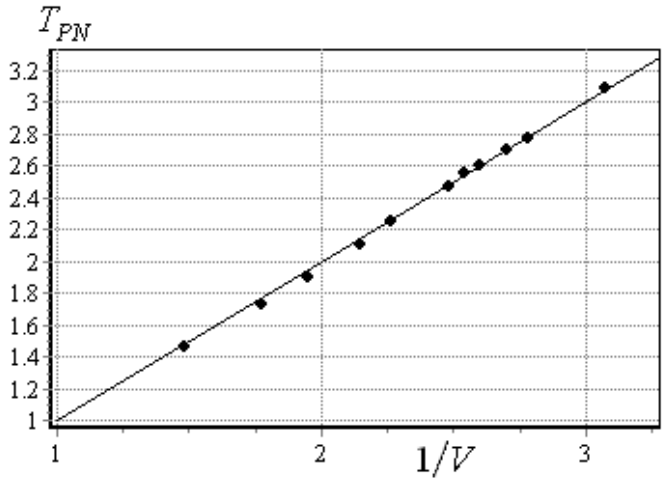
$E = 0.01, \quad \omega = 1, \quad \eta = 1.276, \quad \kappa = 2$

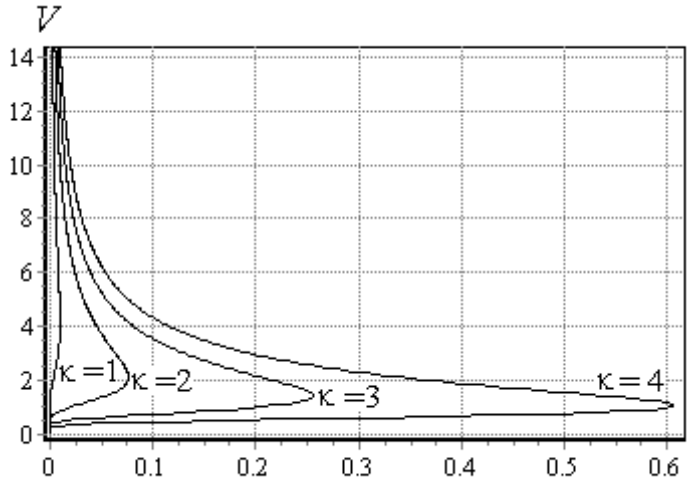


$\kappa = 3$

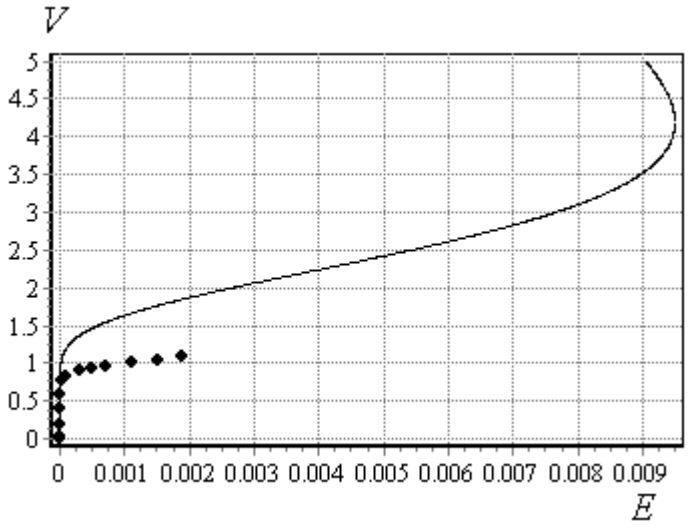
Peierls-Nabarro oscillations $\quad T_{PN} = 1/V, \quad V = dX/d\tilde{t}, \qquad X(\tilde{t}) = \sum_n n\left|b_n(\tilde{t})\right|^2$

Comparison of the theory with numerical experiments





$$E = 2\pi^2 \frac{\omega^4 \eta^2}{\kappa} \frac{1}{V^4} \frac{1}{\sinh^2\left(2\pi\eta\omega/\kappa V\right)}$$



Lakhno V.D., Korshunova A.N., Eur. Phys. J. B, v.79, (2011), p.147-151.

Conclusions

1) In a weak electric field a Holstein polaron moves uniformly experiencing small Peierls – Nabarro oscillation of its shape.
2) At critical value of the electric field intensity polaron starts oscillating at Bloch frequency, retaining its shape.
3) For sufficiently long time soliton becomes a breather that oscillates.
4) In all cases the polaron motion along the chain is infinite.

General approach to calculation of the mobility at high temperatures

Motion equations for Holstein Hamiltonian:

$$i\eta\frac{db_n}{dt} = \alpha' q_n b_n + \nu\left(b_{b+1} + b_{n-1}\right)$$

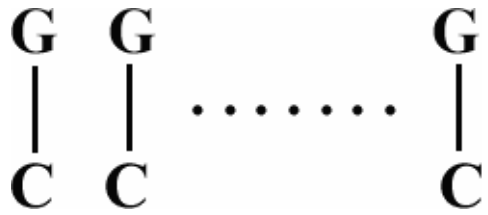
$$M\frac{d^2 q_n}{dt^2} = -\gamma_f \frac{dq_n}{dt} - k\, q_n - \alpha'\left|b_n\right|^2 + A_n(t)$$

$$\left\langle A_n(t)\right\rangle = 0 \qquad \left\langle A_n(t) A_m\left(t+t'\right)\right\rangle = 2T\ \gamma_f \delta_{n\,m}\delta\left(t'\right)$$

$$\mu = \frac{e}{2T}\lim_{\varepsilon\to 0}\varepsilon^2\int_0^\infty \left\langle x^2(t)\right\rangle \exp\left(-\varepsilon t\right) d\, t \qquad x^2(t) = a^2\sum_n n^2\left|b_n(t)\right|^2$$

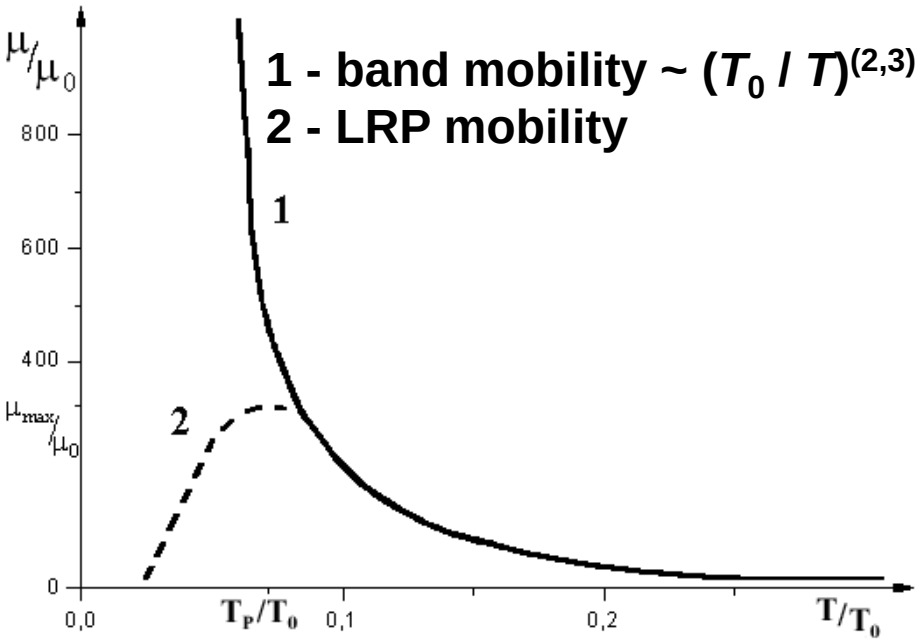
V.D.Lakhno, N.S.Fialko, *JETP Letters*, **78**, 336, (2003).

Temperature dependence of Hole mobility in (PolyG / PolyC)



$\nu = 0{,}084$ eV, $\alpha' = 0{,}13$ eV / Å,

$\omega = \sqrt{K/M} = 10^{12}$ sec^{-1}, $\omega' = \gamma_f / M = 6 \cdot 10^{11}$ sec^{-1}



1 - band mobility ~ (T_0 / T)$^{(2,3)}$

2 - LRP mobility

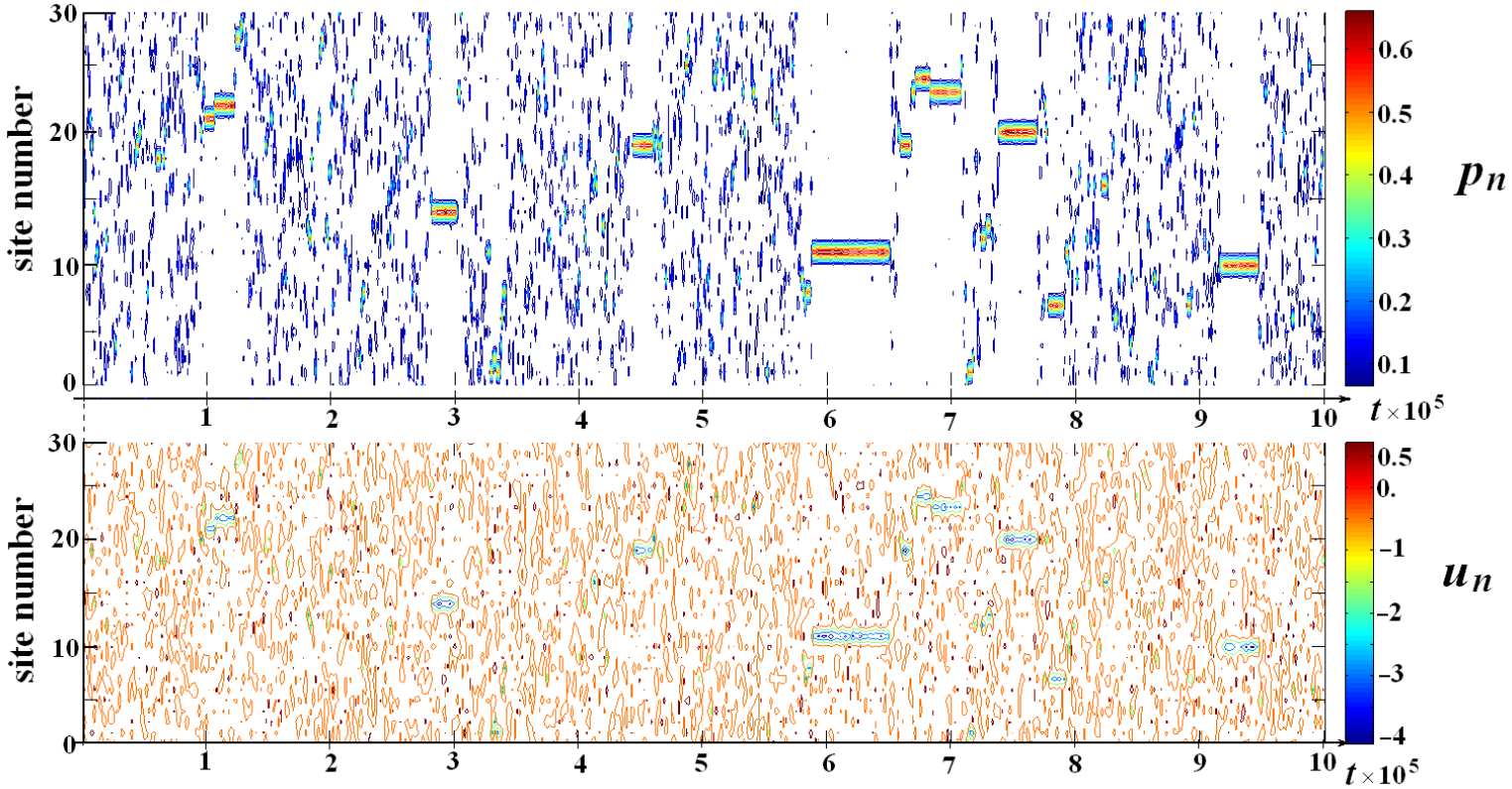
$\eta\omega \approx 7{,}7\,K, \quad T_P \approx 20\,K,$

$\mu_{max} \approx 1500$ cm^2/ V sec,

$\mu_0 = 2{,}87$ cm^2/ V sec -

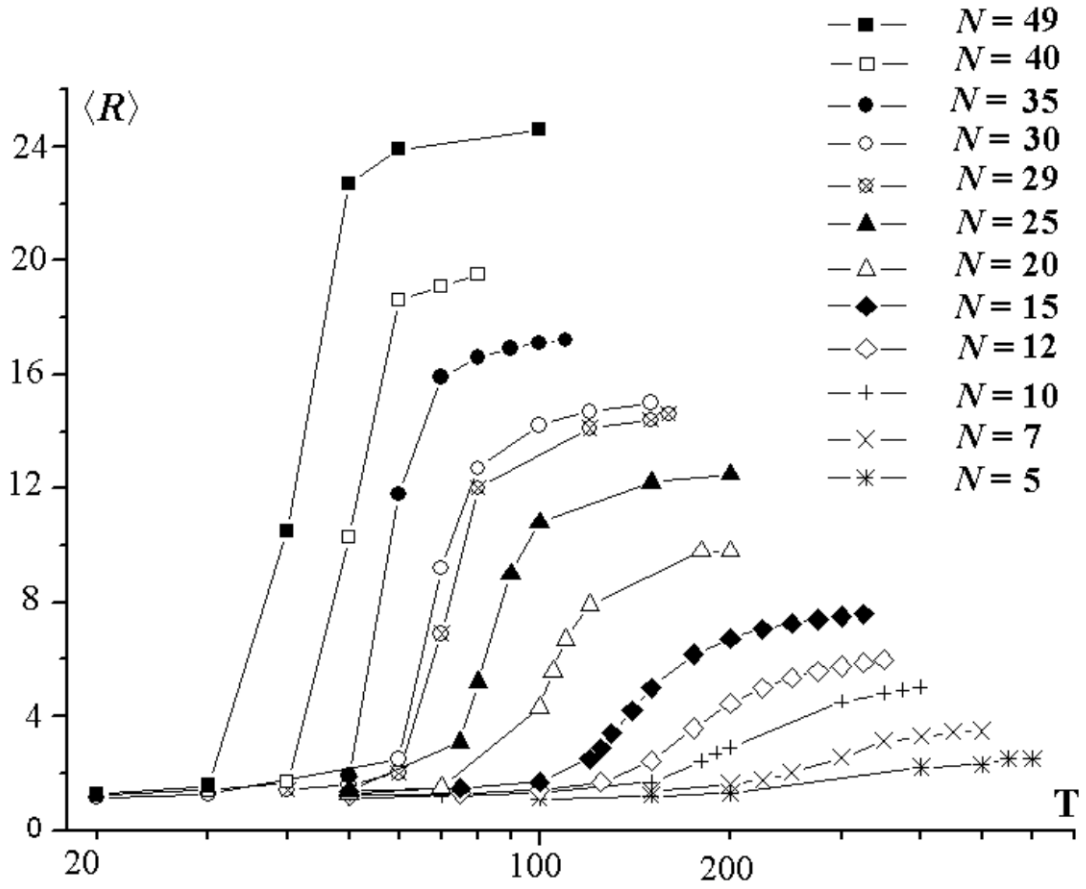
hole mobility at T_0 = 300 K

Small radius polaron near critical temperature



Localized and delocalized charge states

Delocalisation parameter



$$\langle R \rangle = \left\langle \frac{1}{\sum |b_n|^4} \right\rangle$$

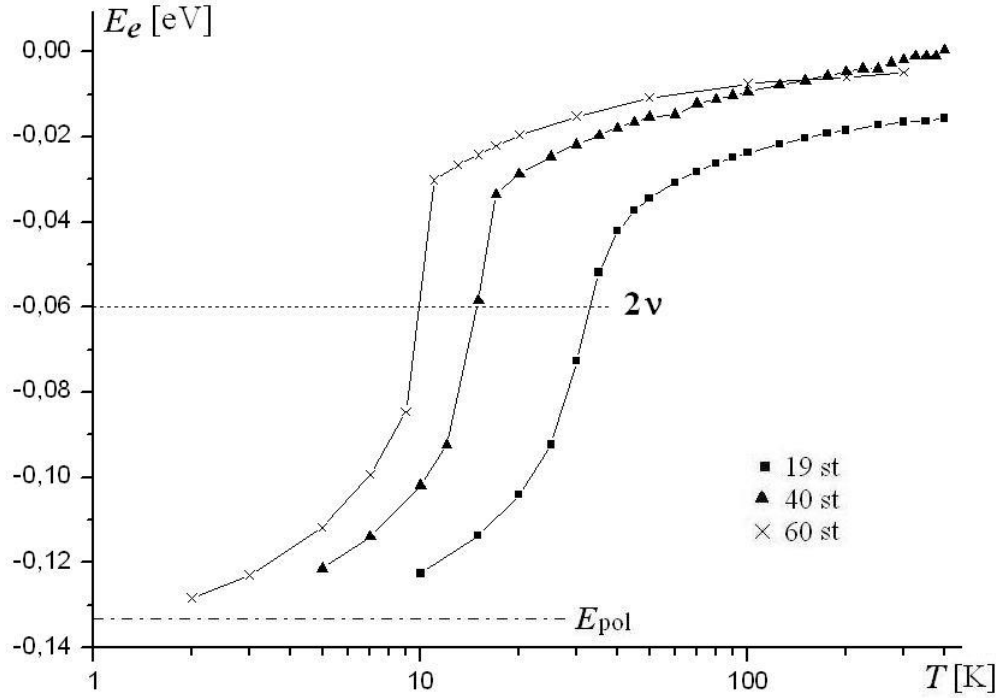
$$\langle R \rangle = 1, \quad |b_n|^2 = \delta_{n,n_0};$$

$$\langle R \rangle = N, \quad |b_n|^2 = 1/N$$

Thermodynamic values of $\langle R(\mathrm{T}) \rangle$ for chains of different lengths N (logarithmic scale).

V.Lakhno,N.Fialko, JETP, v.120,125,(2015)

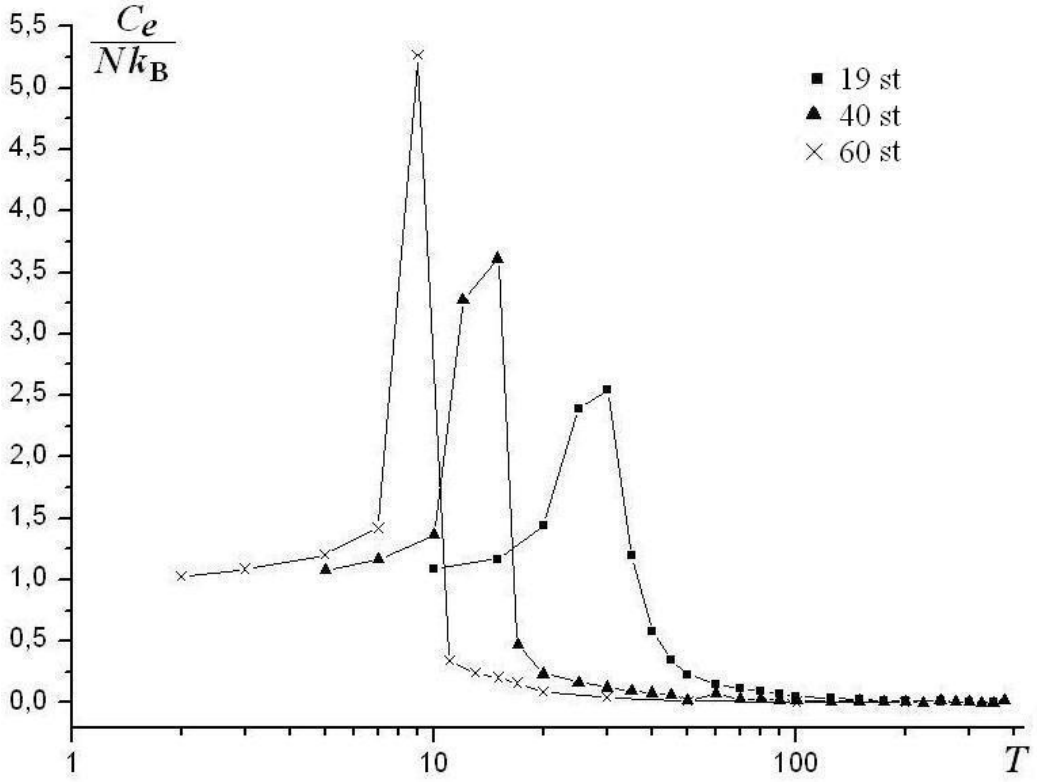
Polaron energy



Results of calculations of thermodynamically equilibrium values.

Electronic part of the total energy Ee(T) for chains of length 19, 40 and 60 sites. Dashed lines show polaron energies Epol and the lower bound of the conductivity band 2ν

Heat capacity



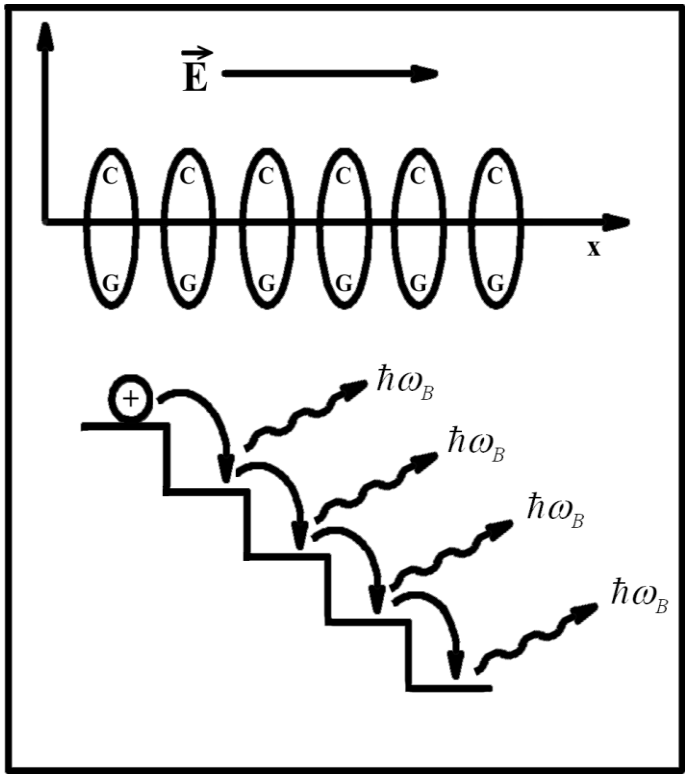
Normalized electronic heat capacity.

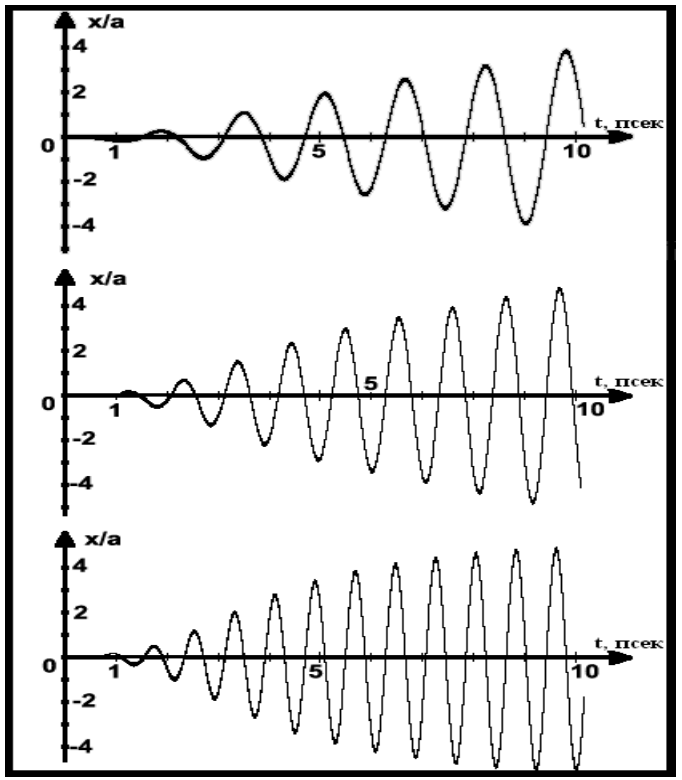
$$C_V = \frac{\partial \langle E_{tot}(T) \rangle}{\partial T} = \frac{1}{k_B T^2} \left(\langle E_{tot}^2(T) \rangle - \langle E_{tot}(T) \rangle^2 \right), \qquad C_e = \frac{\partial E_e}{\partial T} = C_V - Nk_B$$

Conclusion

1. For T=0, $E_e=E_{pol}$, temperature grows,$E_e(T)$ increases and f charge passes on from polaron state to delocalized one.
2. The polaron decay temperature depends not only on the model parameters but also on the chain length: the larger is N, the less is the decay temperature.
3. The peak on the graph of electronic heat capacity is observed at the polaron decay temperature.

DNA-based molecular devices

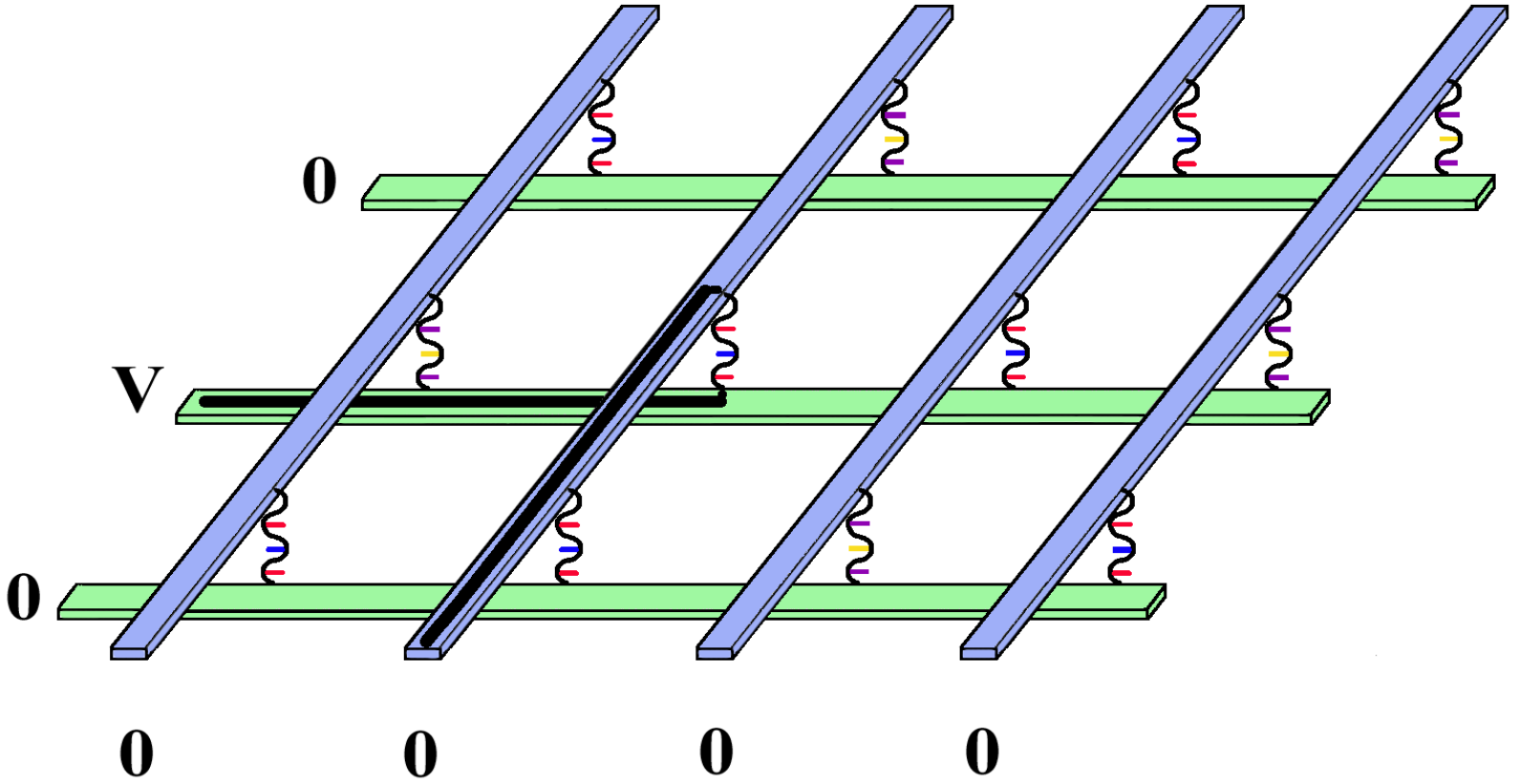




$$\eta\Omega = n\eta\omega_B,\ n = 1,2,3,\text{K}\ \ \eta\omega_B = eEa$$

- **Terahertz emitters of electromagnetic waves**
- **Nanoelements with negative differential conductivity**
- **Nanoelements with absolute negative conductivity**
- **Multiphoton radiation detectors**
- **Cascade lasers**

Nanobiochip



The measuring of current along the separated contour diagnoses its change after hybridization

V. D. Lakhno, V. B. Sultanov.
J. Chem. Theory Comput. **2007, 3, 703-705**

Digital memory device based on tobacco mosaic virus conjugated with nanoparticles

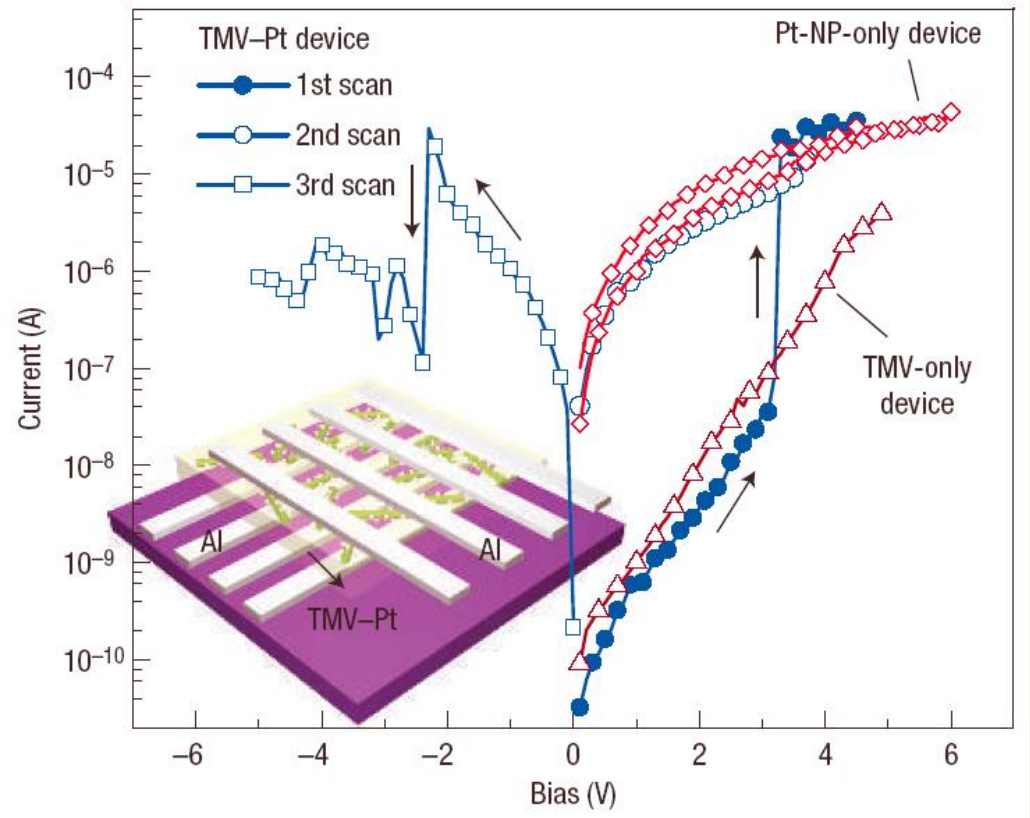
Nature v. 1 Oct. 2006, pp.72-77

R.J. Tseng[1], CH. Tsai[2], L. Ma[1], J. Ouyang[1], C.S. Ozkan[3] Y. Yang[1]

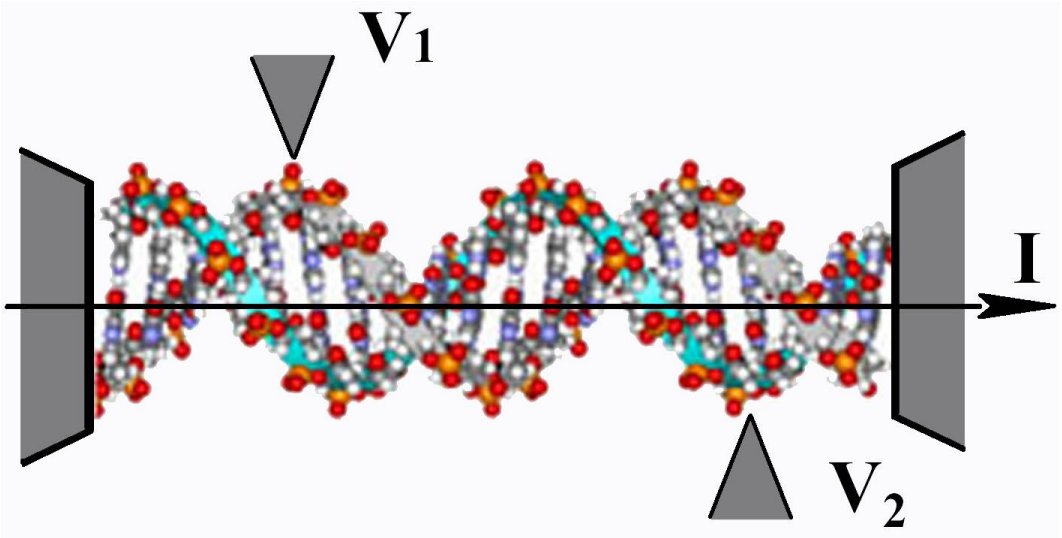
[1]Department of Materials Science and Engineering, University of California_Los Angeles, USA

[2]Department of Electrical Engineering, University of California_Riverside, USA

[3]Department of Mechanical Engineering, University of California_Riverside, USA



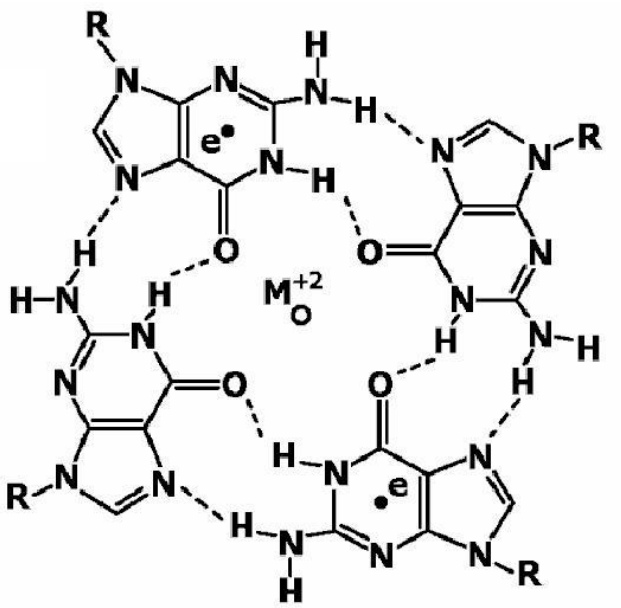
Logical gate XOR



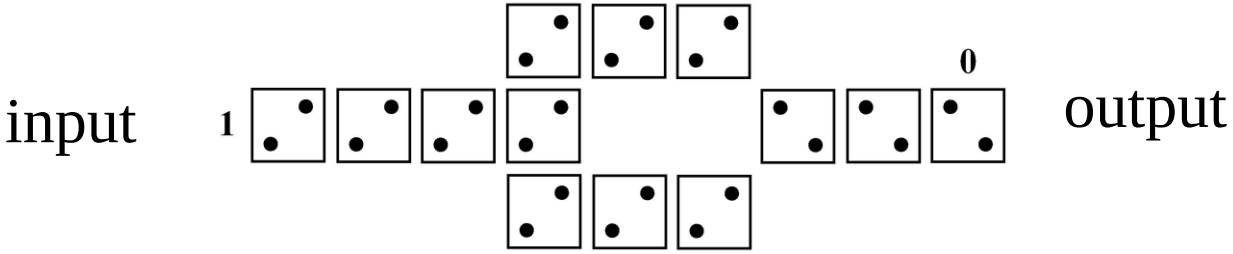
v1	v2	p
1	1	0*
1	0	1
0	1	1
0	0	0

V. D. Lakhno, V. B. Sultanov.
Mathematical biology and bioinformatics,
2006, v.1 (1), pp. 123-126.

DNA quantum cell



G-quadruplex



inverter

A.B.Kotlyar, D.Porath et al. Nature nanotechnology, 2014, pp. 1040-1046.

DOI: 10.1038/NNANO.204.246

The results were obtained in collaboration with my colleagues:

N.Fialko

V.Sultanov

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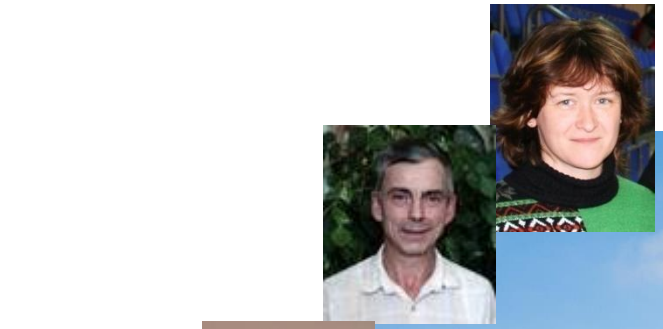
A.Shigaev

E.Sobolev



Thank you for your attention