Some Instances of Updated Nanotechnology Applied in Microbiology

Journal Seminar Presentation
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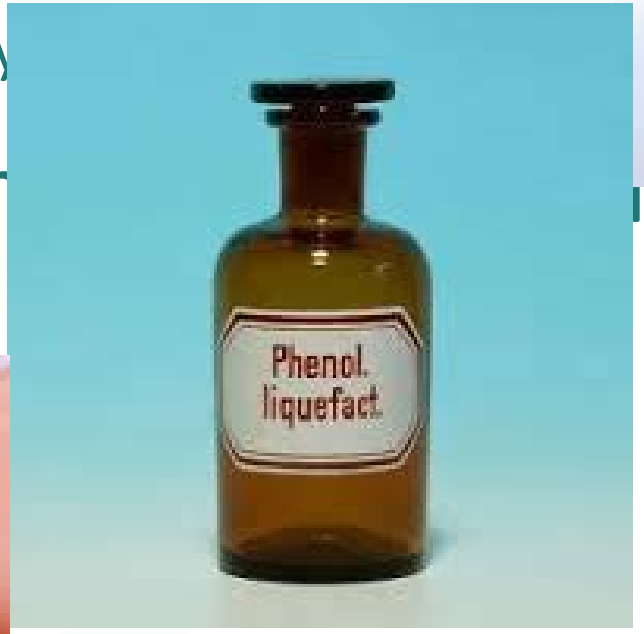
Menu

- Nanotechnology applied in anti-bacteria:
- 1 With small molecule-capped gold nanoparticles
- Nanotechnology applied in detecting bacterial activities:
- 1 Detection by single-walled carbon nanotubes
- 2 Utilization of nanodiamond thermometry

Nowadays Antibacterial Agents

⊙Non-residue-producing antibac

-e.g. alcohols, peroxides, aldehy



⊙Residue-producir

-e.g. heavy metals, phenols

Disinfectants in Consumer Products, Health Council of the Netherlands, No. 2001/05E, 2001
http://images.wisegeek.com/ethanol-bottle.jpg
http://3.imimg.com/data3/VL/BC/MY-5149559/liquid-phenol-250x250.jpg
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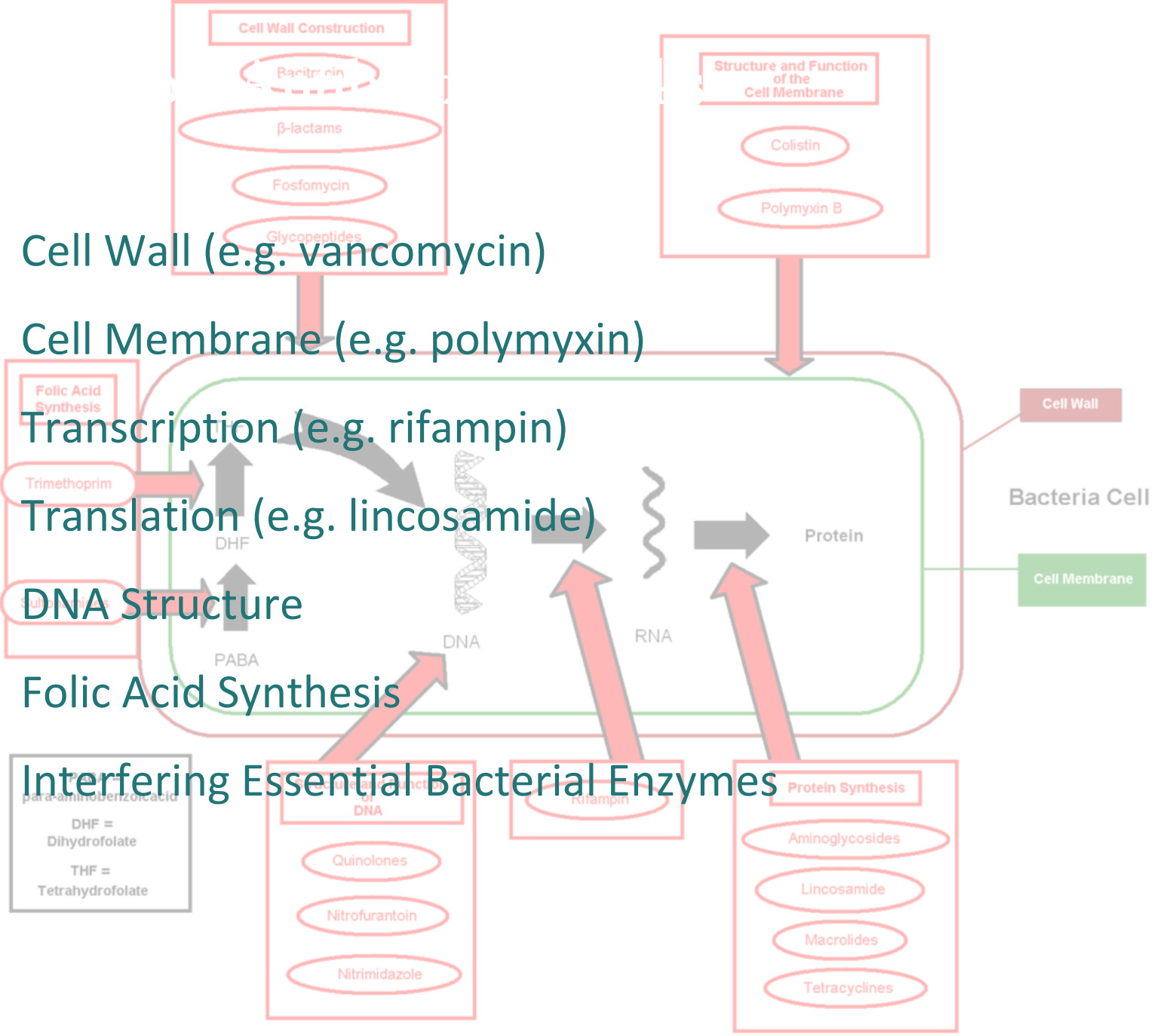
com/science/health/breakthroughs/what-comes-after-antibiotic-5-alternatives-to-stop-superbugs#slide-1
p://www.popularmechanics.com/cm/popularmechanics/images/ev/antibiotic-alternatives-01-1213-de.jpg

- Cell Wall (e.g. vancomycin)
- Cell Membrane (e.g. polymyxin)
- Transcription (e.g. rifampin)
- Translation (e.g. lincosamide)
- DNA Structure
- Folic Acid Synthesis
- Interfering Essential Bacterial Enzymes



http://upload.wikimedia.org/wikipedia/commons/8/87/Antibiotics_action.png

Some Remarks

- Why new Antibacterial Agents?

  Antibiotics resistance (e.g. MRSA).

- What is nano-scale?

  Materials that are studied among 0.1 to 100nm (usually refers to directly utilization of single atom or molecule)

- Why nano-scale?

  Have special characters from original compounds in larger scale

Drexler, K. Eric (1986). Engines of Creation: The Coming Era of Nanotechnology. *Doubleday*.
http://en.wikipedia.org/wiki/Nanotechnology
http://florence20.typepad.com/.a/6a00d83452a77469e20120a704fccf970b-pi

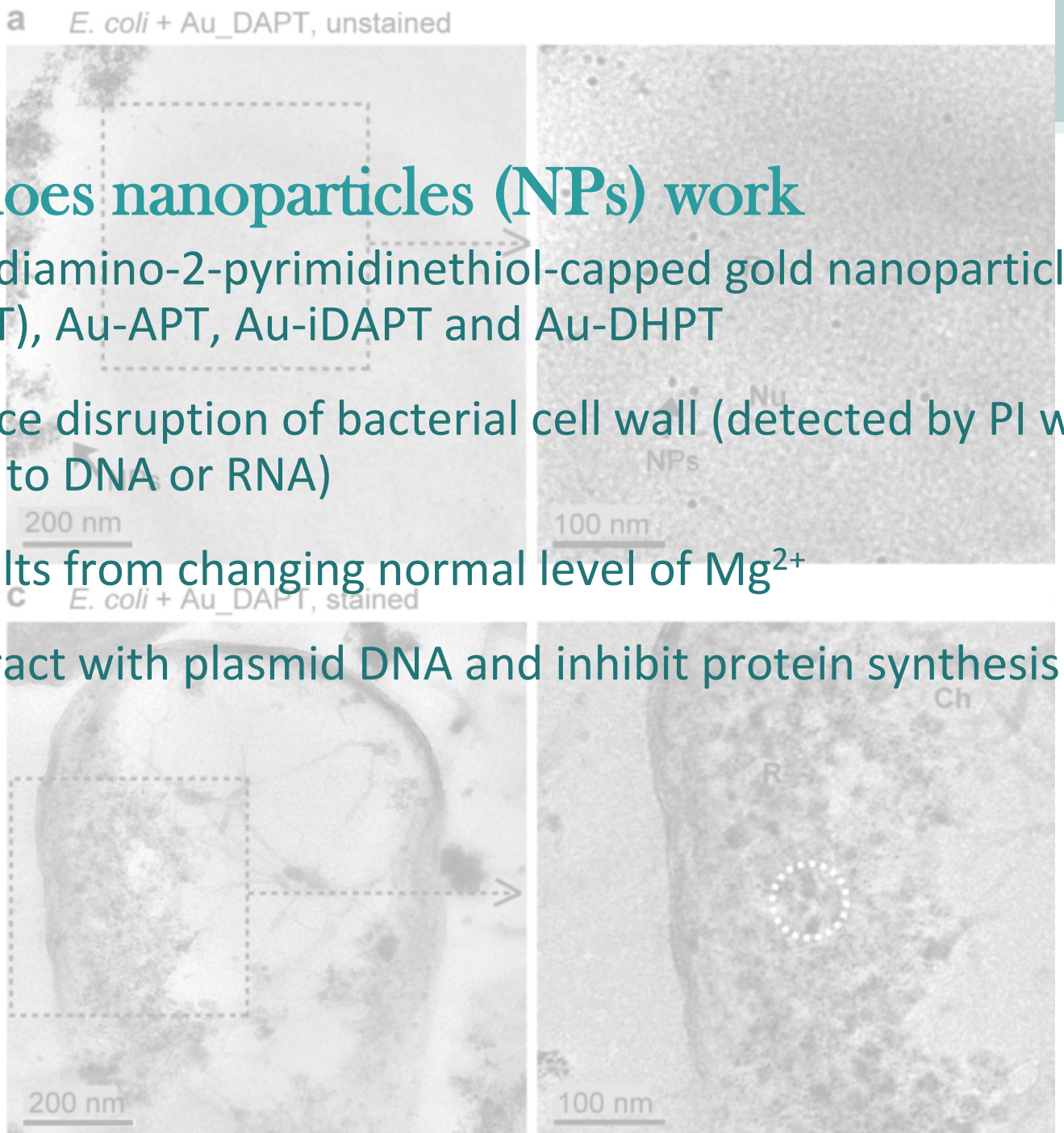
What if we use nano-scale

- Regular scale: Some bacteria have resistance by have pumps that could pump our drugs.
- Nano-scale: easy to cross bacterial membrane
- Possible advantage: interaction with bio-molecules, have multivalue

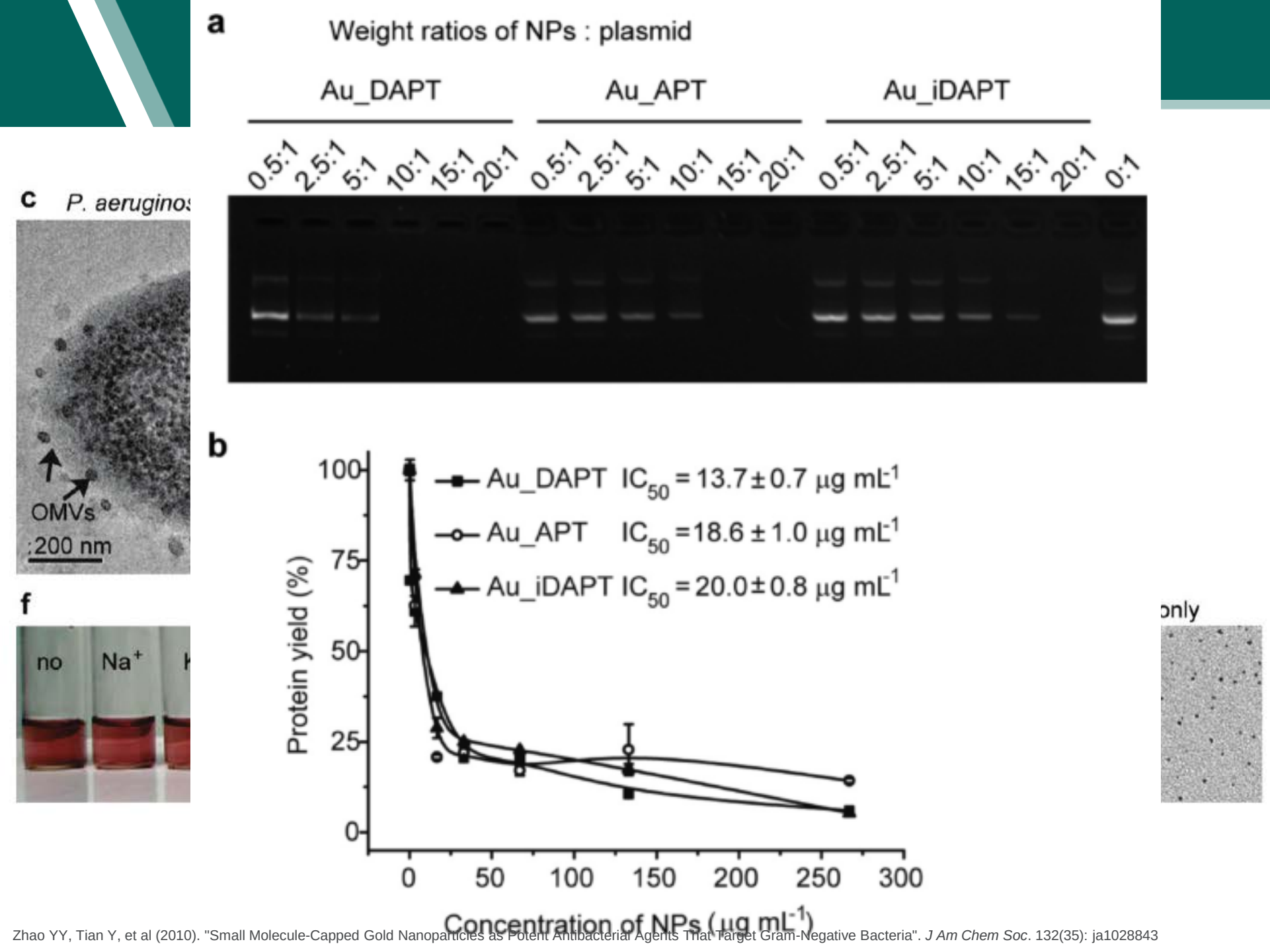
Drexler, K. Eric (1986). Engines of Creation: The Coming Era of Nanotechnology. *Doubleday*.
http://en.wikipedia.org/wiki/Nanotechnology
http://www.nanowerk.com/news/id10732.jpg

How does nanoparticles (NPs) work

- 4,6-diamino-2-pyrimidinethiol-capped gold nanoparticles (Au-DAPT), Au-APT, Au-iDAPT and Au-DHPT
- Induce disruption of bacterial cell wall (detected by PI which bind to DNA or RNA)
- Results from changing normal level of Mg^{2+}
- Interact with plasmid DNA and inhibit protein synthesis



Zhao YY, Tian Y, et al (2010). "Small Molecule-Capped Gold Nanoparticles as Potent Antibacterial Agents That Target Gram-Negative Bacteria". *J Am Chem Soc*. 132(35): ja1028843



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Pros and Cons

- Borden possible drug selection
- Decrease environment pollution during production
- Hard to lead to bacterial resistance
- Low toxicity to mammalian cells

- Expensive production price and relatively high difficulty in production in short term

Zhao YY, Tian Y, et al (2010). "Small Molecule-Capped Gold Nanoparticles as Potent Antibacterial Agents That Target Gram-Negative Bacteria". *J Am Chem Soc*. 132(35): ja1028843.
Yan K, Ma LY (2011). "Nano Antiacterial Agent Could Fight Against Bacterial Resistance". *Newton.* 2011(1):pp10

Real Time Detection

- Why?

  Detect Intracellular molecule could help to study bio-molecule and cell activity

- How?

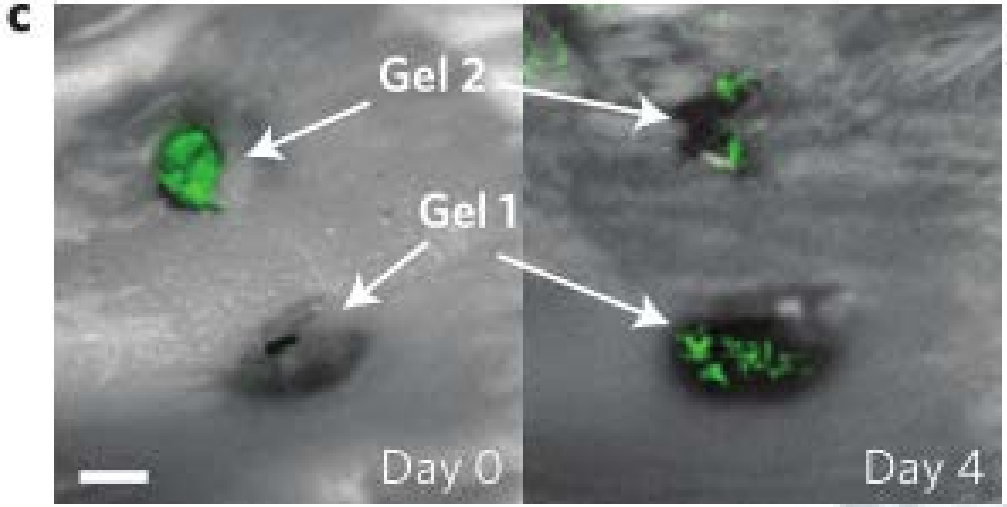
  Usually by monoclonal antibodies, fluorescence or isotope labeling

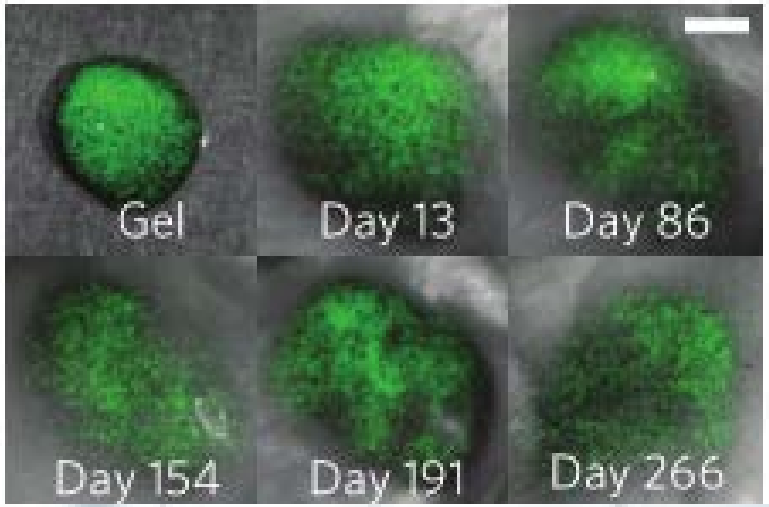
- Why nano-scale?

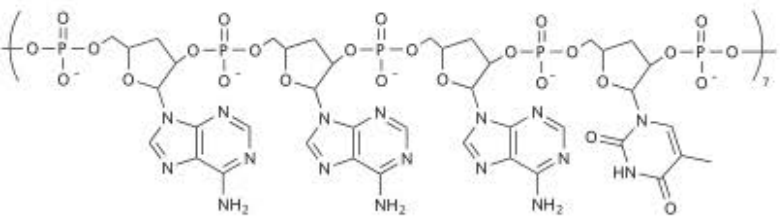
  New way to detect, more accurate, could focus in subcellular structure

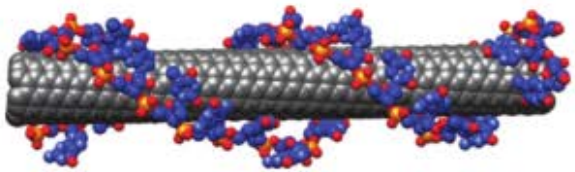
Instance One: SWCN

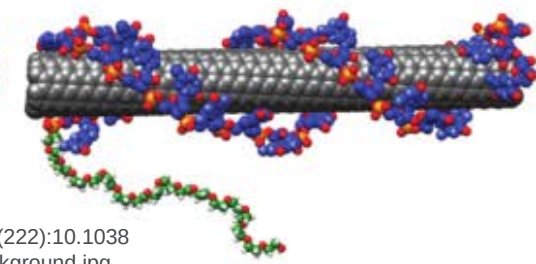
- single-walled carbon nanotubes (SWCN) wrapped with DNA [e.g. $(AAAT)_7$-SWCN] (200ul injection of 50mg/L SWCN)











Nicole M Iverson, et al (2013). "*In vivo* Biosensing via Tissue-localizable Near-infrared-fluorescent Single-walled Carbon Nanotubes". *N Nano*. 8(222):10.1038
http://en.clipdealer.com/preview/image/001/500/072/previews/15--1500072-Multi%20Walled%20Carbon%20Nanotube%20on%20White%20Background.jpg

What is the hint?

- Current study: detect NO and other potential molecules
- Further study: detect blood glucose or insulin
- Potential study: detect key molecules in microorganisms (e.g. radicals or oxidants which identify cell damage)
- Possible study on microbiology: detect real-time intracellular temperature

Dominguez T (2011). "When Will Carbon Nanotubes Save The World?". Discovery Communications. Available from: http://news.discovery.com/tech/biotechnology/carbon-nanotubes-111228.htm
http://static.ddmcdn.com/gif/blogs/6a00d8341bf67c53ef015439094817970c-800wi.jpg

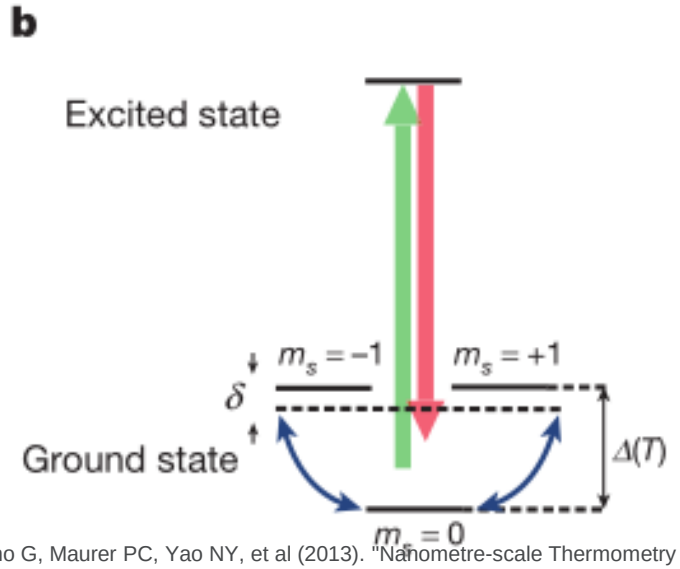
Instance Two: Nanodiamond

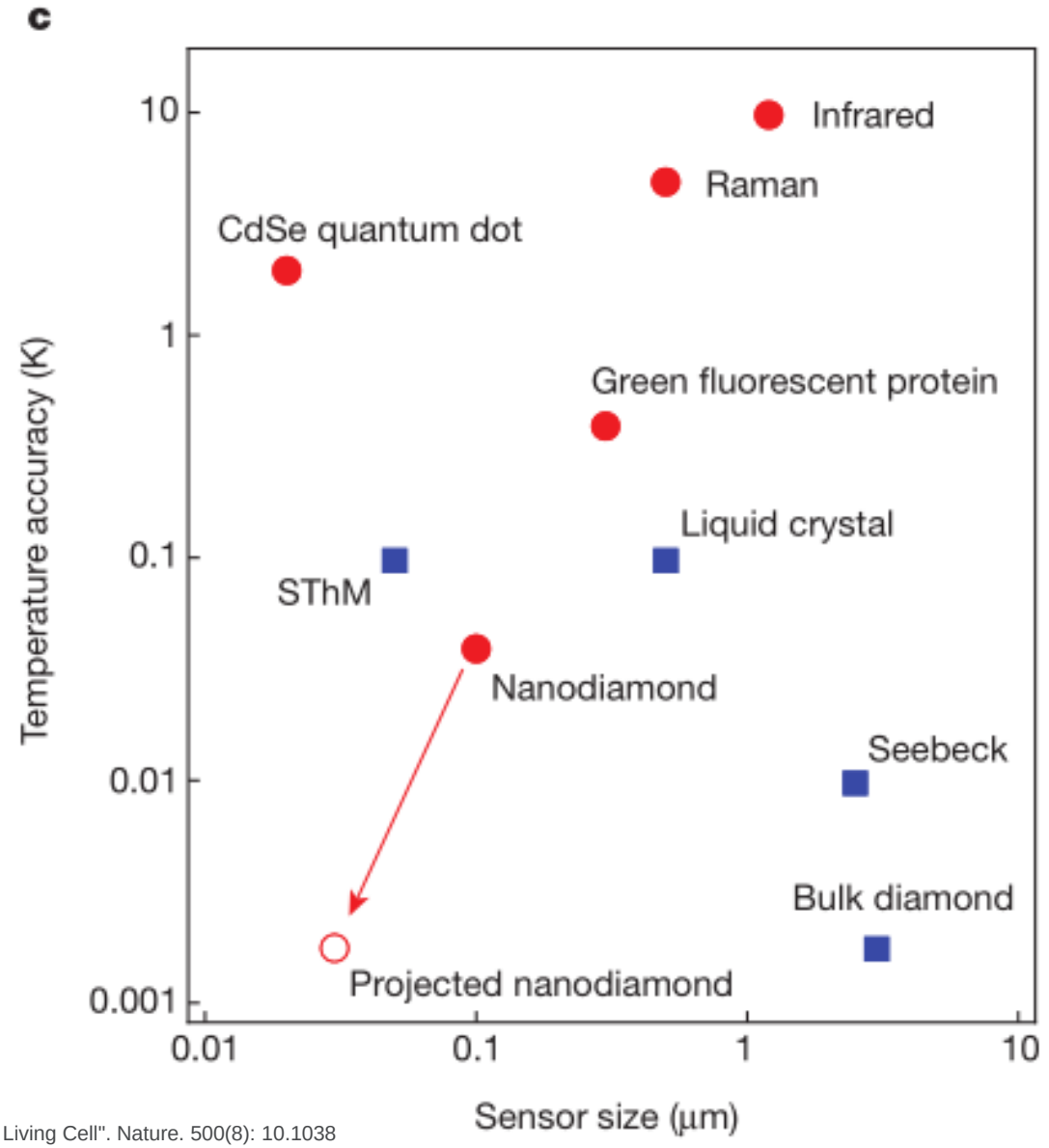
- Intracellular thermometry
- Excitation: 532nm; Detection: greater than 638nm
- Introduced to cell (human embryonic fibroblast) by nanowire-assisted delivery
- Different positions, different temperature, different strength
- Fluorescence strength->nanodiamond temperature->local temperature

Kucsho G, Maurer PC, Yao NY, et al (2013). "Nanometre-scale Thermometry In A Living Cell". Nature. 500(8): 10.1038
Yan K, Ma LY (2013). "Nano-scale Diamond Thermometry". *Newton*. 2013(9):pp14.

How Does It Works?

- Based on nitrogen-vacancy
- Sensitive electron in nitrogen
- 1/1000K

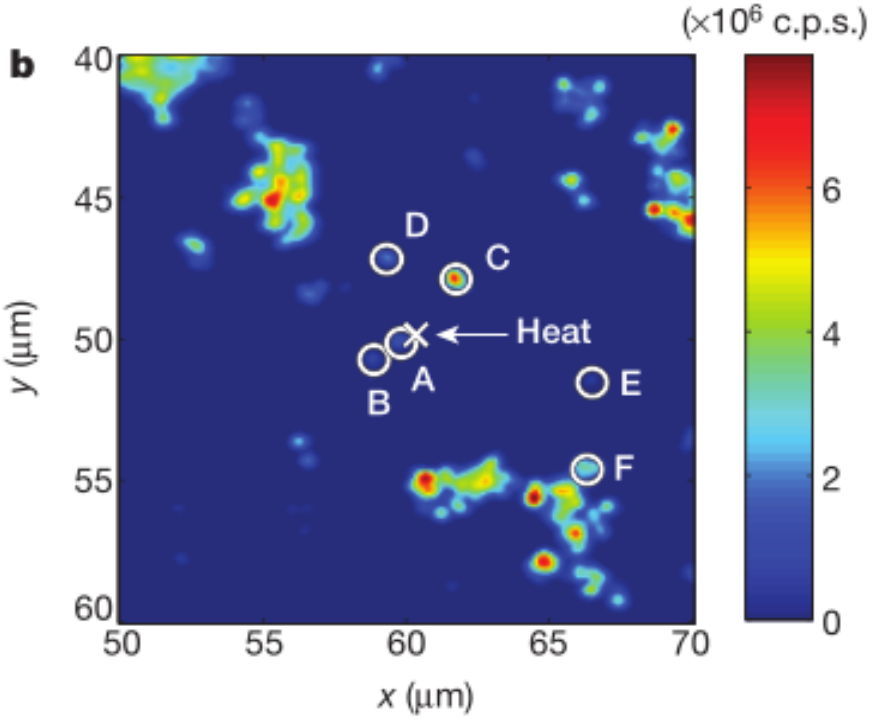


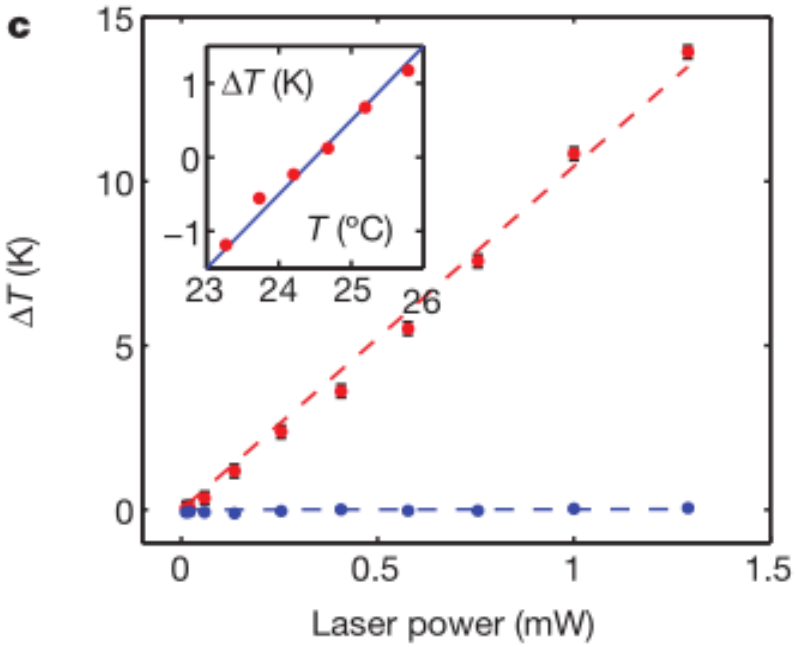


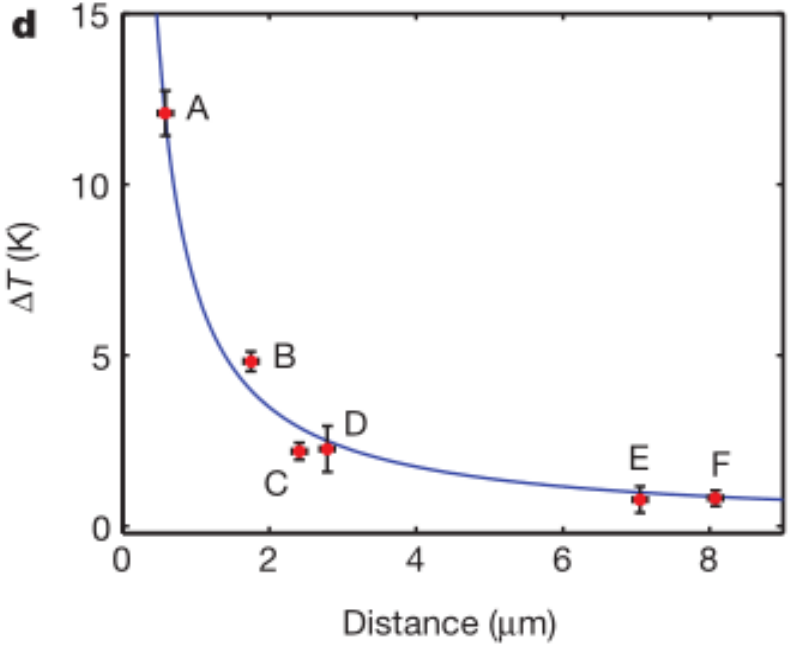
Kucsho G, Maurer PC, Yao NY, et al (2013). "Nanometre-scale Thermometry In A Living Cell". Nature. 500(8): 10.1038

How to Detect?

- Cross: heat by laser on gold nanoparticle
- Circle: nanodiamond







Kucsho G, Maurer PC, Yao NY, et al (2013). "Nanometre-scale Thermometry In A Living Cell". Nature. 500(8): 10.1038

What is the hint?

- Accurately control intracellular temperature
- Study cell pathways (e.g. metabolism of particular key compounds)
- Pros: high sensitivity and high accuracy
- Cons: relatively high price and difficulty in production in short term; need to deal with individual cells

Conclusion

- Nanotechnology releases new direction for microbiology study
- Have advantages compared to traditional methods
- Need further develop
- Not in large-scale utilization

Q & A session

All are welcoed

Q: How could we use nanotubes and nanodiamonds to help us in microbiology?

A: Thank you for your question. I think I have introduced this in previous slide that we could use nanotechnology to help us to study some pathways and metabolisms. Maybe I'd better use an example here. Let's suggest that now we need to study expression of a new protein under stress out of cells. Stress would transduct into cell trhough pathways, lead to transcription of DNA and eventually leads to protein expression. If we put nanodiamonds near DNA which might express or particular recepters, we could knwo which and how much the particular site is affected in this pathway by detecting its temperature changed. So...

Q: But how could you make sure nanodiamonds stay there and would not affect, e.g. transcription?

A: Actually, I believe that scientists have there way to localize the nanoparticles according to the experiment about relationship between temperature and distance. And nanodiamonds are not necessarily need to bind to the DNA, thus I believe it would not affect cell activity during detection.

Q: Why NPs has low toxicity to mammalian cells and can lower environment pollution?

A: Thank you for your question. Actually according to the paper that introduced gold NPs, it has been tested with human cells and it has been proved that the nanoparticles did not affect human cell growth. However, I am sorry that I could not answer why NPs affect Mg level in bacterial cell but do not affect mammalian cell because the paper proved this point by experimental result instead of mechanism and I must accept that I do not know the principle either.

For your second question, (why can NPs lower the pollution, right?) I quoted the summary from the paper which announced that by producing nanoparticles, production could be simplified. But since I don't the exact manufactory of production, I could not tell how it can lower environment pollution detailedly. Hope that I could answer your question.

Zhao YY, Tian Y, et al (2010). "Small Molecule-Capped Gold Nanoparticles as Potent Antibacterial Agents That Target Gram-Negative Bacteria". *J Am Chem Soc*. 132(35): ja1028843.
Yan K, Ma LY (2011). "Nano Antiacterial Agent Could Fight Against Bacterial Resistance". *Newton.* 2011(1):pp10

Q: Why do we need to use "tubes" and how does it work?

A: Thank you Professor. We use carbon nanotubes since carbon atoms line in a particular way in tubes. It is the same as nanodiamond, but their ways of lining are different. In the particulat ways of lining, elctron could be transducted across nanotube quickly after being excited. Actually, some of the mechanisms and principles of nanotechnology are still under study by scientists, and to be honest, I don't know the detail of these peinciples either.

Q: How does nanodiamond work?

A: Thanks for your question, professor. As I showed previously, electrons in nitrogen-vacancy are sensitive, and could easily be excited and give fluorescence under exitation light. Different temperature differences give different strengths when the electrons exited. (So... I still haven't introduced clearly? OK, I will try to explain further.) We know that diamonds are made by carbon atoms. However, among the carbon atoms there are randomly nitrogen-vacancy which has one electron more than carbon. This free electron could not bind with any carbon and can not form any covelent bond. As we know, FREEDOM is dangerous compared to ORDER, and the free electron is sensitive. I hope that I could answer your question?

Q: Could we use nanotubes or nanodiamonds to inhibit bacterial growth?

A: Thank you for your question. Actually, for your second question, I do not go through any paper that talks about nanodiamonds which could kill bacterial cell. However, for your first part, I should say yes, your are right, carbon nanotubes could really inhibit bacterial growth. In fact, there are some papers that always report that carbon nanotubes could inhibit bacterial growth. However, why sometimes nanotube could help us to detect temperature but sometimes could kill bacteria... I believe that it is because different material binds to carbon nanotubes. For example, if nanotube is wrapped by particular DNA, it could detect temperature; if it binds to other particular compounds and even kill bacterial cell. Hope this could help to answer your question.

Nepal D, et al. (2008) "Strong Antimicrobial Coatings: Single-Walled Carbon Nanotubes Armored with Biopolymers". *Nano lett*. **2008** 8(7), pp 1896-1901

Q: Could nanoparticles be used to cure cancer?

A: Your point is really excellent. Actually, many smart scientists have thought as you and some of them have found the way. Remember that I just introduced that scientists used laser to focus on nanodiamond which could give heat. Scientists also use this character to cure cancer. Cancer cells grow rapidly, thus they adsorb nutritions. Thus if we treat patient with nanoparticles, their majority will stay in cancer cell. After that, we could use lights or sounds like ultrasound which could give energy from outside body, and energy would be mostly adsorbed by nanodiamond, eventually lead to temperature increasing and cancer cell deadth. This has been reported by papers, but is from animal models like mice, and I still have not seen any paper about directly curing cancer on human being, but I believe real pratice would come soon, and thank you for your question.

Reference

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Thank You!