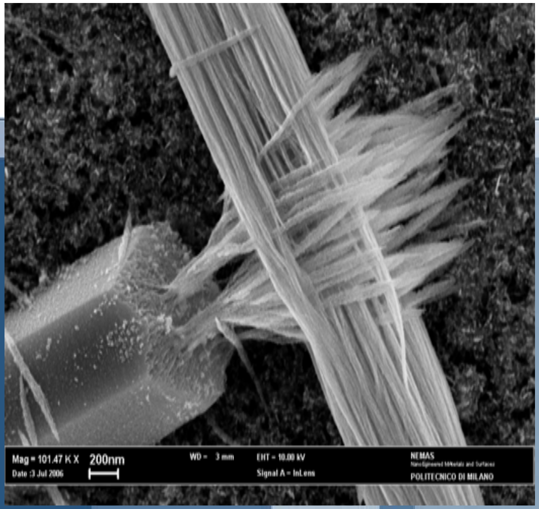
NEMAS (www.nemas.polimi.it)

Centre for Nano Engineered MAterials and Surfaces



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Nanotechnologies:

a general introduction

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Nuclear Engineering Department

(www.nanolab.polimi.it)

1 Nanotechnologies: a general introduction

(C.E. Bottani, Politecnico di Milano, Italy)

2 Nanomedicine

(Mauro Ferrari, University of Texas, Houston, USA)

3 The scanning probe microscope: an essential tool for nanotechnologies

(Andrea Li Bassi, Politecnico di Milano, Italy)

SUMMARY

- **Definitions**
- **Social and economic relevance**
- **The surprising story of direct imaging and manipulation of atoms (from Feynman’s dream to the real birth of nanotechnologies)**
- **Quantum confinement: the singular properties of low-dimensional and nanoscopic objects**
- **One more colour on the palette**
- **Nanobiotechnology and Nanomedicine**

Birth of the word “*nanotechnology*”

The term nanotechnology was coined by the Tokyo Science University professor Norio Taniguchi in 1974 to describe the precision manufacture of materials with nanometer tolerances, and was unknowingly appropriated by Drexler in his 1986 book “*Engines of Creation: The Coming Era of Nanotechnology*” to describe what later became known as *molecular nanotechnology*

Definitions of nanotechnology

puristic (Feynman 1959)

- **First definition: *"a technology that exploits quantum confinement and/or the capability of manipulating individual atoms and molecules"***

etymological

- **Second definition: *"a technology that works at the nanoscopic scale(L < 1 μm)"***

opportunistic

- **Third definition: *"Any technology involving small objects (everything below 1 mm is o.k.) one can write about in a funding proposal with the hope for getting a lot of money without need of knowing atomic and molecular physics and chemistry"***

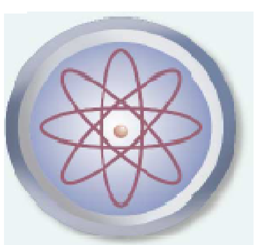
What is “nano” ?

- 1 nanometer (nm) = 10^{-9} m
- roughly a thousand atoms in a $(2.5\ \text{nm})^3$ cube
- smallest structures in integrated circuits:
  roughly 250 nm
- protein size:
  1-20 nm
- hair diameter:
  10 μm (= 10000 nm)

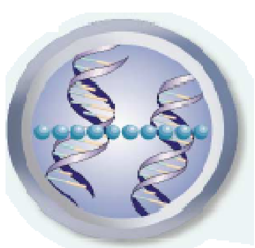
Though, apparently, microtechnologies belong to what we have called the *opportunistic* definition, they constitute, of course, a very important field of present research tightly connected to nanotechnologies (microelectronics, Micro Electro-Mechanical Systems - MEMS, biotechnologies….)

In the case of devices and materials (inorganic, organic, biologic) the researcher/designer must always face a *multiscale problem* (from the atom scale to the man scale)

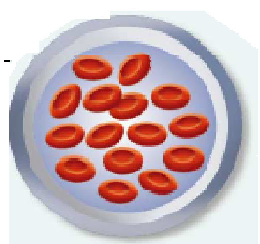
mimic natural nanostructures…



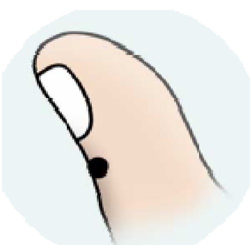
Less than a nanometer
Individual atoms are up to a few angstroms, or up to a few tenths of a nanometer, in diameter.



Nanometer
Ten shoulder-to-shoulder hydrogen atoms (blue balls) span 1 nanometer. DNA molecules are about 2.5 nanometers wide.



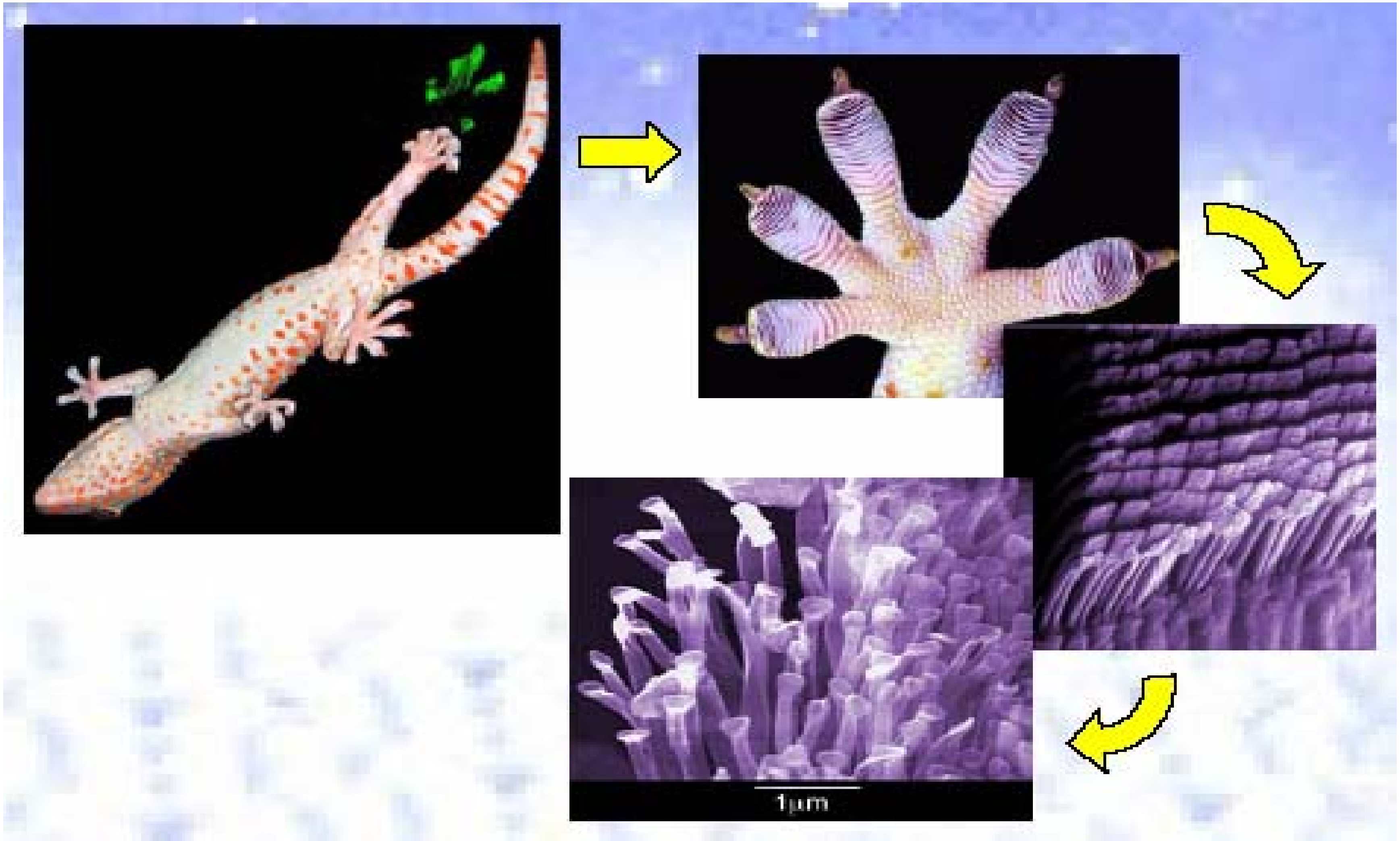
Thousands of nanometers
Biological cells, like these red blood cells, have diameters in the range of thousands of nanometers.



A million nanometers
The pinhead sized patch of this thumb (circled in black) is a million nanometers across.

Billions of nanometers
A two meter tall male is two billion nanometers tall.

Gecko's legs and van der Waals forces



Social and economic relevance

Nanotechnology is predicted to become the basis for remarkably powerful and inexpensive computers, fundamentally new medical technologies that could save millions of lives, sensors important in military application as well as environmental protection, and new zero-pollution manufacturing methods that could create greater material abundance for all.

According to key policy makers, the development of nanotechnology as the latest mega trend in science and engineering will bring a wave of radical innovation and perhaps, because of its potentially broad impact, spark a new industrial revolution.

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Economic relevance

2. Nanotechnology Markets

2.1 Market growth and size

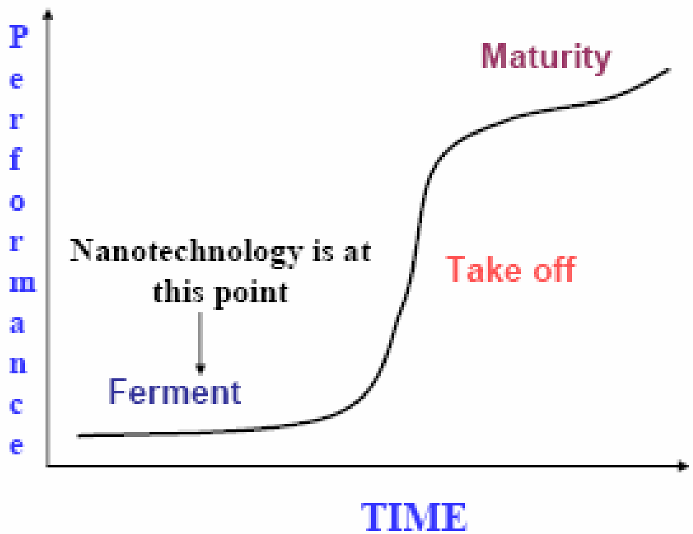
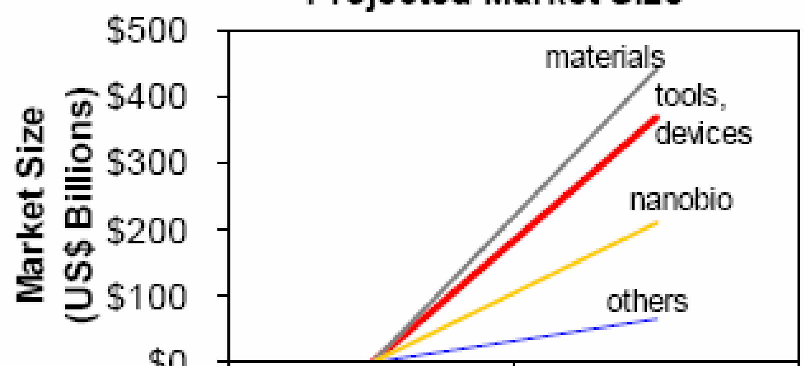
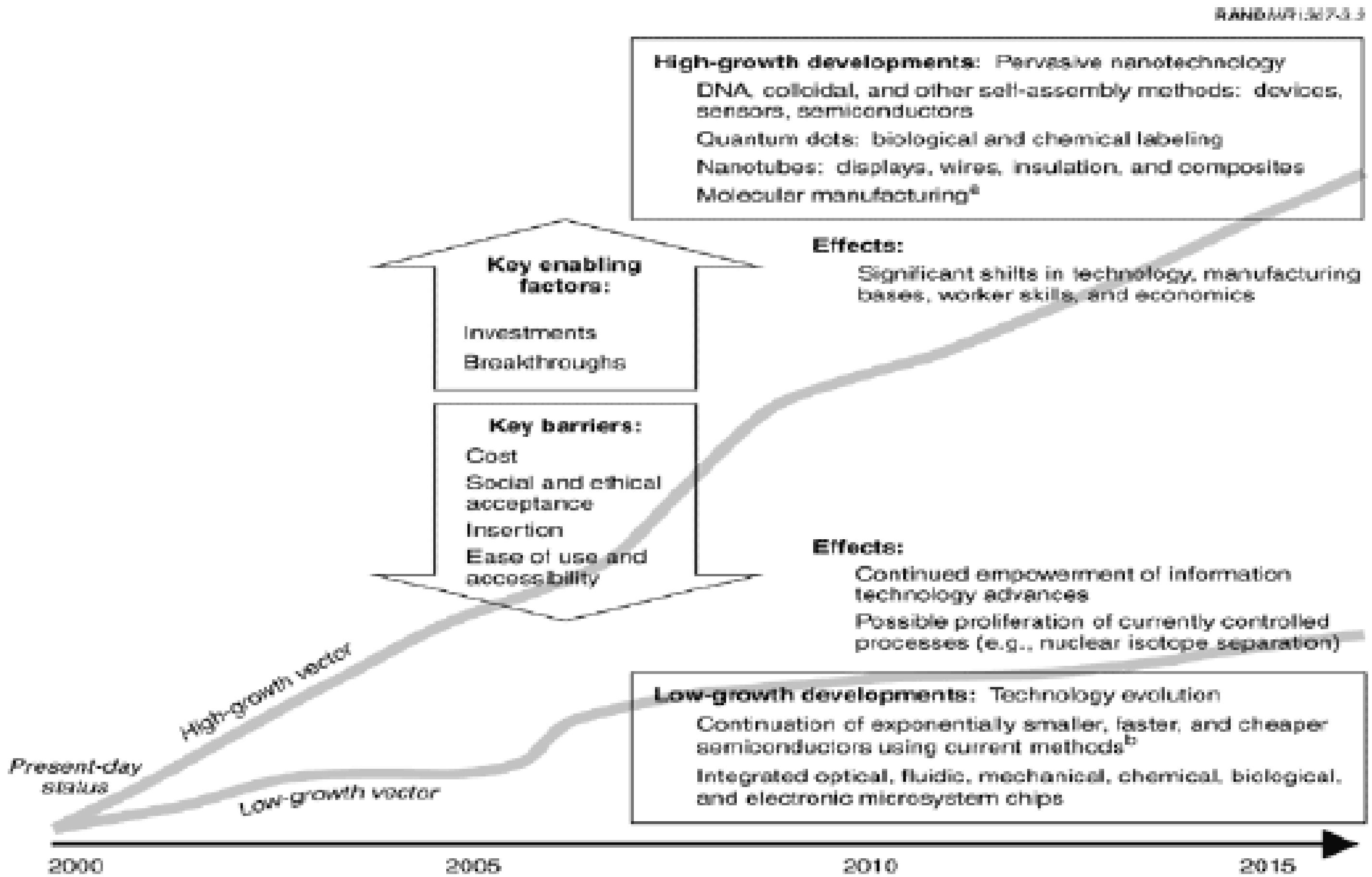


Figure 1: A clear point in the industrial life cycle of nanotechnology development



	1990-2000	2000-2010
Tool and devices	$0	$370
Others	$0	$65
Materials	$0.13	$440
Nanobio	$0	$210

Figure 2: Market size vs. Time for all Nanotechnology Products



[a]See Drexler, 1987, 1992 [162, 163].

[b]See SEMATECH, 1999 [190].

Figure 3: Range of Possible Future Developments of Nanotechnology

Fields of application

- While nanotechnology is in the “pre-competitive” stage (meaning its applied use is limited), nanoparticles are being used in a number of industries. Nanoscale materials are used in electronic, magnetic and optoelectronic, biomedical, pharmaceutical, cosmetic, energy, catalytic and structural applications. Areas producing the greatest revenue for nanoparticles reportedly are chemical-mechanical polishing, magnetic recording tapes, sunscreens, automotive catalyst supports, biolabeling, electroconductive coatings and optical fibers.

- Today most computer hard drives contain giant magnetoresistance (GMR) heads that, through nano-thin layers of magnetic materials, allow for an order of magnitude increase in storage capacity. Other electronic applications include non-volatile magnetic memory, automotive sensors, landmine detectors and solid-state compasses.

- Nanomaterials, which can be purchased in dry powder form or in liquid dispersions, often are combined with other materials today to improve product functionality.

- Step assists on vans
- Bumpers on cars
- Paints and coatings to protect against corrosion, scratches and radiation
- Protective and glare-reducing coatings for eyeglasses and cars
- Metal-cutting tools
- Sunscreens and cosmetics
- Longer-lasting tennis balls
- Light-weight, stronger tennis racquets
- Stain-free clothing and mattresses
- Dental-bonding agent
- Burn and wound dressings
- Ink
- Automobile catalytic converters.

Nanotechnology is rapidly advancing, with more than 300 nanoproducts already on the market.

Future Applications

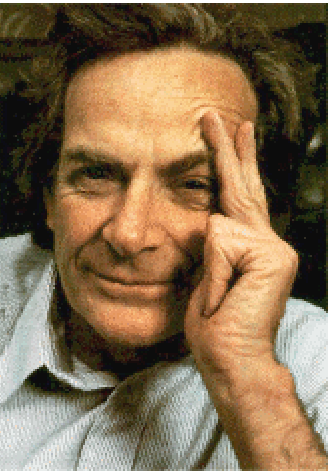
The pharmaceutical and chemical industries are being impacted greatly by nanotechnology. New commercial applications of nanotechnology that are expected in two to five years in these and other industries include:

- Advanced drug delivery systems, including implantable devices that automatically administer drugs and sensor drug levels;
- Medical diagnostic tools, such as cancer tagging mechanisms and lab-on-a-chip, real time diagnostics for physicians;
- Cooling chips or wafers to replace compressors in cars, refrigerators, air conditioners and multiple other devices, utilizing no chemicals or moving parts;
- Sensors for airborne chemicals or other toxins;
- Photovoltaics (solar cells), fuel cells and portable power to provide inexpensive, clean energy, and
- New high-performance materials.

National Nanotechnology Initiative USA (since 1996)

Recent achievements in nanotechnology funded in whole or in part by the National Nanotechnology Initiative:

- **Use of the bright fluorescence of semiconductor nanocrystals (quantum dots) for dynamic angiography in capillaries hundreds of micrometers below the skin of living mice—about twice the depth of conventional angiographic materials and obtained with one-fifth the irradiation power.**
- **Nano-electro-mechanical sensors that can detect and identify a single molecule of a chemical warfare agent—an essential step toward realizing practical field sensors.**
- **Nanocomposite energetic materials for propellants and explosives that have over twice the energy output of typical high explosives.**
- **Prototype data storage devices based on molecular electronics with data densities over 100 times that of today's highest density commercial devices.**
- **Field demonstration that iron nanoparticles can remove up to 96% of a major contaminant (trichloroethylene) from groundwater at an industrial site.**



"There's Plenty of Room at the Bottom"

An Invitation to Enter a New Field of Physics

Richard P. Feynman 1959

(annual meeting of the American Physical Society at the California Institute of Technology)

"The principles of physics, as far as I can see, do not speak against the possibility of maneuvering things atom by atom. It is not an attempt to violate any laws; it is something, in principle, that can be done; but in practice, it has not been done because we are too big. "

"Rearranging the atoms

But I am not afraid to consider the final question as to whether, ultimately---in the great future---we can arrange the atoms the way we want; the very *atoms*, all the way down! What would happen if we could arrange the atoms one by one the way we want them (within reason, of course; you can't put them so that they are chemically unstable, for example)."

The special laws of quantum mechanics
"*on a small scale*"

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"Atoms on a small scale behave like *nothing* on a large scale, for they satisfy the laws of quantum mechanics. So, as we go down and fiddle around with the atoms down there, we are working with different laws, and we can expect to do different things. We can manufacture in different ways. We can use, not just circuits, but some system involving the quantized energy levels, or the interactions of quantized spins, etc."

Richard P. Feynman 1959

First example: melting temperature

Nanoparticles $R > 15$ nm (Semenchenko)

$$T_M = T_0 \exp\left(-\frac{2\gamma_{sl}}{\rho L R}\right)$$

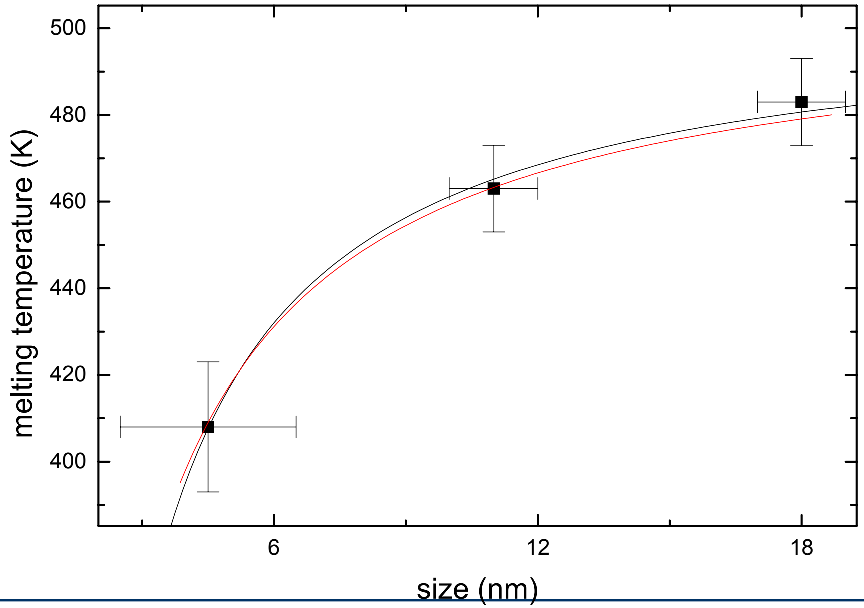
T_M particle melting temperature

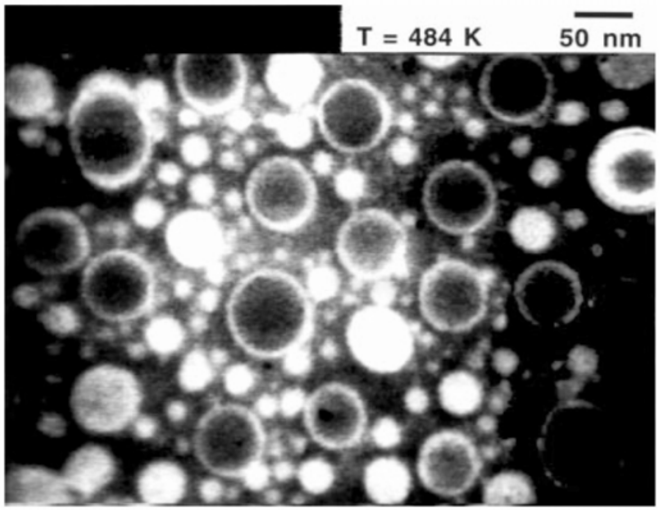
T_0 bulk melting temperature

ρ volume mass density

L latent heat of fusion

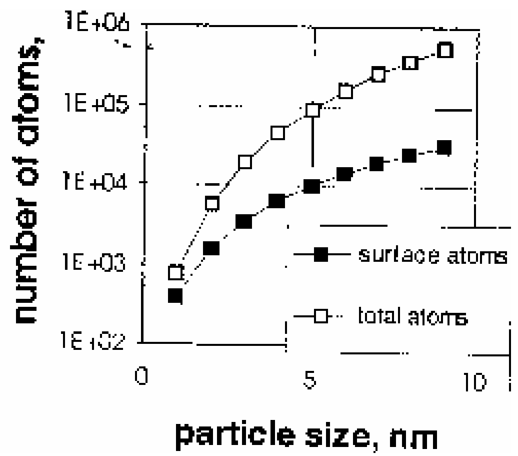
γ_{sl} interfacial free energy between solid and liquid



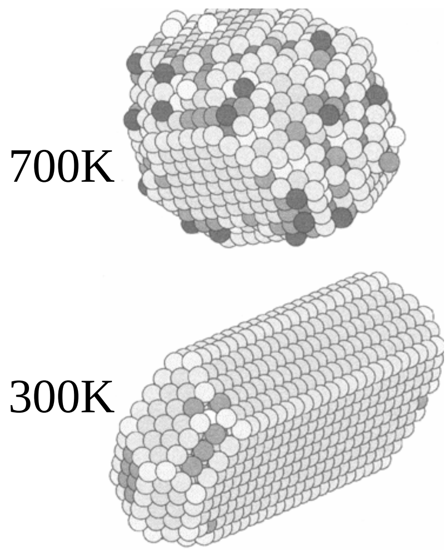


Nanoclusters (aggregates of 10-1000 atoms)

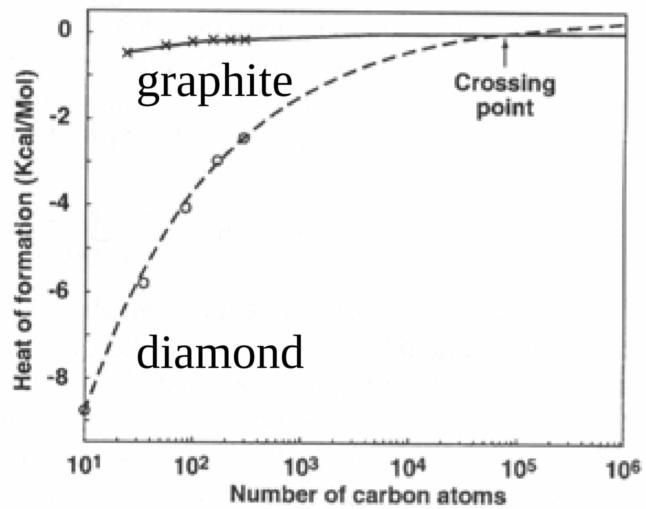
Surface role



Shape changing



Phase stability vs size



Critical parameter: fraction of surface atoms

The atomic structure of matter

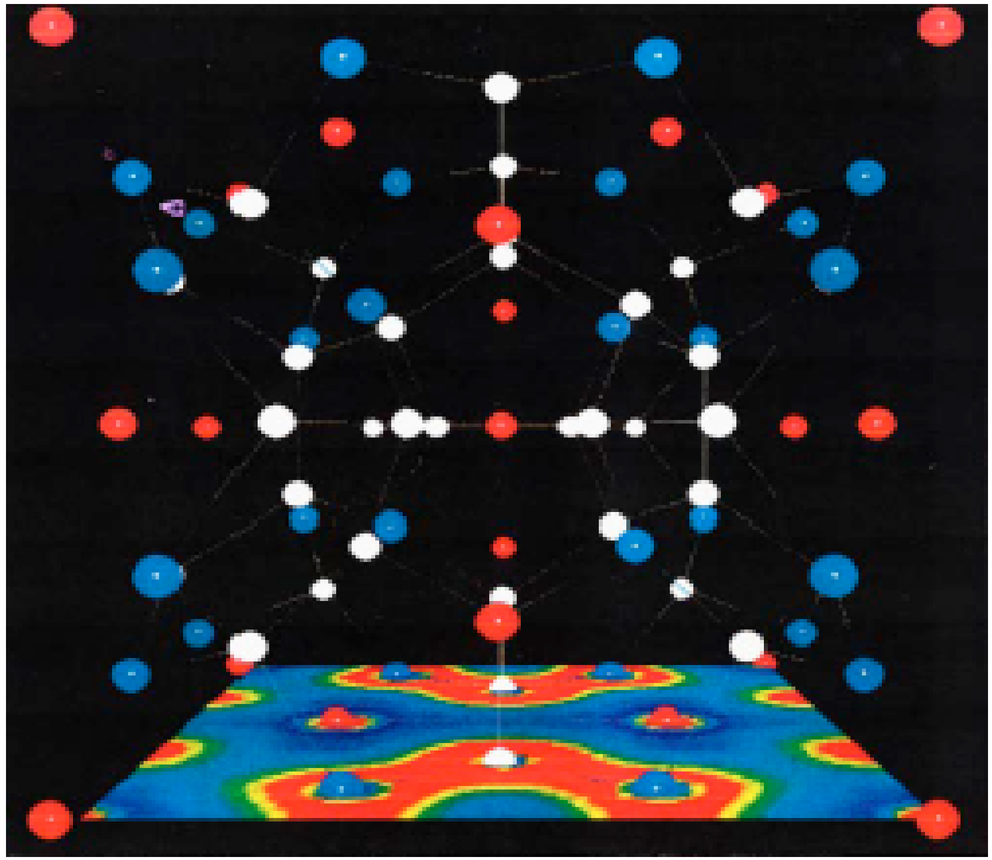


FIG. 2. The geometric structure of the clathrate $Sr_8Ga_{16}Ge_{30}$ (Sr, red; Ga, blue; Ge, white) and its charge density in a plane bisecting the centers of the cages. DFT calculations have shown that the Sr atoms are weakly bound and scatter phonons effectively, thereby lowering thermal conductivity. However, contrary to intuitive expectations, the Sr atoms do not donate electrons to the frame and are practically neutral. Conductivity is due to electrons traveling through the frame, not through the one-dimensional Sr "wires" in the structure; there is thus little scattering of conduction electrons by Sr vibrations. For these reasons, the compound is a metal with a large Seebeck coefficient (unlike ordinary metals). The calculation suggests that other compounds of this type may be even better thermoelectrics (theory by N. P. Blake and H. Metiu, submitted for publication) [Color].

"…it should be possible to see the individual atoms. What good would it be to see individual atoms distinctly?"

There's Plenty of Room at the Bottom

An Invitation to Enter a New Field of Physics

by Richard P. Feynman **1959**

This transcript of the classic talk that Richard Feynman gave on December 29th 1959 at the annual meeting of the American Physical Society at the California Institute of Technology was first published in the February 1960 issue of Caltech's Engineering and Science, which owns the copyright.

John Dalton (1766-1844) was born into a poor family near Manchester, England. He supported himself to some extent by teaching from the age of twelve, when he started his own small Quaker school. Dalton wrote ***A New System of Chemical Philosophy***, from which the following quotes are taken:

Matter, though divisible in an* extreme degree*, is nevertheless not* infinitely *divisible. That is, there must be some point beyond which we cannot go in the division of matter. The existence of these ultimate particles of matter can scarcely be doubted, though they are probably much too small ever to be exhibited by microscopic improvements. I have chosen the word* atom *to signify these ultimate particles … .

Do atoms *exist* ?

No one experimental result exists regarding the geometric shape of a particle or even of an atom. It is true that, thinking of an atom, in the effort for formulating theories in agreement with the experimental facts, very often we have to draw a geometric sketch on the blackboard, or on a piece of paper, or more often only in our mind, while the precise details of the representation are given by a mathematical formula. […] Yet the geometric forms shown in those drawings do not represent anything one could directly observe in real atoms. […] It is certainly an *adequate* description; but as far as its *truthfulness* is concerned, the important question to be asked is not whether it is true or false, but whether it has the possibility of being true or false. Most probably, this possibility does not exist.

Erwin Schroedinger – *Science and Humanism. Physics in our time* (1953)

Percy W. Bridgman 1959

"…it seems to me that facts prove that theoretical physicists profitably employ concepts which by no means can be reduced to instrumental operations. Quantum mechanics is full of such examples: the wave function Ψ is perhaps the simplest"

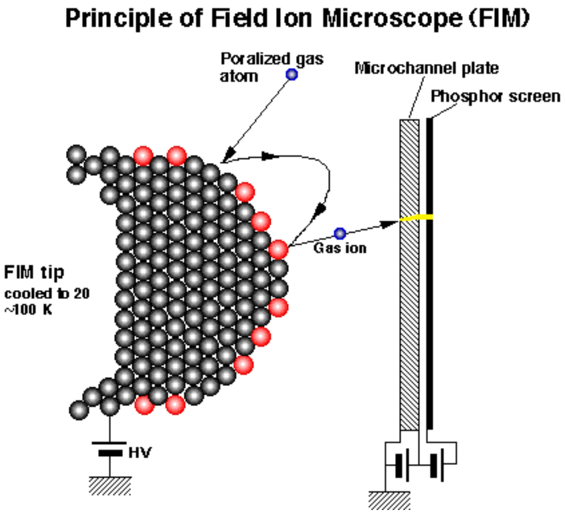
"I have already pointed out that, being strictly rigorous, something like a *microscopic world* does not exist, but simply a modified world of macroscopic experience does. A different way to say that our meanings are to be looked for at the macroscopic level is to say that the isolation operation fails when we try to apply it at the microscopic level".

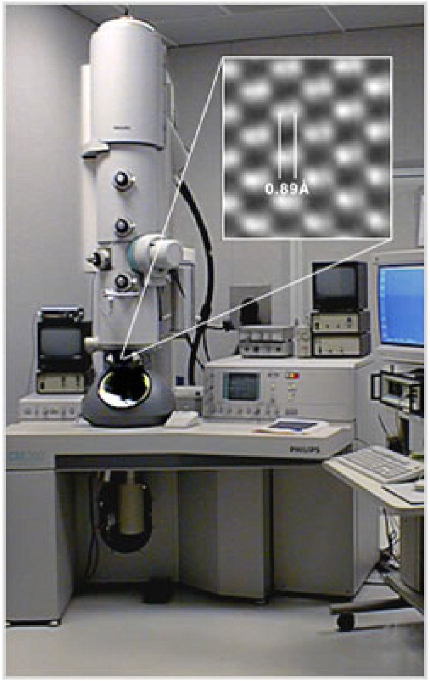
(P.W. Bridgman, 1882-1961, Nobel laureate 1946,

in *The way things are,*

Harvard University Press, Cambridge, Mass., 1959).

2005: 50 years since the first image with atomic resolution





TEM

Field ion microscope

Erwin Wilhelm Müller

Invention 1951

Atomic resolution 1955

J.W. Menter 1956

first HRTEM with resolution

better than 4 Å about 1970

Press Release: The 1986 Nobel Prize in Physics

15 October 1986

The Royal Swedish Academy of Sciences has decided to award the 1986 Nobel Prize in Physics by one half to

1931

Professor. **Ernst Ruska**, Fritz-Haber-Institut der Max-Planck-Gesellschaft, Berlin, Federal Republic of Germany, **for his fundamental work in electron optics, and for the design of the first electron microscope**

and the other half, jointly to

1982

Dr **Gerd Binnig** and Dr **Heinrich Rohrer**, IBM Research Laboratory, Zurich, Switzerland, **for their design of the scanning tunnelling microscope**.

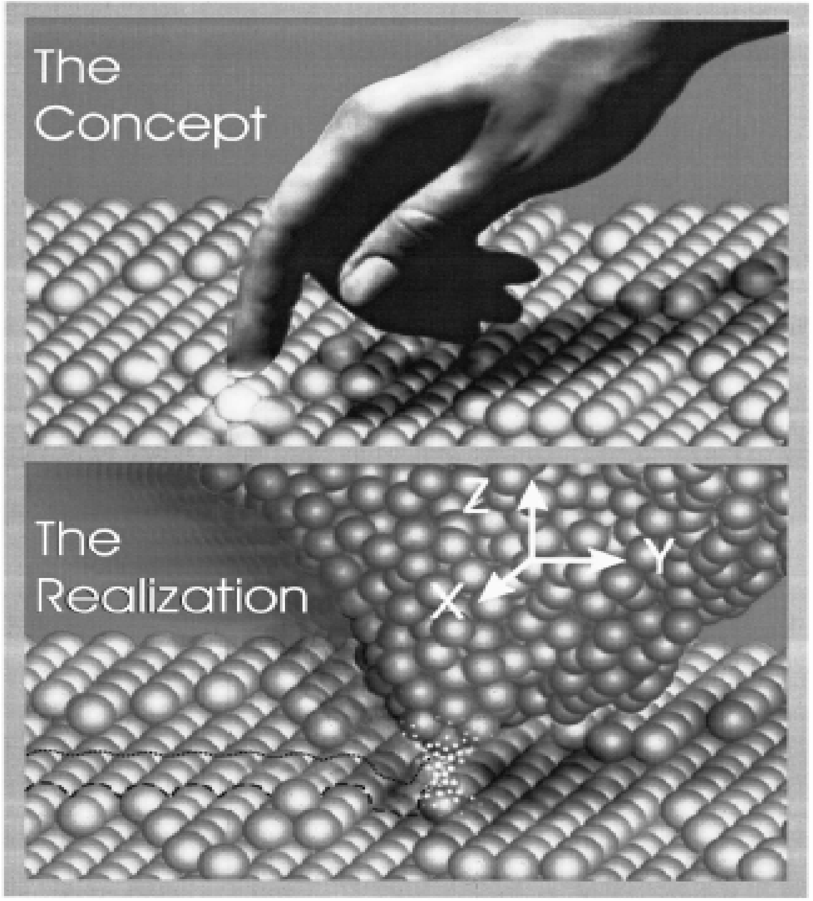
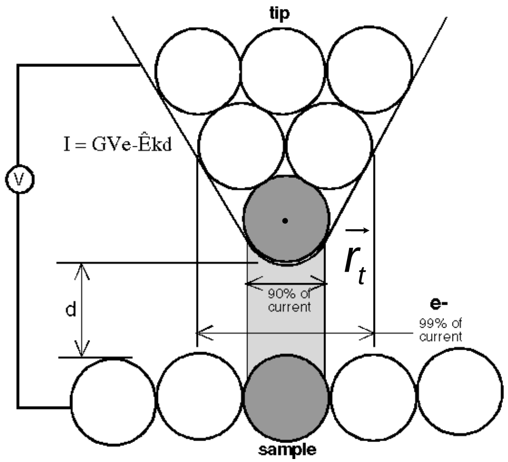


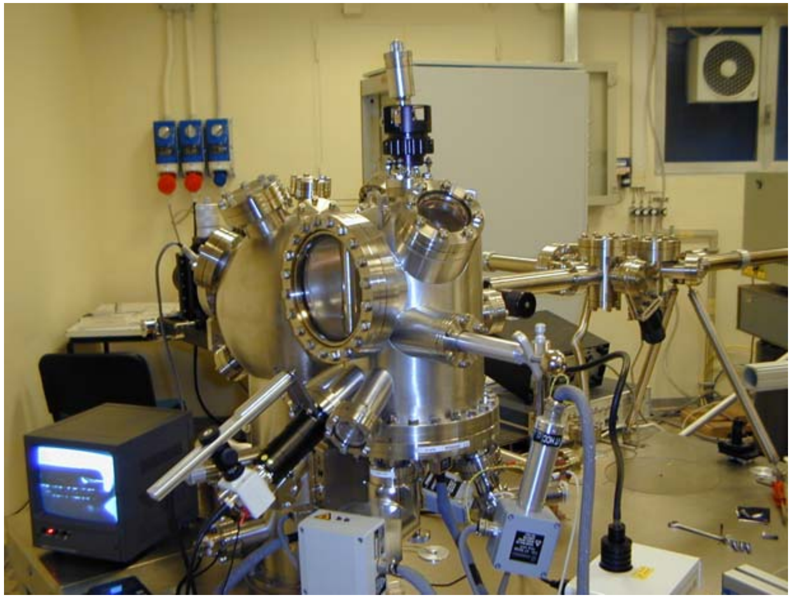
FIG. 1. Principle of a local probe: The gentle touch of a nanofinger. If the interaction between tip and sample decays sufficiently rapidly on the atomic scale, only the two atoms that are closest to each other are able to "feel" each other.

Scanning Tunneling Microscopy (STM)



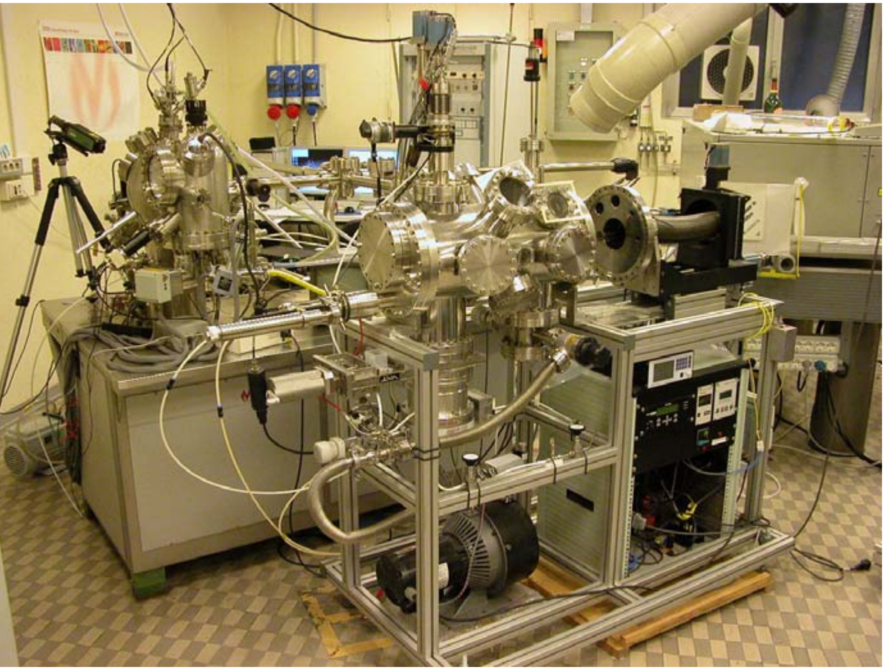
$$I \propto T = \exp(-2\sqrt{2m\phi/\hbar^2}\,z)$$

$$\frac{dI}{dV} \propto T \sum_j |\psi_j(\vec{r}_t)|^2\, \delta(E_F + eV - E_j)$$



-Scanning tunneling spectroscopy (electronic surface density of states)
- Current Imaging Tunneling Spectroscopy

Micro- and Nano-Structured Materials Laboratory



http://www.nanolab.polimi.it

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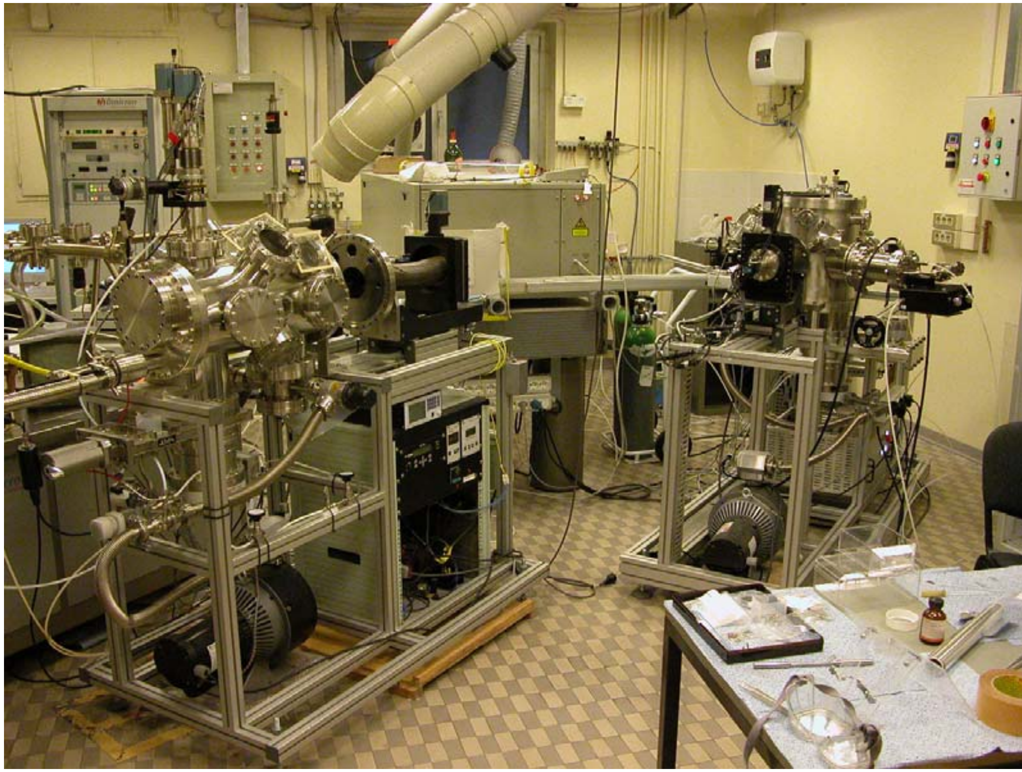
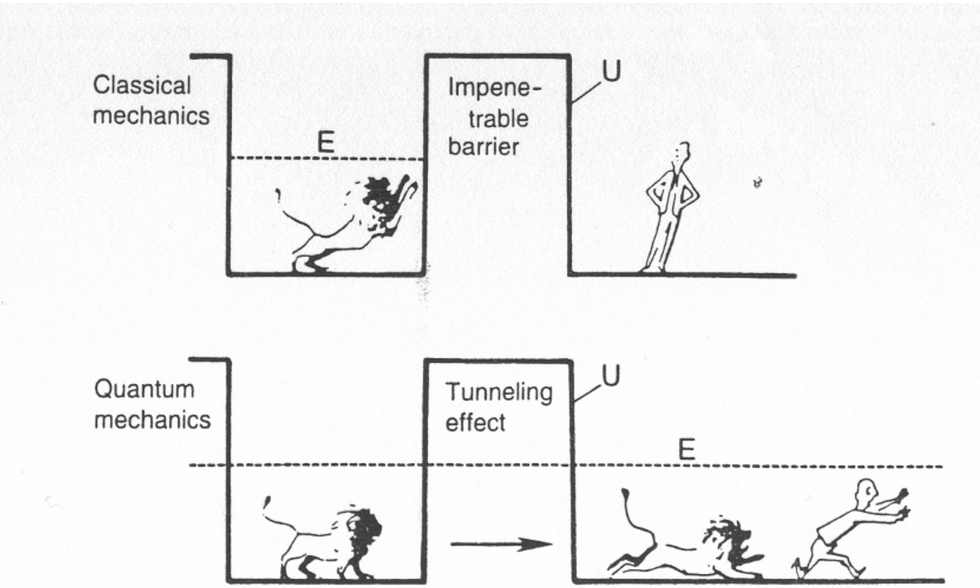
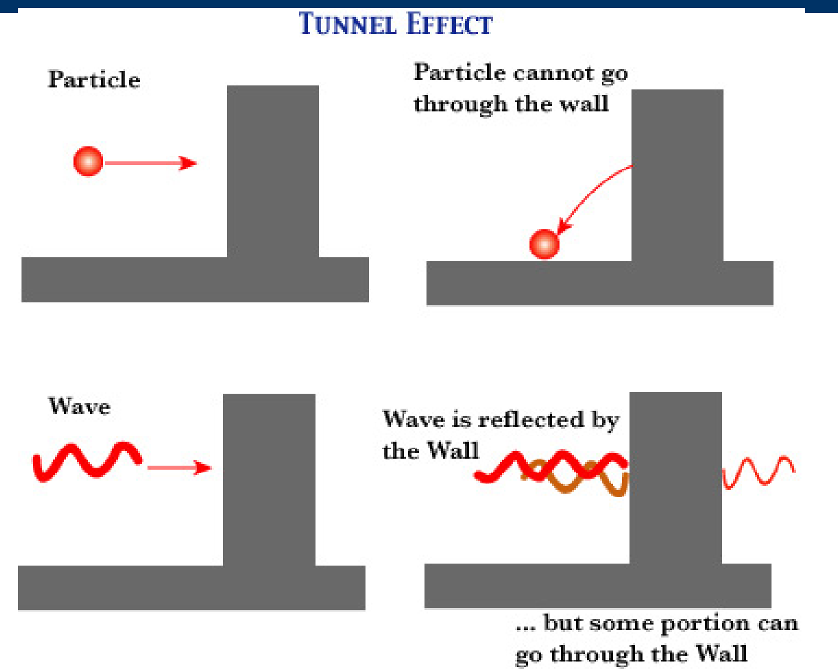
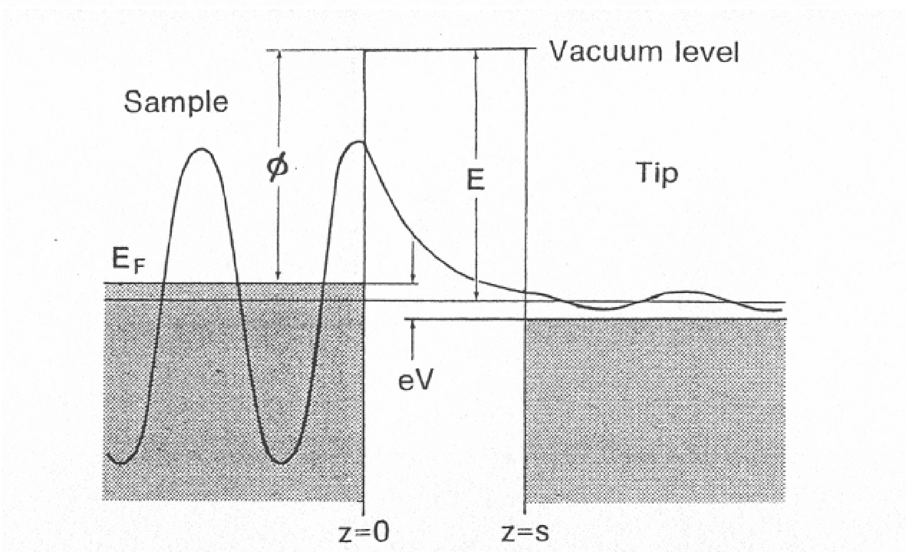
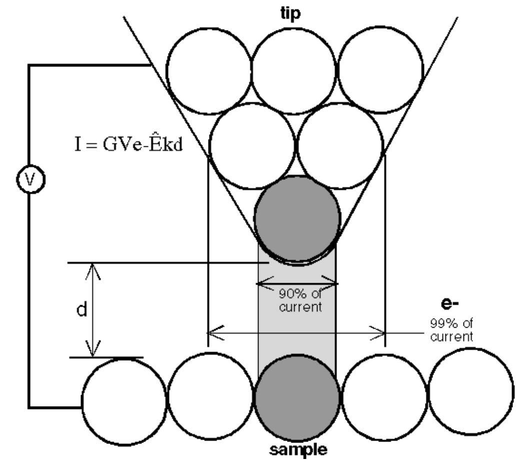


Tunnel effect and Heisenberg uncertainty principle

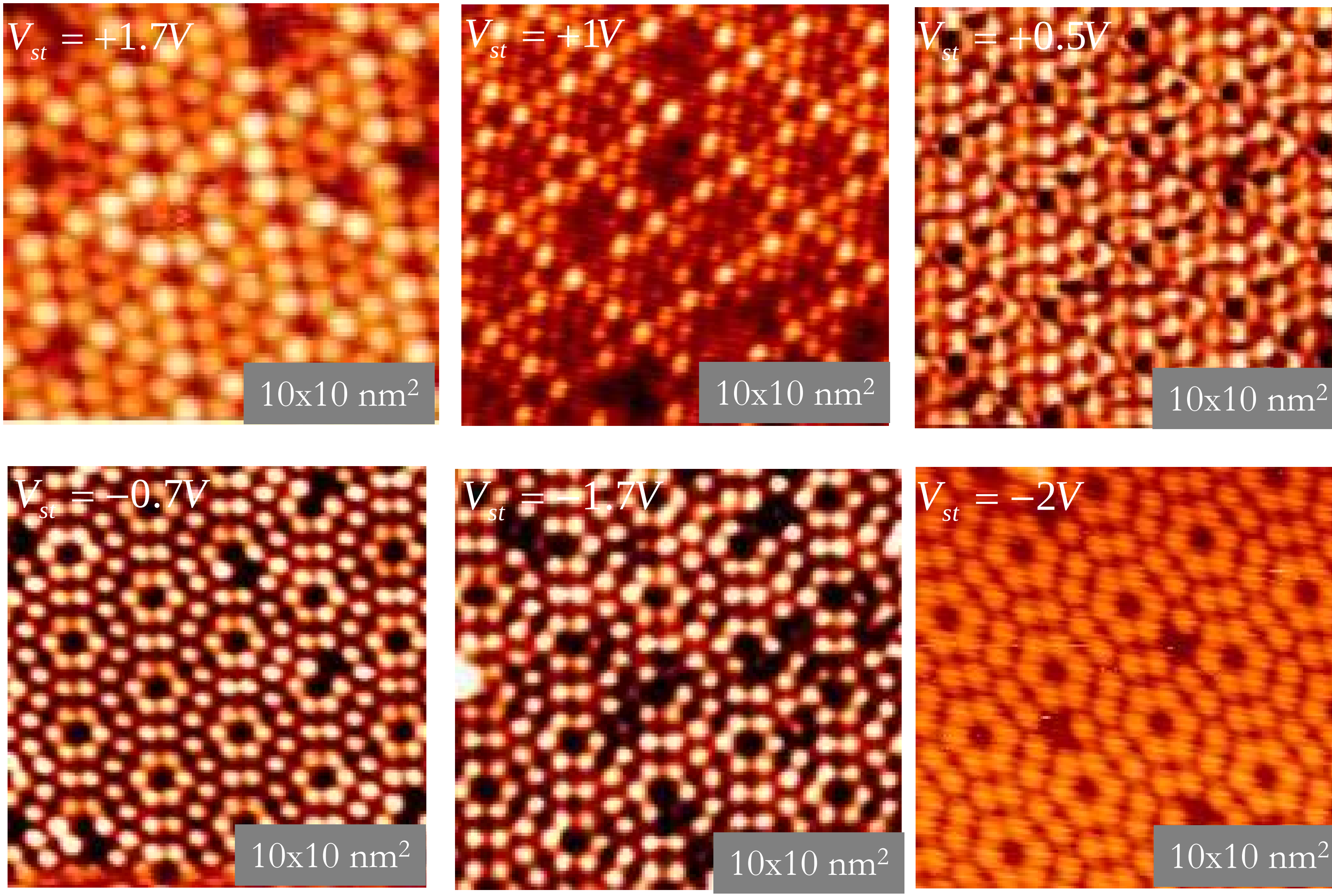




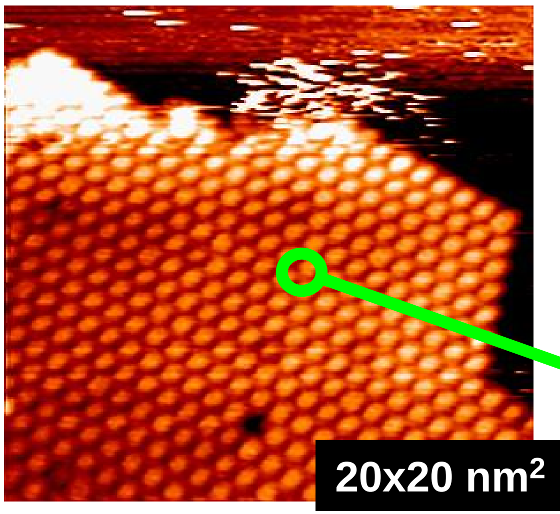


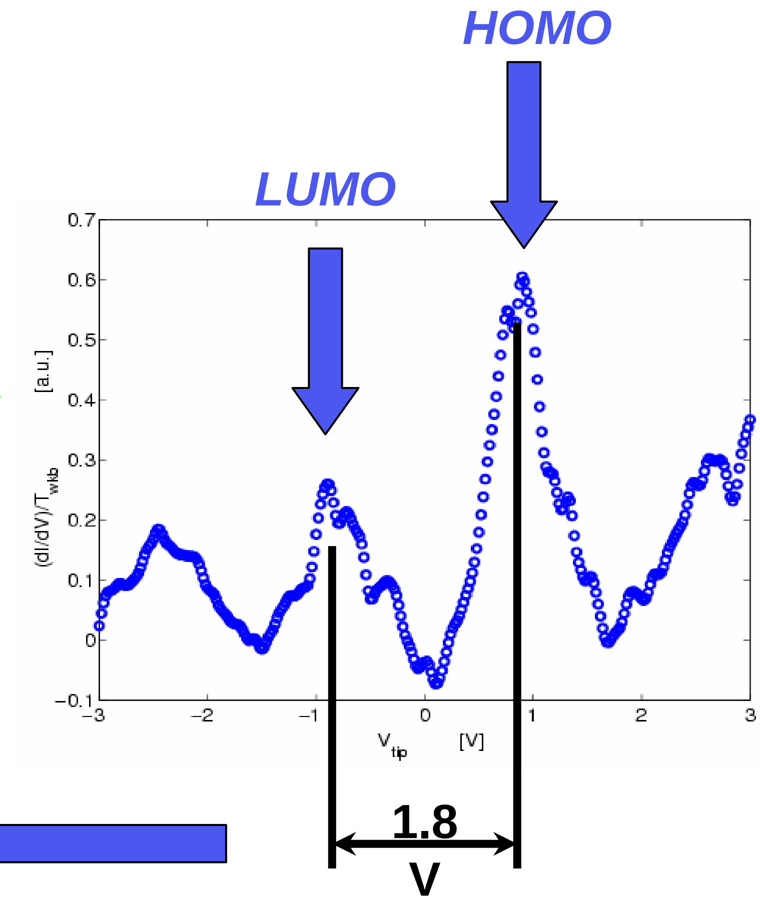


Imaging *occupied* and *empty* states



Local STS measurements on C60 deposited on Au(111)





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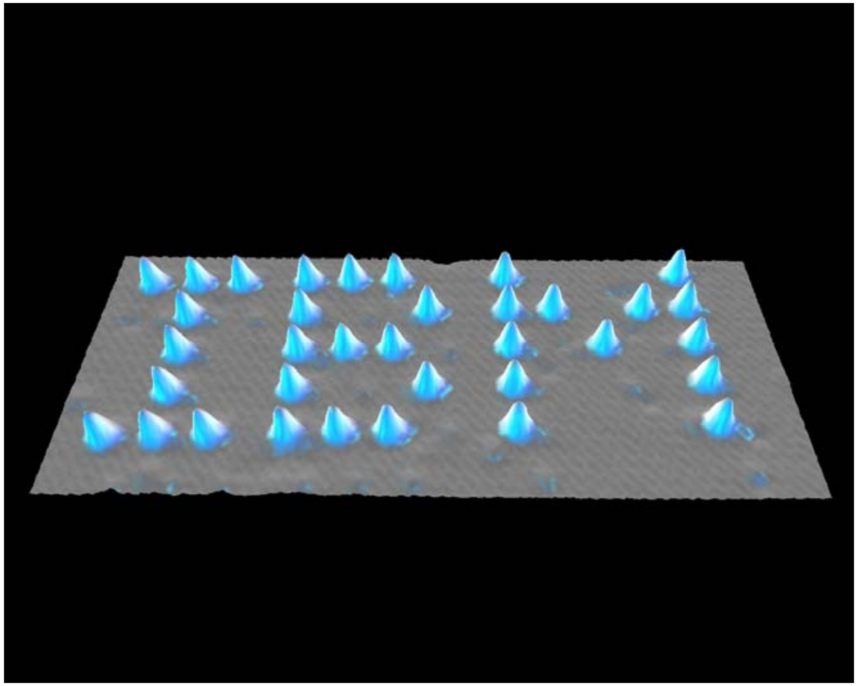
numeric simulations data 1.9 eV

Writing with atoms and manipulating atoms



Xenon on Nickel (110)

G. Binnig and H. Rohrer: In touch with atoms S327

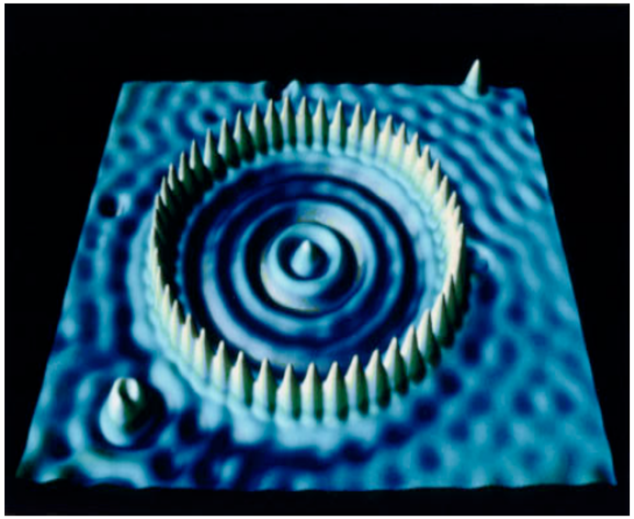


FIG. 2. (Color) STM image of a quantum corral for electrons built with 48 iron atoms on copper. The same tip is used to position the iron atoms into a 12.4-nm-diameter ring and to image them and the wave-structure interior caused by the confined surface-state copper electrons. Courtesy D. Eigler, IBM Research Center, Almaden, CA.

E. Schrödinger.

***Quantisation as an eigen value problem,* Annalen der Physik, 79 (4) p. 361 (1926)**

$$i\hbar\frac{\partial\Psi}{\partial t}=\hat{H}\Psi$$

$$\hat{H}=-\frac{\hbar^2}{2m}\nabla^2+U(\vec{r})$$

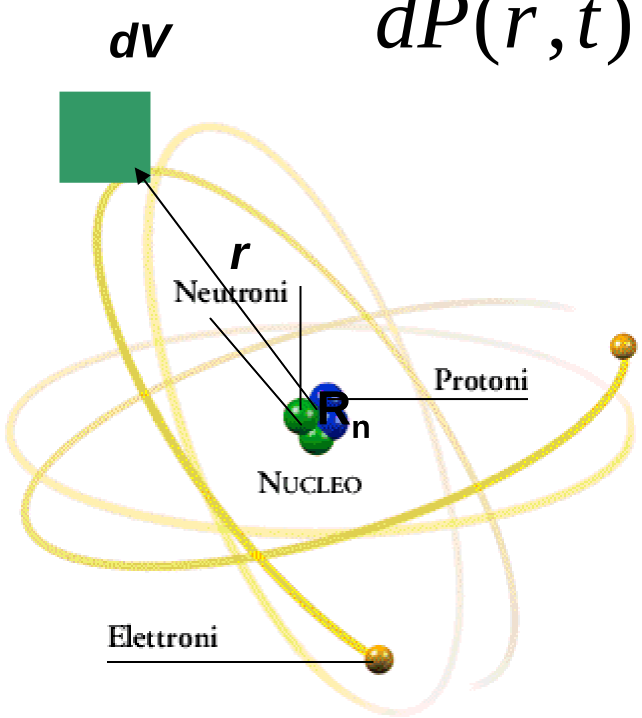
$$\Psi(\vec{r},t)=\psi(\vec{r})e^{-i\frac{E}{\hbar}t}$$

$$-\frac{\hbar^2}{2m}\nabla^2\psi(\vec{r})+U(\vec{r})\psi(\vec{r})=E\psi(\vec{r})$$

Schrödinger

Max Born

The “planetary” structure of the atom substituted by a probabilistic description



$$dP(\vec{r},t) = |\Psi(\vec{r},t)|^2 dV$$

$$R_a \approx 10^{-10} m$$

$$R_n \approx A^{1/3} 10^{-15} m$$

$$R_e \approx 0\,?$$

Today to *directly see* an atom means to see its *independent* electrons orbitals that is

“to see probability waves”

D.R.Hartree – Proc. Camb. Phil. Soc. 24, p. 111-132 (1927)

$$\Psi(\vec{r}_1,\vec{r}_2,\ldots,\vec{r}_i,\ldots,\vec{r}_Z)=\psi_1(\vec{r}_1)\psi_2(\vec{r}_2)\ldots\psi_i(\vec{r}_i)\ldots\psi_Z(\vec{r}_Z)$$

$$-\frac{\hbar^2}{2m}\nabla^2\psi_i(\vec{r}_i)+U_{eff}(r_i)\psi_i(\vec{r}_i)=E_i\psi_i(\vec{r}_i)$$

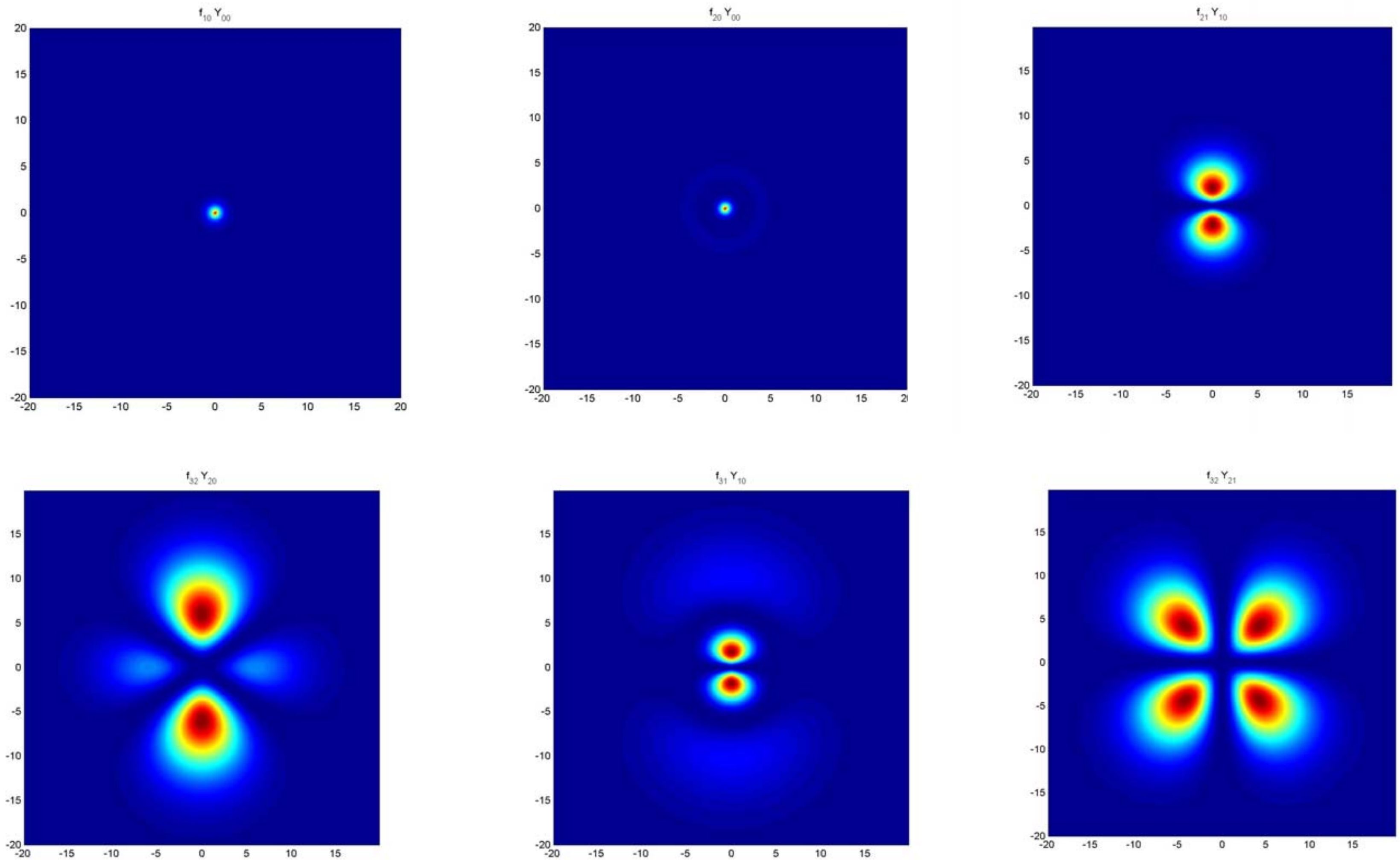
$$U_{eff}(r_i)=-\frac{Ze^2}{r_i}+\left\langle\sum_{j\neq i}^{1,Z}\frac{e^2}{r_{ij}}\right\rangle$$

mean field

$$d\Omega_i = \sin\vartheta_i d\vartheta_i d\varphi_i$$

$$\left\langle\sum_{j\neq i}^{1,Z}\frac{e^2}{r_{ij}}\right\rangle=\frac{1}{4\pi}\int\left(e^2\sum_{j\neq i}^{1,Z}\int\frac{\left|\psi_j(\vec{r}_j)\right|^2}{\left|\vec{r}_j-\vec{r}_i\right|}d\vec{r}_j\right)d\Omega_i$$

$$\psi_{nlm_l m_s}(r,\vartheta,\varphi) = \frac{F_{nl}(r)}{r} Y_{lm_l}(\vartheta,\varphi)\chi_{m_s}$$



Atomic number : 37

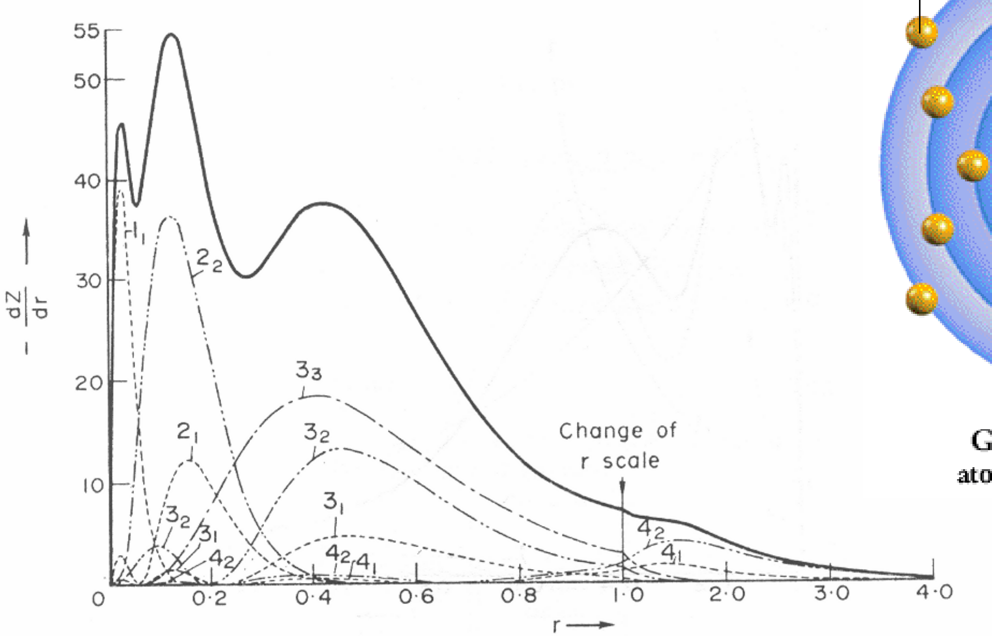
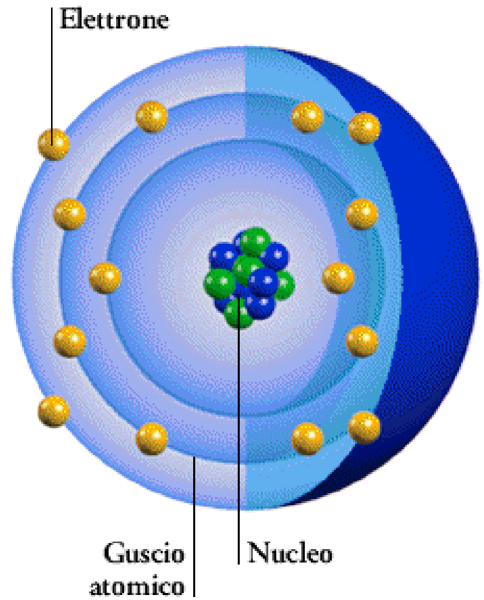


FIG. 2. Radial distribution of charge for Rb^+ and contributions from different groups of core electrons. Radial density $-(dZ/dr)$ in electrons per atomic unit plotted against r in atomic units. ——— Total for all core electrons ········· Contributions from groups with $l = 0$ $(k = 1)$ —··—··— Contributions from groups with $l = 1$ $(k = 2)$ —— – —— – Contributions from groups with $l = 2$ $(k = 3)$

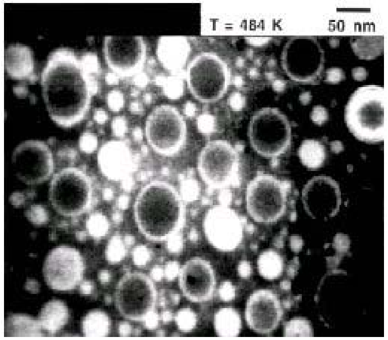


Wolfgang Pauli

Thermodynamic potential

Statistics

$$F = U - TS = -k_B T \ln Z$$



$$Z = \sum_n g_n e^{-\frac{E_n(\text{chem, size, stress})}{k_B T}}$$

Atomic energy levels

Symmetry

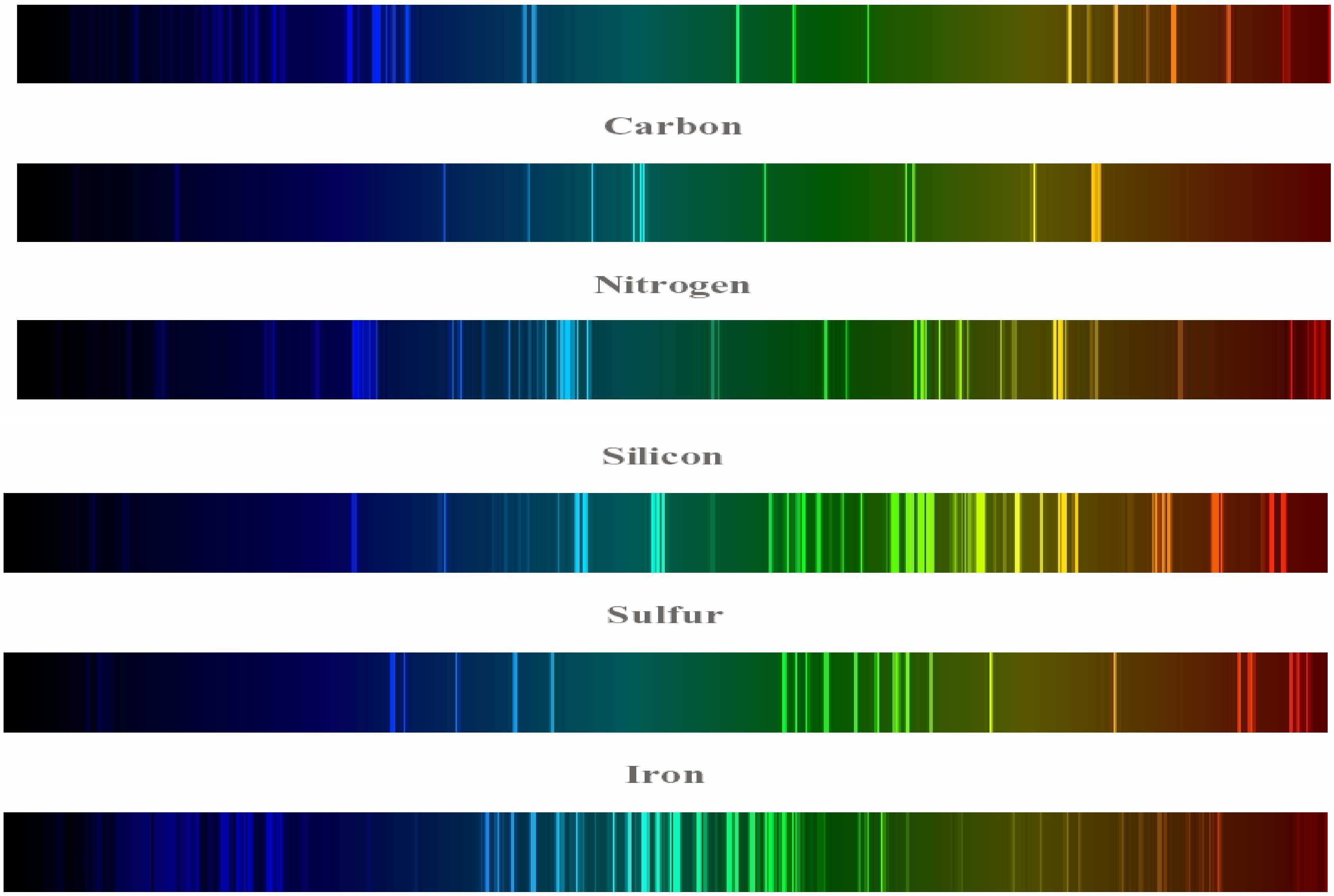
Joint density of states

Absorption coefficient

$$\sigma(\omega) = \frac{\pi e^2 \omega}{V} \sum_{ij} \left| \langle \psi_j | \vec{n} | \psi_i \rangle \right|^2 \left(f(E_j) - f(E_i) \right) \delta\left(E_j - E_i - \hbar\omega \right)$$

Pauli principle

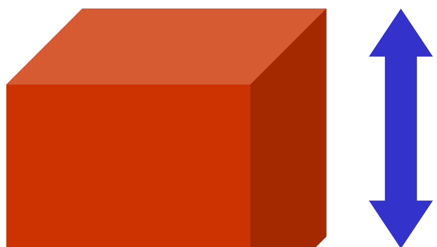
Discrete energy levels: line spectra of atoms



How many atoms in a given volume? (solid state)

•0.1 nm 1 atom

•2.5 nm 10x10x10=1000 atoms



L_i

•100 nm 50000000 di atoms

Si Wafer

• 0.01 m more than 1000000000000000000000 atoms

The density of states (DOS) of the confined free electron gas

$$E(\vec{k}) = \frac{\hbar^2}{2m^*}\sum_{i=1}^{D} k_i^{\,2}$$

m*** ***effective mass***, ***D*** **dimension**, ***a_i* *lattice spacing***

N_i* *number of lattice cells in i-direction

$$k_i = \frac{2\pi}{N_i a_i}\left(0,\pm1,\pm2,\ldots\right)$$

Traveling waves, no confinement: N_i>>10

Continuous spectrum of energy levels

like in bulk solids

$$k_i = \frac{\pi}{N_i a_i}\left(1,2,3,\ldots\right)$$

Standing waves, confinement: N_i<10

Discrete spectrum of energy levels

like in atoms

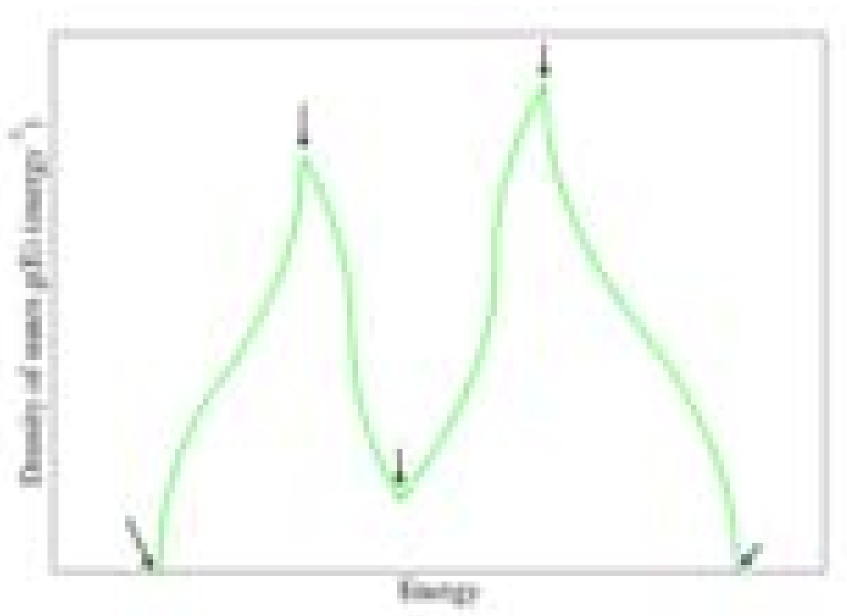
Density of states (DOS)

$$DOS = g(E) = \sum_{\vec{k}} \delta(E - E(\vec{k})) = \frac{V}{4\pi^3} \int \frac{dS_{\vec{k}}}{\left|\nabla E(\vec{k})\right|}$$

$\nabla E(\vec{k}) = 0$ **Van Hove singularities**

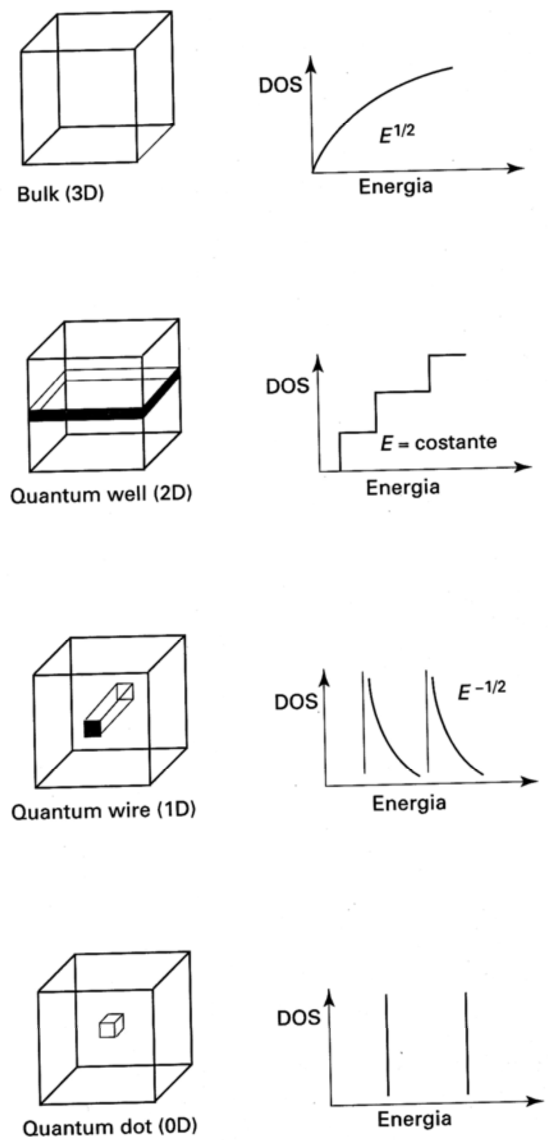
$$\frac{dg}{dE} = \infty$$

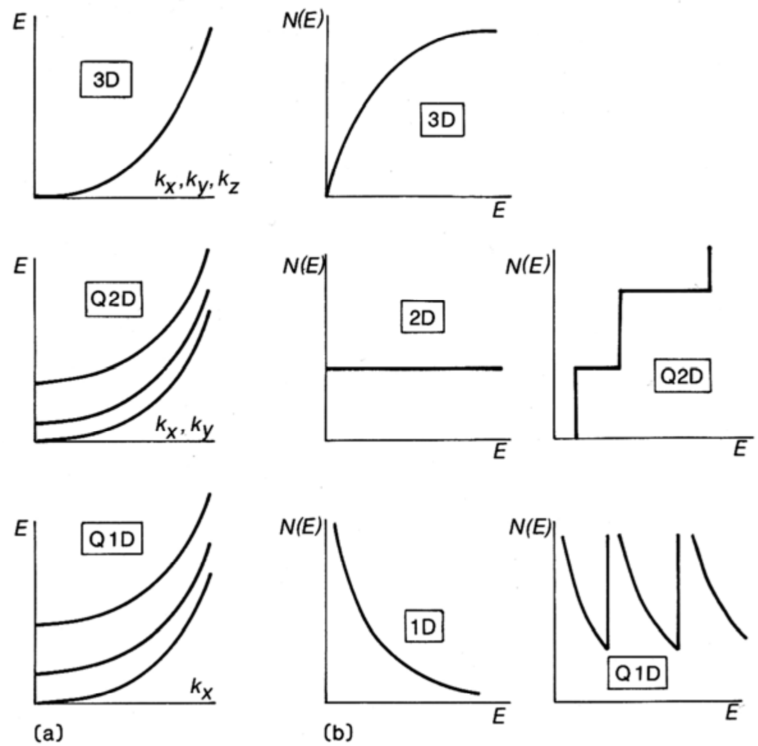
$g(E)$



E

The role of dimensionality and size: the free electron gas DOS





Continuous energy levels: band spectra of solids

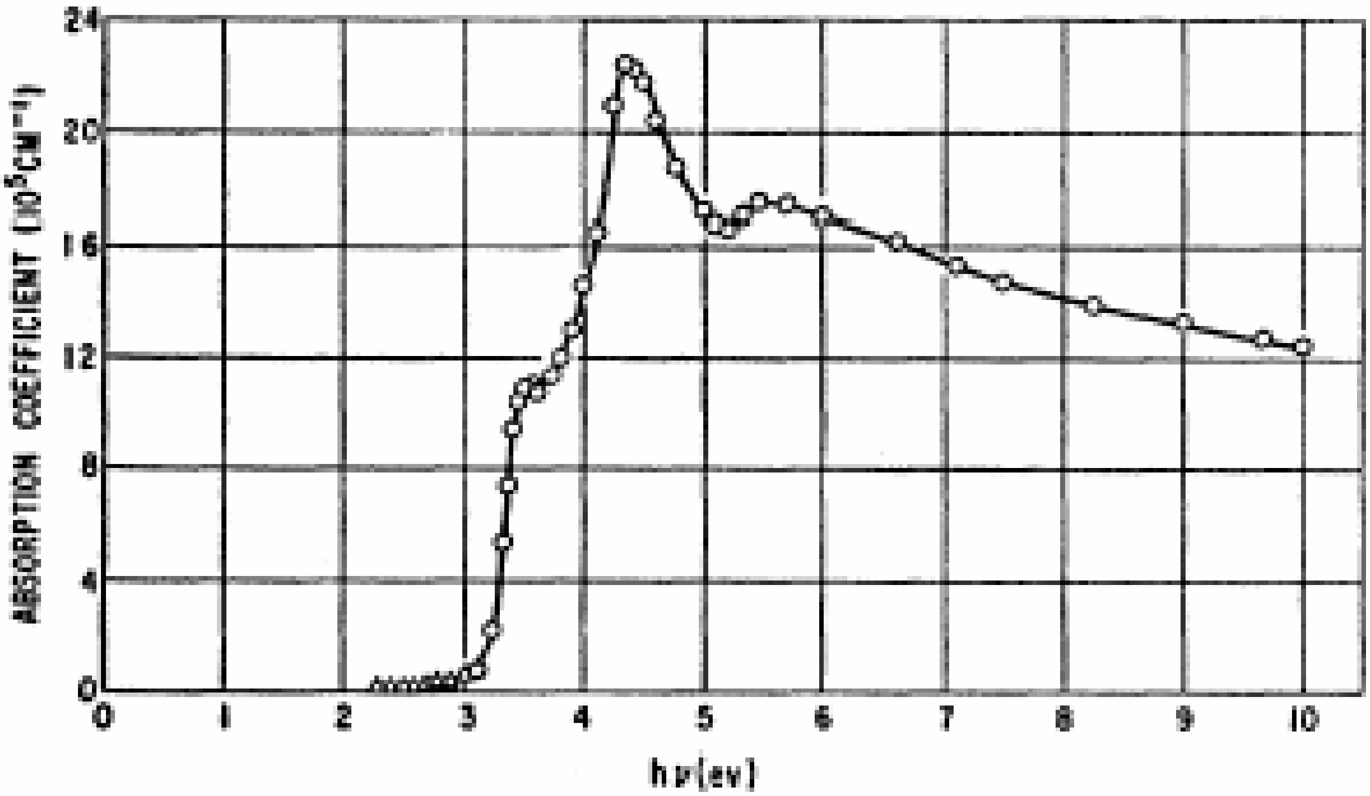
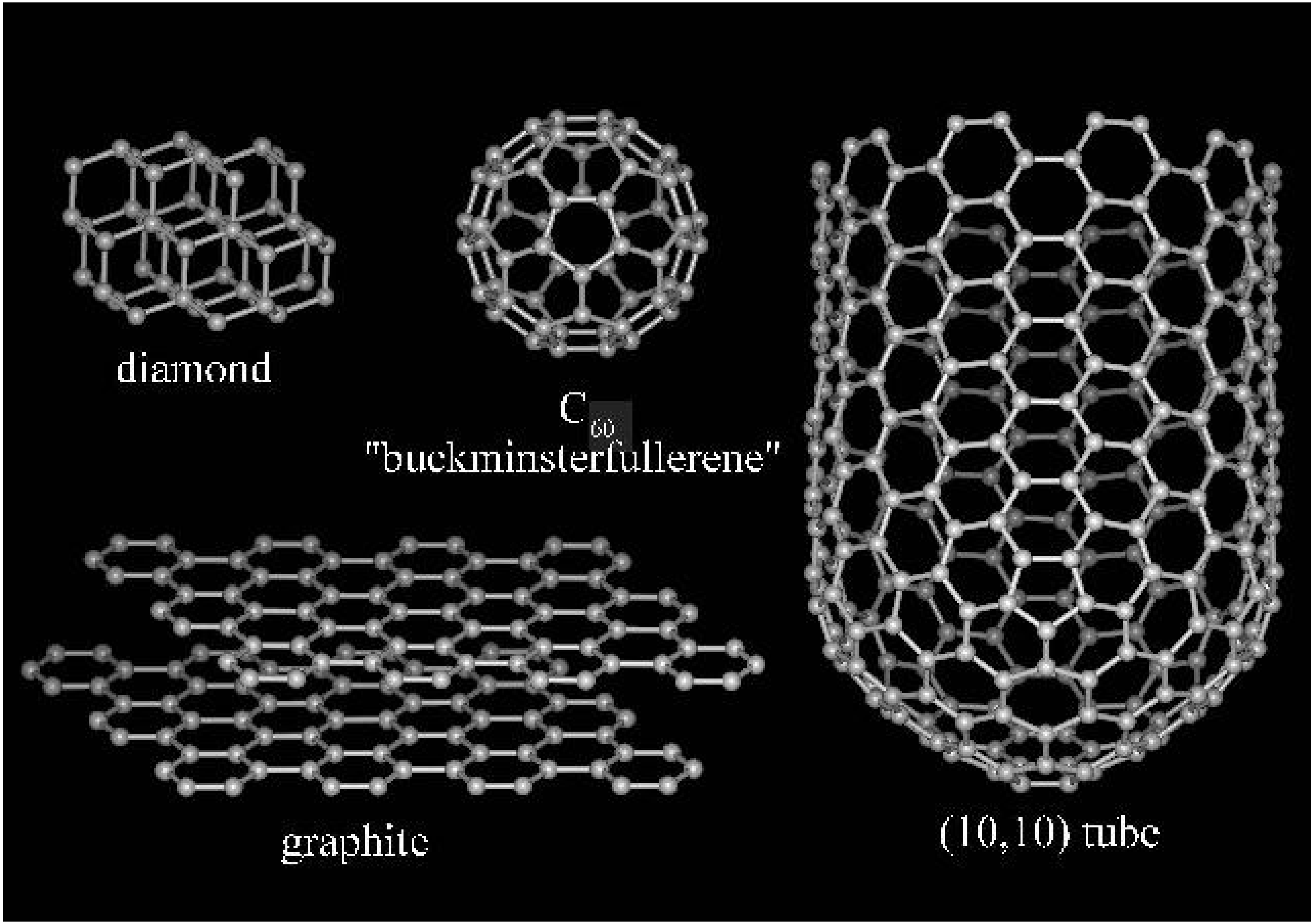
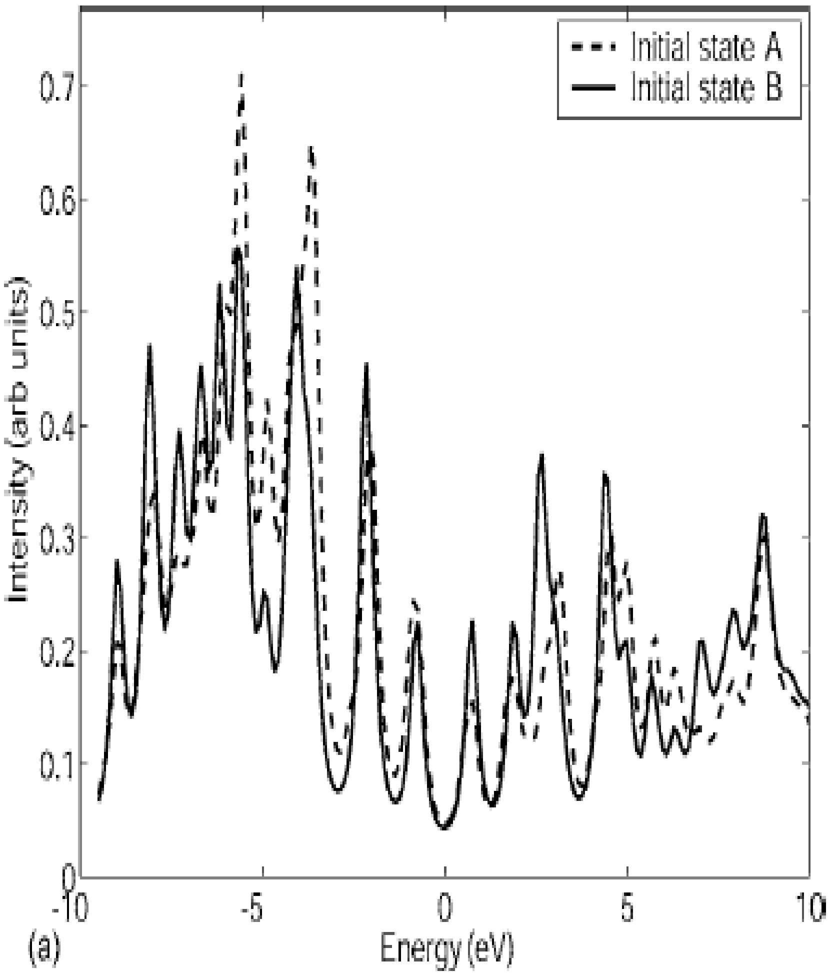


FIG. 4. Spectral dependence of the absorption coefficient ($\alpha = 4\pi k/\lambda$) of Si.

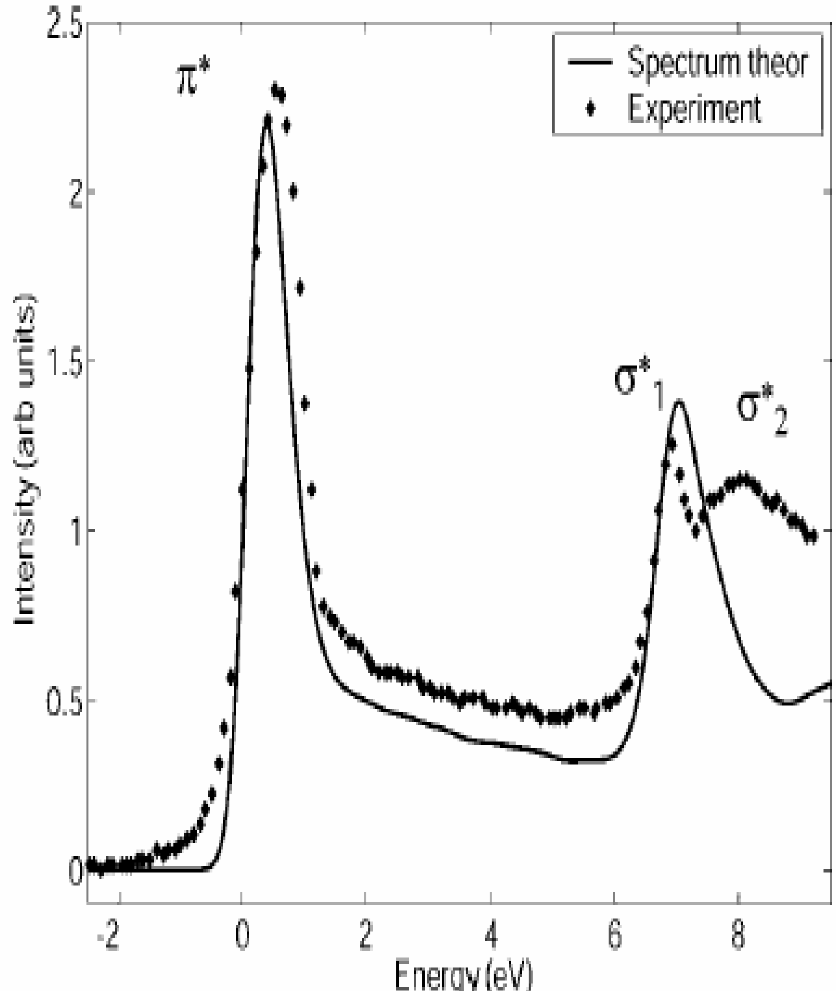
Nanostructures

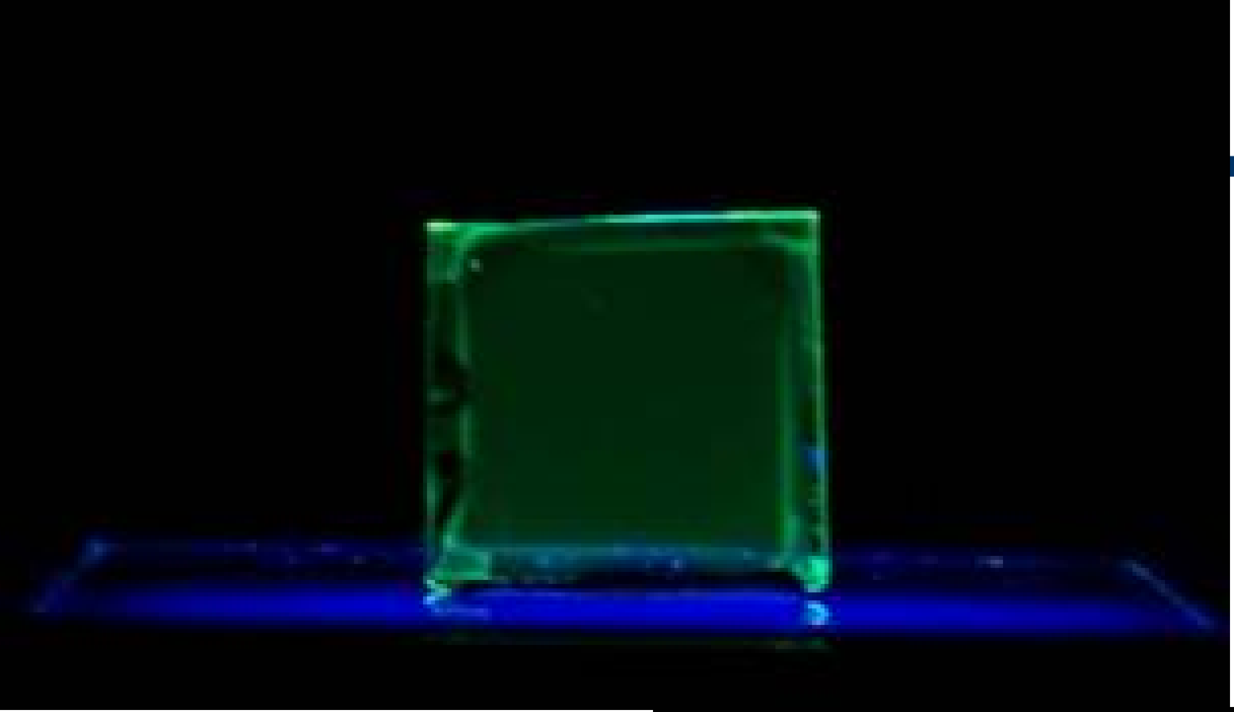


Carbon nanotube



Graphite basal plane



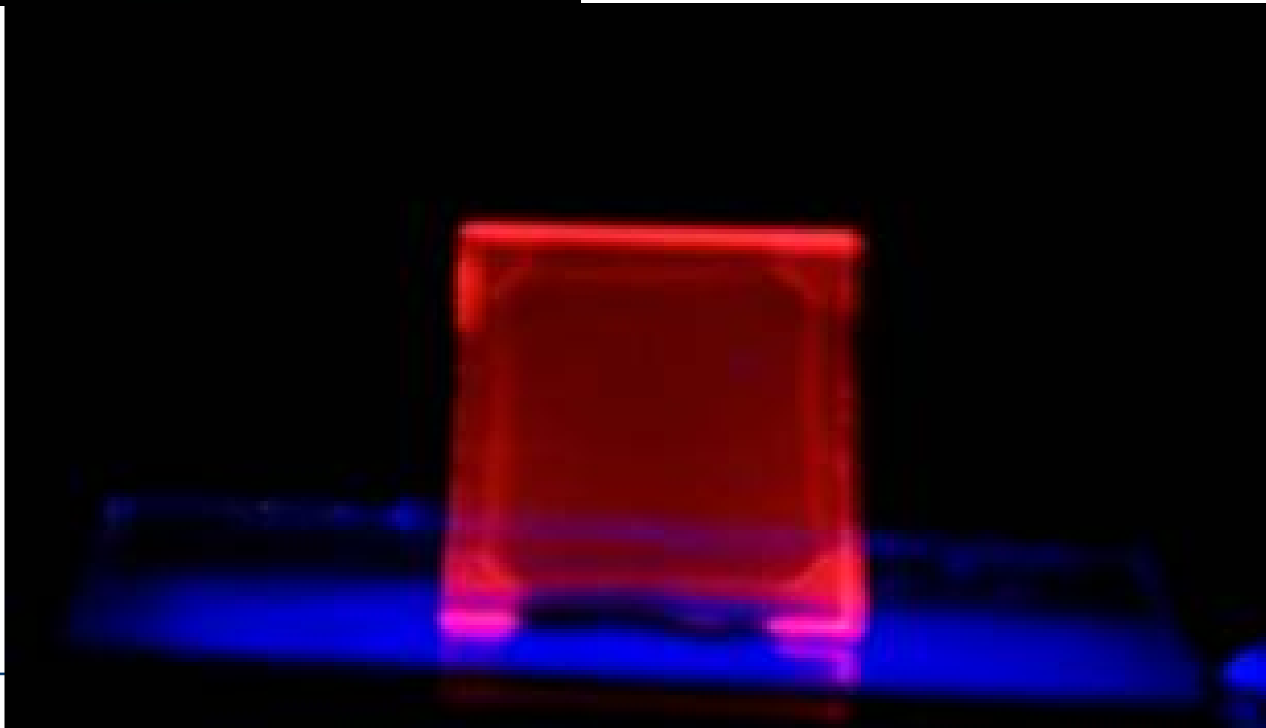


•green

•3 nm

•red

•4 nm



Superatoms: quantum dots. Attention to size control!

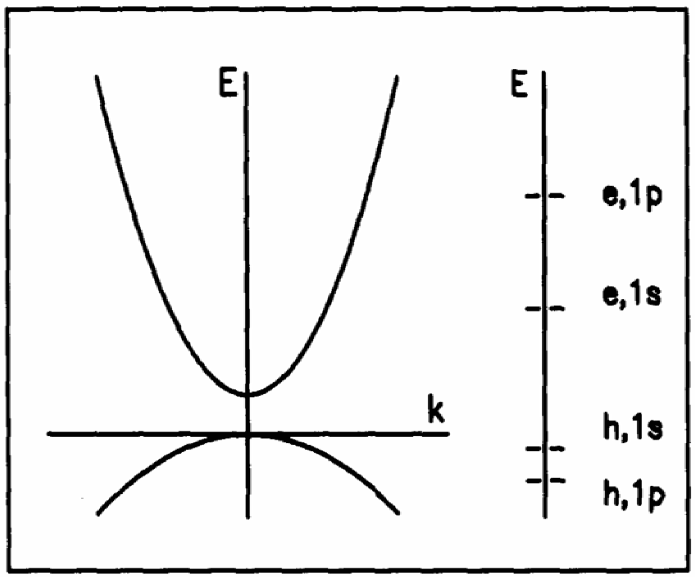


Fig. 2.3: Schematic plot of the single particle energy spectrum in bulk semiconductors (left). The single particle energies for electrons (*e*) and holes (*h*) in small quantum dots are shown in the right part of the figure.

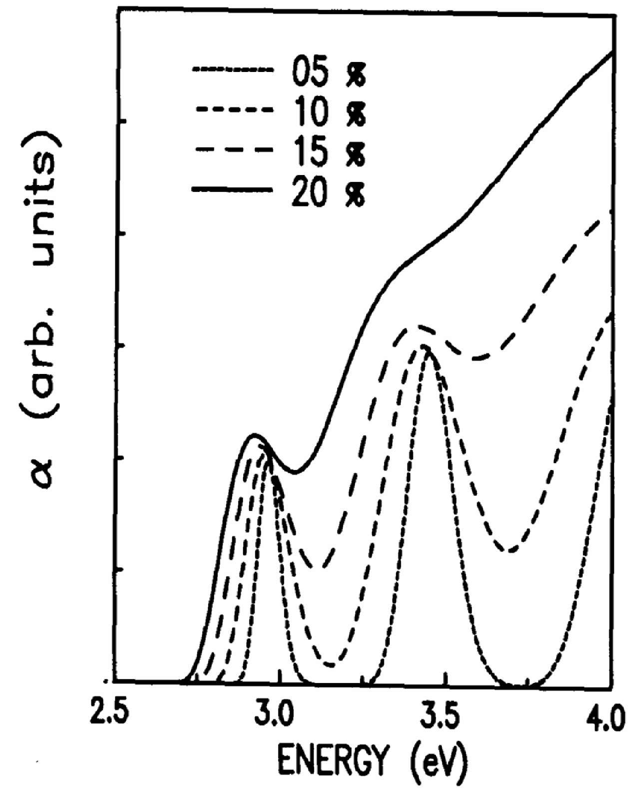


Fig. 2.5: Linear absorption for quantum dots with a Gaussian size distribution. The different curves are for the widths of the Gaussian size distribution indicated in the figure.

What is so special about nanoscale?

- Every property has a **critical length scale** where the **fundamental physics** of that property starts to **change** (typical: **some nm**)

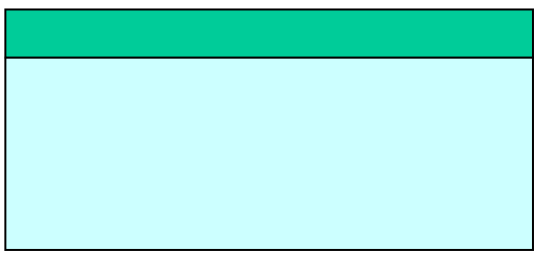
- Nanostructures assembled by **nanoscale building blocks** are within these critical length scales

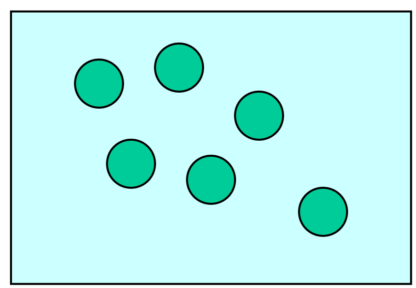
- Nanoscale building blocks impart to the **nanostructures** **new and improved properties** and functionalities

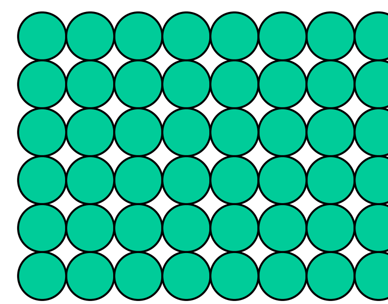
- Material **properties** can be **engineered** through the controlled **size-selective synthesis** and assembly of nanoscale building blocks

Nanostructured materials

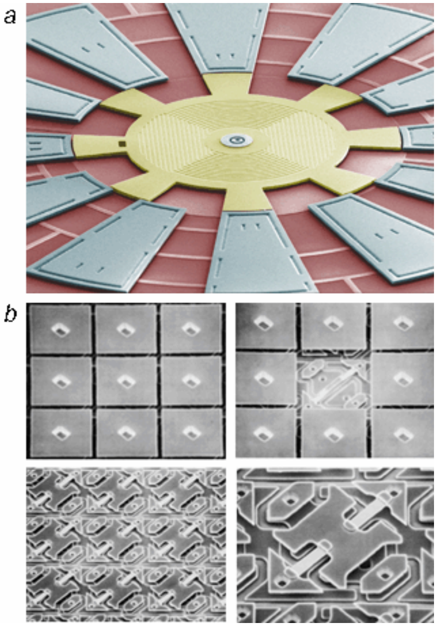
- films and multilayers of nanometric thickness
- nanopowders
  - disperse
  - assembled



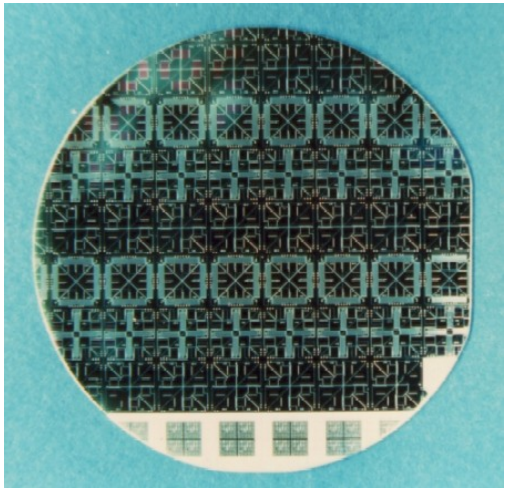




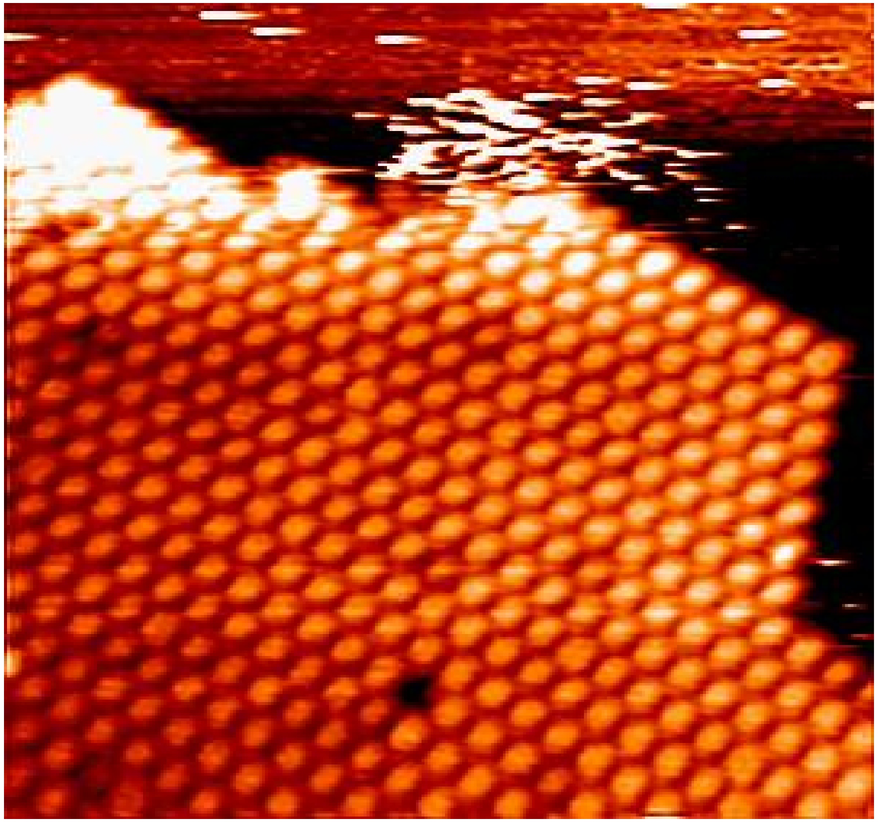
Fabrication techniques



Top down



Bottom up



Richard Feynman and biology (1959)

What are the most central and fundamental problems of biology today? They are questions like: What is the sequence of bases in the DNA? … How are proteins synthesized? … Where do the proteins sit? Where do the amino acids go in? In photosynthesis, where is the chlorophyll; how is it arranged; where are the carotenoids involved in this thing? What is the system of the conversion of light into chemical energy?

It is very easy to answer many of these fundamental biological questions; you just *look at the thing!*"

In the year 2000, when they look back at this age, they will wonder why it was not until the year 1960 that anybody began seriously to move in this direction.

10.1098/rsta.2003.1194

THE ROYAL SOCIETY

Protein folding and misfolding: a paradigm of self-assembly and regulation in complex biological systems

By Michele Vendruscolo[1], Jesús Zurdo[1], Cait E. MacPhee[2] and Christopher M. Dobson[1]

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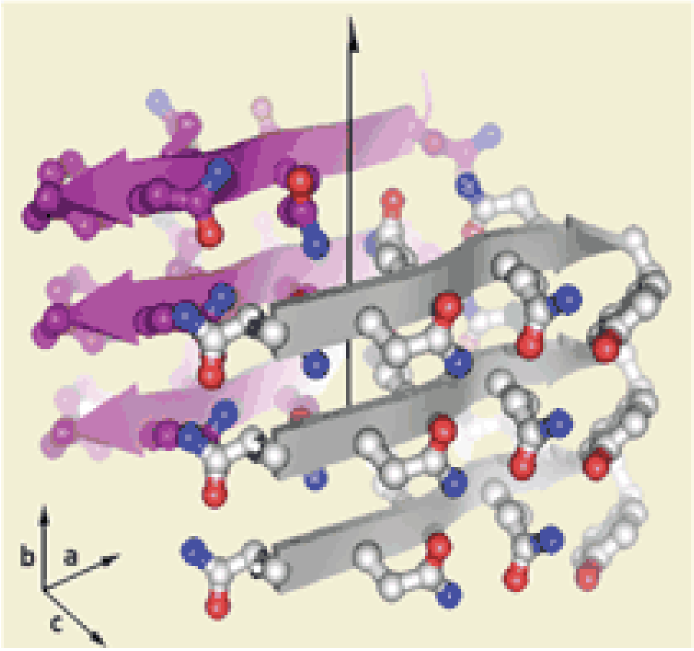
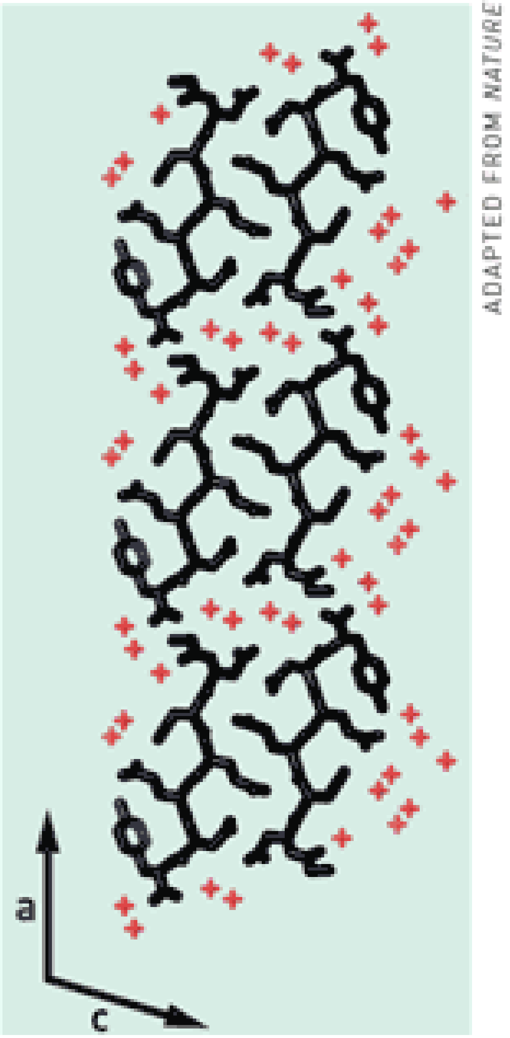
Published online 6 May 2003

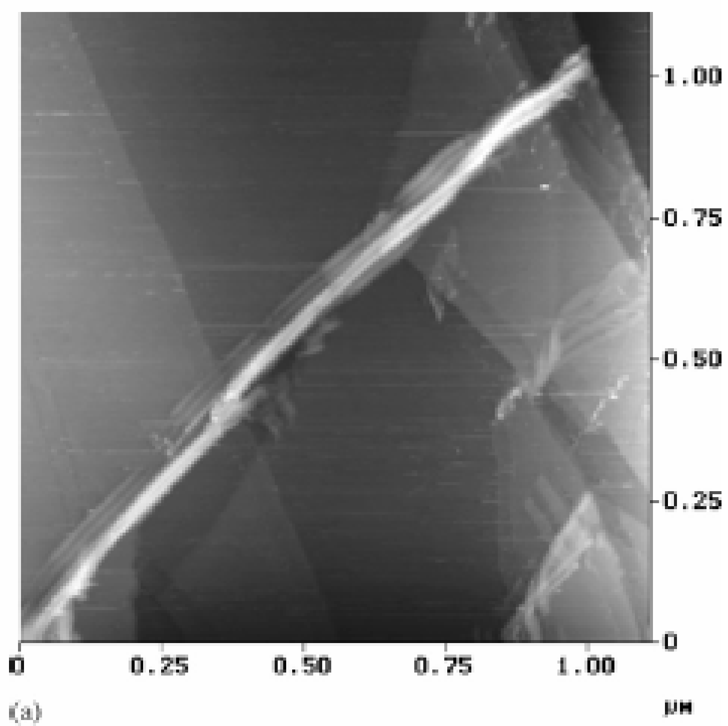
Nelson et al. *Nature* **2005,** *435,* 773

First **atomic view** of amyloid fibrils by means of synchrotron x-rays **diffraction of nanocrystals**.





STM measurments of the aggregation of β-amyloid (Aβ42) peptide on hydrophobic graphite



(**Z. Wang et al.**, Ultramicroscopy (2003), 97: 73–79)

POLITECNICO DI MILANO

Research motivations

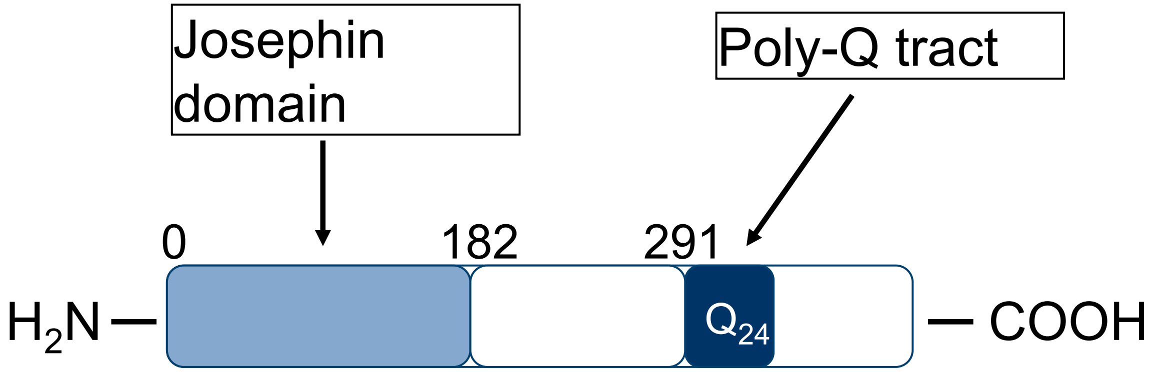
“The deposition of proteins in the form of **amyloid fibrils** and plaques is the characteristic feature of more than **20 degenerative conditions** affecting either the central nervous system or a variety of peripheral tissues.”

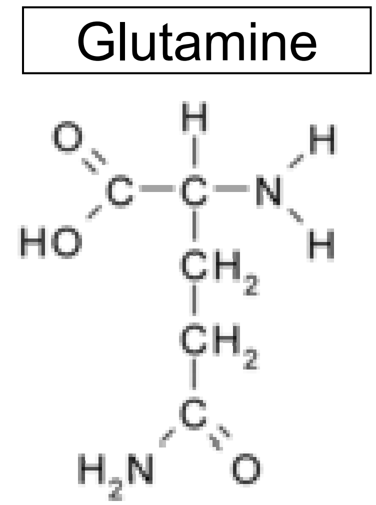
“Much remains to be learned about the mechanism by which the proteins associated with these diseases aggregate and form amyloid structures**.”**

(**Massimo Stefani and Christopher M. Dobson** J Mol Med (2003) 81:678–699)

Comprehension of the fibrillogenesis mechanism has the final task to **determine strategies to prevent the aggregation** of these toxic aggregates.

The protein Ataxin-3





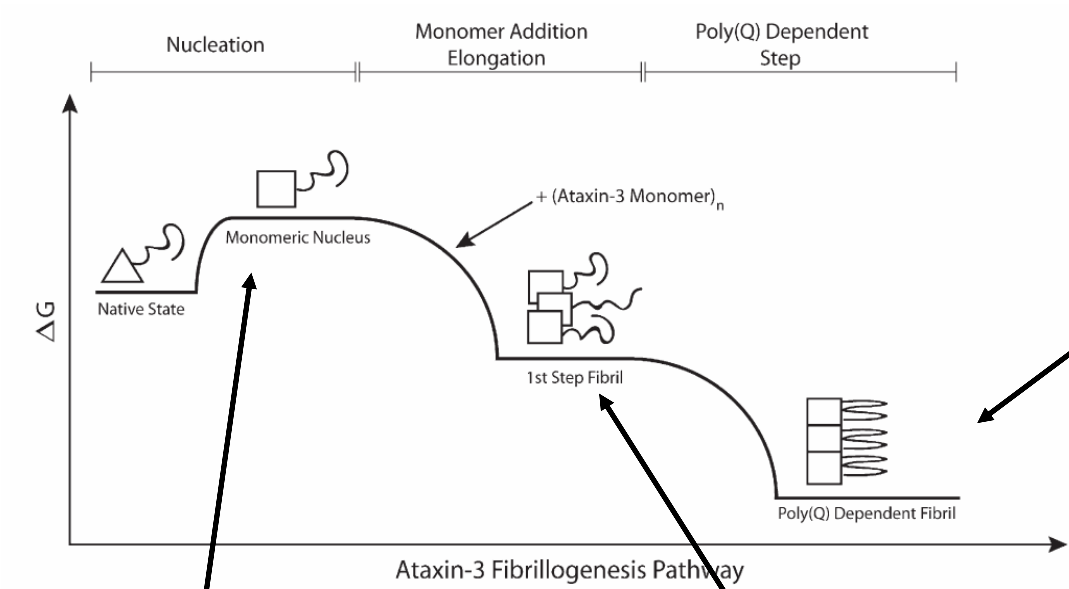
Ataxin-3 is thought to play a role in the intracellular protein degradation process.

The **SPINOCREBELLAR ATAXIA TYPE 3** is characterized by the presence of **large intranuclear amyloid AT-3 aggregates**.

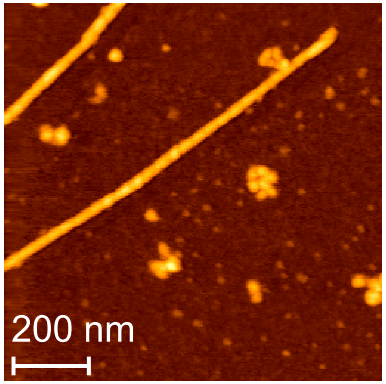
The appearance of the disease is strictly related to the **abnormal expansion of the poly-Q tract** over a critical length of about **36-40 residues**.

The 2-stage model

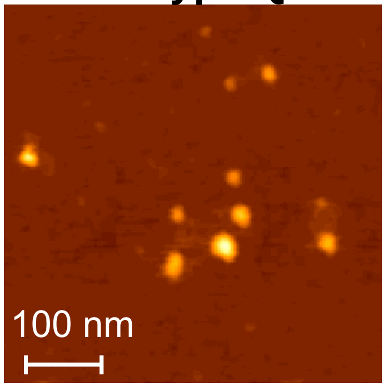
Ellisdon A.M. J. Mol. Biol. 2007



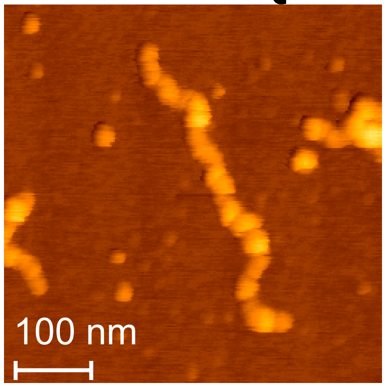
Annealed Q36



Wild type Q6



Annealed Q6



The **first stage** is a **poly-Q tract independent** nucleated growth **polymerization mechanism** in which the single proteins act as monomers presumably activated by **structural rearrangements of Josephin domain**; the **second stage** is **poly-Q dependent**, it occurs **only in expanded AT-3** and it leads to the formation of **long fibrils**.

Molecular nanotechnology (MNT) is the concept of engineering functional mechanical systems at the molecular scale.

An equivalent definition would be "machines at the molecular scale designed and built atom-by-atom". This advanced form of nanotechnology (or *molecular manufacturing*) would make use of positionally-controlled mechanosynthesis guided by molecular machine systems. MNT would involve combining physical principles demonstrated by chemistry, other nanotechnologies, and the molecular machinery of life with the systems engineering principles found in modern macroscale factories. Detailed theoretical investigation have investigated the feasibility of molecular nanotechnology, but the topic remains controversial.

Perhaps the eventual *Technology Roadmap for Productive nanosystems* will exhibit a more hopeful tone: attend the second lecture…