Exploring the Nano World

Key Stage 4 Programme

Pupil Name	Name
Handbook Designed by	Dr Y Hamidizadeh

Timetable and Assignment Submission

Timetable – Tutorials

1			
2			
3			
4			
5			
6 (Feedback)			

Timetable – Homework Assignments

Tutorial 1		
Tutorial 2		
Tutorial 3		
Tutorial 4		
Tutorial 5		

Assignment Submission – Lateness and Plagiarism

Lateness	
Submission after midnight on 9th August	10 marks deducted
Plagiarism	
Some plagiarism	10 marks deducted
Moderate plagiarism	20 marks deducted
Extreme plagiarism	Automatic fail

The Brilliant Club KS4 Programme – Pupil Feedback Report

Grade	Marks	What this means
1st	70+	Performing to an excellent standard at A-level
2:1	60-69	Performing to a good standard at AS-level
2:2	50-59	Performing to an excellent standard at GCSE
3rd	40-49	Performing to a good standard at GCSE
Working towards a pass	0-39	Performing below a good standard at GCSE
Did not submit	DNS	No assignment received by The Brilliant Club

Lateness	
Any lateness	10 marks deducted
Plagiarism	
Some plagiarism	10 marks deducted
Moderate plagiarism	20 marks deducted
Extreme plagiarism	Automatic fail

Name of PhD Tutor			
Title of Assignment			
Name of Pupil			
Name of School			
ORIGINAL MARK / 100		FINAL MARK / 100	
DEDUCTED MARKS		FINAL GRADE	

If marks have been deducted (e.g. late submission, plagiarism) the PhD tutor should give an explanation in this section:

Learning Feedback Comment 1 - ***Enter Key Learning Priority Here***	
What you did in relation to this Key Learning Priority *Enter feedback here*	How you could improve in the future *Enter feedback here*
Learning Feedback Comment 2 – ***Enter Key Learning Priority Here***	
What you did in relation to this Key Learning Priority *Enter feedback here*	How you could improve in the future *Enter feedback here*
Learning Feedback Comment 3 – ***Enter Key Learning Priority Here***	
What you did in relation to this Key Learning Priority *Enter feedback here*	How you could improve in the future *Enter feedback here*
Resilience Comment	
How you showed learning resilience during the course *Enter feedback here*	How you could build learning resilience in the future *Enter feedback here*

Contents

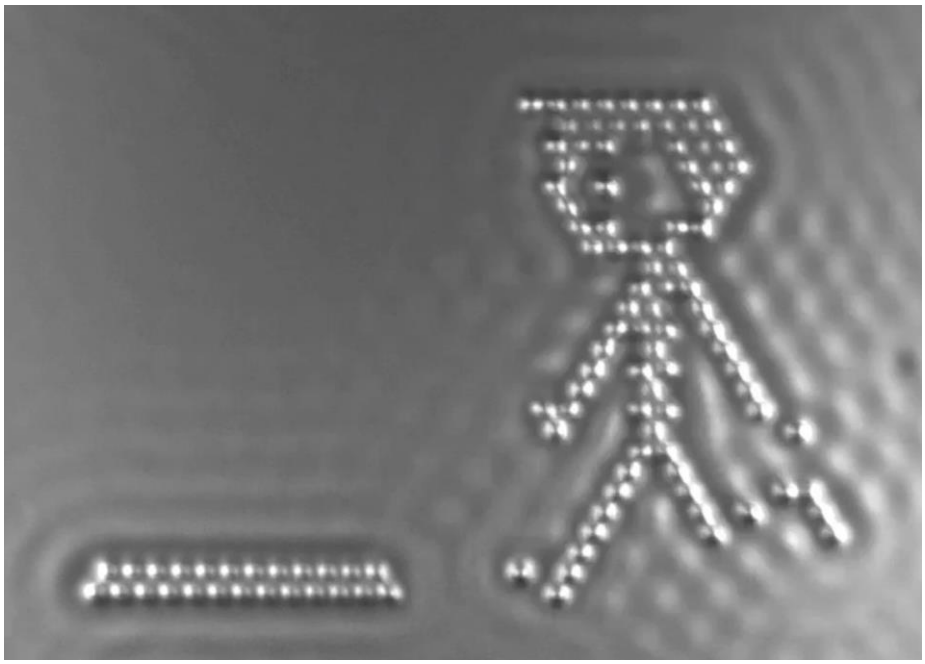
Course Rationale 5
Mark Scheme 6
Glossary of Keywords 9
Tutorial 1 Nanotechnology 10
1.1 How big is "nano"?! 12
1.2 History of nanotechnology 13
Homework 1 15
Tutorial 2 Applications (Part I) 17
2.1 Different types of Nanotechnology 19
2.2 Metrology: Forensics 20
Homework 2 23
Tutorial 3 Applications (Part II) 31
3.1 Electronics and Sensors: Si NW Chemical Sensors and their Issues 33
3.2 Aims and Research Goals 35
What is IETS?! 35
Homework 3 36
Tutorial 4 My PhD Project 38
4.1 Fabrication of Si NW / SiO2 / Al NW Tunnel junction 39
4.2 Measurements and Results 40
4.3 How to design a scientific poster 42
Homework 4 43
Tutorial 5 Future and Risks 45
5.1 Future 1 47
5.2 Risks 48
Final Assignment 50
Tutorial 6 Feedback Tutorial 52
Reflecting on Uni Pathways 53
Appendices 54
Appendix 1 Referencing correctly 54
Appendix 2 Using the VLE 56

Course Rationale

Imagine if you climbed out of the shower only to discover you'd shrunk in the wash by about 1500 million times! If you stepped into your living room, what you'd see around you would not be chairs, tables, computers, and your family but atoms, molecules, proteins, and cells. Shrunk down to the "nanoscale" you'd not only see the atoms that everything is made from—you'd actually be able to move them around! Now suppose you started sticking those atoms together in interesting new ways, like tiny LEGO® bricks of nature. You could build all kinds of fantastic materials, everything from brand new medicines to ultra-fast computer chips. Making new things on this incredibly small scale is called nanotechnology and it's one of the most exciting and fast-moving areas of science and technology today.[1]

In this course, we are going to explore the nano world. To do this, initial tutorial will introduce students the basic concepts of nanotechnology such as: What is nanotechnology? Where is it come from? and Why is it important to us?! Pupils will then learn about different types of nanotechnology and their applications in day to day life. Pupil will also learn about the current risks of nanotechnology and the risks it might have in future. Finally, we will have a discussion about future of nanotechnology.

For the final assignment, pupil will be asked to choose a type of nanotechnology, do a research and design a scientific poster about it based on what they've learned during the course. They will also be asked to think about an application that they might build in future based on this technology.



2

[1] Nanotechnology by Chris Woodford (http://www.explainthatstuff.com/nanotechnologyforkids.html)
[2] IBM Research – Zurich (Available at: https://www.nationalgeographic.org/topics/nanotechnology/)

Mark Scheme Table

	Skills	1st (70–100)	2:1 (60–69)	2:2 (50–59)
Subject knowledge	Knowledge and Understanding	○ All content included is relevant to the general topic and to the specific question/title ○ Good understanding of all the relevant topics. ○ Scientific terms are defined and used accurately throughout ○ Clear justification on how the content included is related to the specific issues that are the focus of the assignment	○ Most of the content included is relevant to the general topic and to the specific question/title ○ Good understanding of most the relevant topics ○ Scientific terms are used accurately but not always clearly defined. ○ Adequate justification on how the content included is related to the specific issues that are the focus of the assignment	○ Some of the content included is relevant to the general topic and to the specific question/title ○ Good understanding on some of the relevant topics but occasional confusion on others. ○ Scientific terms are used mostly accurately with occasional confusion and often not defined. ○ Some justification on how the content included is related to the specific issues that are the focus of the assignment
Critical thinking	Research and Evidence	○ Inclusion of rich sources of research findings, data, quotations or other sourced material as evidence for the claims/ ideas ○ Use evidence/calculations to support claims/assertions /ideas, consistently clearly and convincingly ○ Evidence of further reading beyond materials provided which were used in an appropriate context ○ Data is effectively analysed and appropriate assumptions/conclusions are reached	○ Inclusion of adequate sources of research findings, data, quotations or other sourced material as evidence for the claims/ ideas ○ Use evidence/calculations to support claims/assertions/ideas, mostly clearly and convincingly ○ Evidence of further reading beyond materials provided ○ Data is analysed and the assumptions/conclusions that are reached are mostly appropriate	○ Inclusion of some sources of research findings, data, quotations or other sourced material as evidence for the claims/ ideas ○ Use evidence/calculations to support claims/assertions/ideas, at times clearly and convincingly ○ Limited evidence of further reading beyond materials provided ○ There is an attempt to analyse data is and draw assumptions/conclusions

	Developing an Argument	○ A point of view or position in relation to the title or question is consistently clear ○ Argument/proof exceptionally well-developed and well-justified ○ A position is clearly established in relation to the question, and is developed effectively and consistently throughout the essay ○ Makes links effectively between subjects that have not previously been associated ○ Uses concepts from the tutorials in an unfamiliar context, and does so accurately and confidently. ○ Content is analysed effectively to support the argument	○ A point of view or position in relation to the title or question is adequately clear ○ Argument/proof clear and well-developed and position justified ○ A position is established in relation to the question, and is well-developed in most of the essay ○ Some evidence of linking subjects that have not previously been associated ○ Use some concepts from the tutorials in an unfamiliar context, but not always accurate ○ Analysis of content to support the argument	○ A point of view or position in relation to the title or question is somewhat clear ○ Argument/proof clear but not well-developed ○ A position is established in relation to the question, and is well-developed in parts of the essay ○ Limited evidence of linking subjects that have not previously been associated ○ Limited use of concepts from the tutorials in other contexts ○ Some analysis of content to support the argument
	Critical Evaluation	○ Moved beyond description to an assessment of the value or significance of what is described ○ Evaluative points are consistently explicit/systematic/reasoned/justified ○ Effective critiques on the reliability of sources provided	○ Mostly description but some assessment of the value or significance of what is described ○ Evaluative points are mostly explicit/systematic/reasoned/justified ○ Some evidence of critiques on the reliability of sources provided	○ Only description with minimal assessment of the value or significance of what is described ○ Evaluative points are at times explicit/systematic/reasoned/justified ○ Limited evidence of critiques on the reliability of sources provided
Written communication	Structure and Presentation	○ Ideas are presented in paragraphs and arranged in a logical structure that is appropriate for the assignment ○ The introduction clearly outlines how the essay/report will deal with the issues	○ Ideas are presented in paragraphs and arranged in a structure that is mostly appropriate for the assignment ○ The introduction adequately describes how the essay/report will deal with the issues	○ Ideas are presented in paragraphs and arranged in a structure ○ The introduction mentions how the essay/report will deal with the issues ○ The conclusion summarises some of the main points clearly

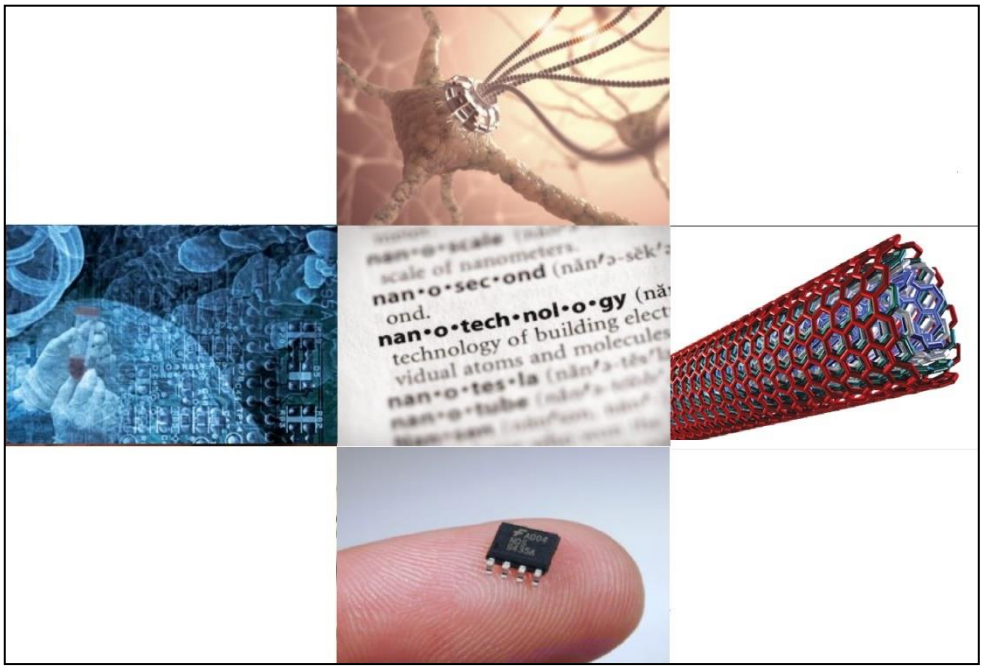
		○ The conclusion summarises all the main points clearly and concisely ○ All calculations, formulas and methods are clearly structured, clear to follow and correct ○ Tables and graphs are effectively constructed including appropriate headings, units and scales. ○ All sources are referenced correctly in an agreed format	○ The conclusion summarises most of the main points clearly ○ Calculations, formulas and methods are mostly structured, clear to follow and correct ○ Most tables and graphs are well constructed ○ Most sources are referenced correctly in an agreed format	○ Calculations, formulas and methods are not always structured, clear to follow and correct. ○ Some tables and graphs are well constructed but contains some errors ○ Some sources are referenced correctly in the agreed format with occasional errors
	Language and Style	○ No spelling, grammar or punctuation errors ○ Units and significant figures are presented accurately throughout ○ Writing style consistently clear, appropriate for scientific documents and easy to follow ○ Accurate and consistent use of technical language and vocabulary	○ Minimal spelling, grammar or punctuation errors ○ Units and significant figures are presented accurately throughout ○ Writing style mostly clear, appropriate for scientific documents and easy to follow ○ Some attempts of using technical language and vocab alary, but not always accurate	○ Some spelling, grammar or punctuation errors ○ Units and significant figures are presented accurately throughout with occasional errors ○ Writing style moderately clear, appropriate for scientific documents and easy to follow ○ Use of simple language and vocabulary effectively but struggles to use technical language

Glossary of Keywords

Tip: Fill this out as we go through the course. If you are unclear about a term or a concept, write it down here and we'll go over it in the tutorial.

Word	Definition	In a sentence

Tutorial 1 – Nanotechnology



What is the Purpose of Tutorial 1?

- To understand How big is "nano"?
- What is Nanotechnology?!
- History of Nanotechnology

Before we begin ...

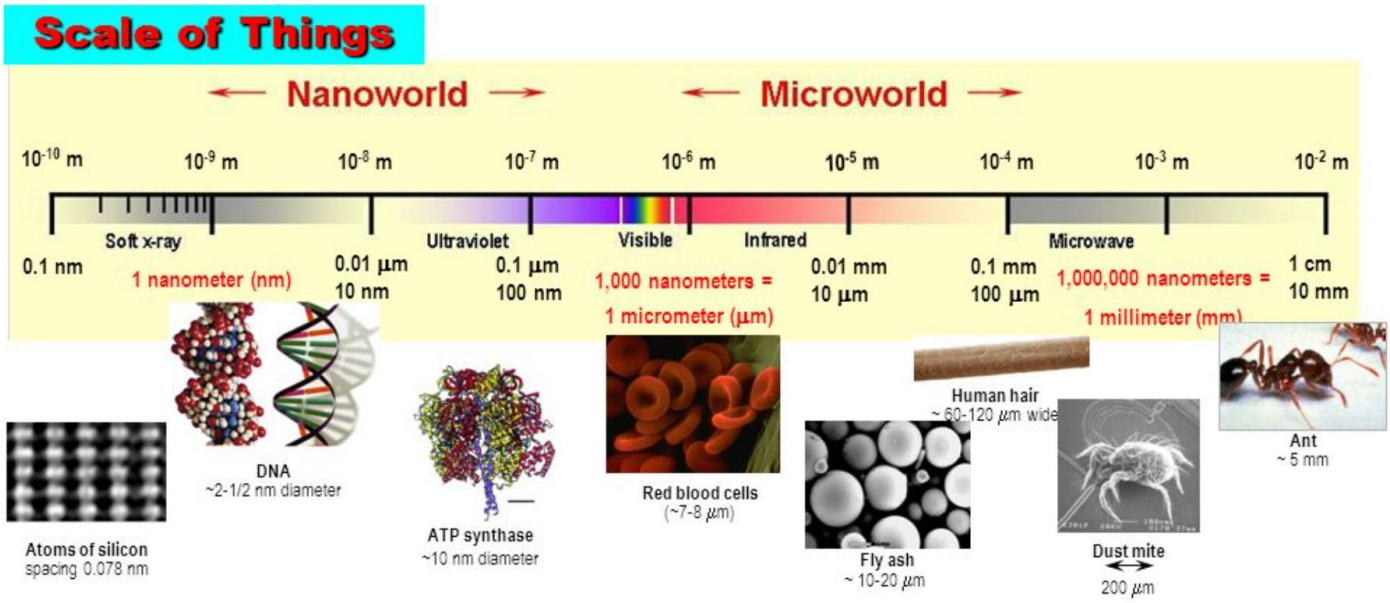
On a post-it, write down the smallest thing you can name and guess how small it is?!

On a different post-it, write down what you know about nano and how small you thing it is?!

1.1 How big is "nano"?!

We live on a scale of meters and kilometres (thousands of meters), so it's quite hard for us to imagine a world that's too small to see. You've probably looked at amazing photos in science books of things like dust mites and flies photographed with electron microscopes. These powerful scientific instruments make images that are microscopic, which means on a scale millionth of a meter wide. Nanoscopic involves shrinking things down to a whole new level. Nano means "billionth", so a nanometer is one billionth of a meter. In other words, the nanoscale is 1000 times smaller than the microscopic scale and a billion (1000 million) times smaller than the world of meters that we live in.

Ordinary objects are absolutely huge measured on what scientists call the nanoscale:



Task 1) Sort card

Look at the pictures and sort them based on their size.

1.2 History of Nanotechnology

Nanotechnology is as old as life itself, but the concept of the nanoscale, nanoscience we can study, and nanotechnology we can harness are all relatively new developments.

Task 2) Reading

Read the History of Nanotechnology section on the article, and create a time-line on Nanotechnology.

Special issue

HET

Human and Experimental Toxicology
2015, Vol. 34(12) 1318–1321
© The Author(s) 2015
Reprints and permission:
sagepub.co.uk/journalsPermissions.nav
DOI: 10.1177/0960327115603588
het.sagepub.com
SAGE

Nanotechnology: History and future

JE Hulla[1], SC Sahu[2] and AW Hayes[3]

History of nanotechnology

Human dreams and imagination often give rise to new science and technology. Nanotechnology, a 21st-century frontier, was born out of such dreams. Nanotechnology is defined as the understanding and control of matter at dimensions between 1 and 100 nm where unique phenomena enable novel applications.[1] Although human exposure to nanoparticles has occurred throughout human history, it dramatically increased during the industrial revolution. The study of nanoparticles is not new. The concept of a "nanometer" was first proposed by Richard Zsigmondy, the 1925 Nobel Prize Laureate in chemistry. He coined the term nanometer explicitly for characterizing particle size and he was the first to measure the size of particles such as gold colloids using a microscope.

Modern nanotechnology was the brain child of Richard Feynman, the 1965 Nobel Prize Laureate in physics. During the 1959 American Physical Society meeting at Caltech, he presented a lecture titled, "There's Plenty of Room at the Bottom", in which he introduced the concept of manipulating matter at the atomic level. This novel idea demonstrated new ways of thinking and Feynman's hypotheses have since been proven correct. It is for these reasons that he is considered the father of modern nanotechnology.

Almost 15 years after Feynman's lecture, a Japanese scientist, Norio Taniguchi, was the first to use "nanotechnology" to describe semiconductor processes that occurred on the order of a nanometer. He advocated that nanotechnology consisted of the processing, separation, consolidation, and deformation of materials by one atom or one molecule. The golden era of nanotechnology began in the 1980s when Kroto, Smalley, and Curl discovered fullerenes and Eric Drexler of Massachusetts Institute of Technology (MIT) used ideas from Feynman's "There is Plenty of Room at the Bottom" and Taniguchi's term nanotechnology in his 1986 book titled, "Engines of Creation: The Coming Era of Nanotechnology." Drexler proposed the idea of a nanoscale "assembler" which would be able to build a copy of itself and of other items of arbitrary complexity. Drexler's vision of nanotechnology is often called "molecular nanotechnology." The science of nanotechnology was advanced further when Iijima,[2] another Japanese scientist, developed carbon nanotubes.

The beginning of the 21st century saw an increased interest in the emerging fields of nanoscience and nanotechnology. In the United States, Feynman's stature and his concept of manipulation of matter at the atomic level played an important role in shaping national science priorities. President Bill Clinton advocated for funding of research in this emerging technology during a speech at Caltech on January 21, 2000. Three years later, President George W. Bush signed into law the 21st Century Nanotechnology Research and Development Act. The legislation made nanotechnology research a national priority and created the National Technology Initiative (NNI).[1] Today, the NNI is managed within a framework at the top of which is the President's Cabinet-level National Science and Technology Council (NSTC)[3] and its Committee on Technology. The Committee's Subcommittee on Nanoscale Science, Engineering, and Technology (NSET) is responsible for planning, budgeting, implementation, and review of the NNI and is comprised of representatives from 20 US departments and independent agencies and commissions (Table 1).

Future of nanotechnology

In a timeframe of approximately half a century, nanotechnology has become the foundation for remarkable

[1]US Army Corps of Engineers, Sacramento, CA, USA
[2]Division of Toxicology, Office of Applied Research and Safety Assessment, Center for Food Safety and Applied Nutrition, US Food and Drug Administration, Laurel, MD, USA
[3]Harvard University, Cambridge, MA, USA

Corresponding author:
AW Hayes, Harvard University, Cambridge, MA 02138, USA.
Email: awallacehayes@comcast.net

Conclusion

The nanoscale is good because it lets us do nanoscience: it helps us understand why things happen by studying them at the smallest possible scale. Once we understand nanoscience, we can do some nanotechnology: we can put the science into action to help solve our problems. That's what the word "technology" means and it's how technology (applied science) differs from pure science, which is about studying things for their own sake.

Homework 1

This homework assignment for the first tutorial is a baseline test to see your initial level of attainment in this subject area. The assignment will test for some, or all, of the subject specific skills that are required later in the final assignment. However, it is shorter than the final assignment and it will be an introduction to the subject as well as the challenge!

Do not worry too much about doing "well" or "badly" on the baseline test. It takes into account the fact that you may not be familiar with the subject area. It is designed to help you and your teacher identify where you are the start of the program and to help you measure your progress along the way.

For the assignment, write an essay (500 words):

Nanoscale is very interesting and quite impressive, but how can we use it in science and technology?

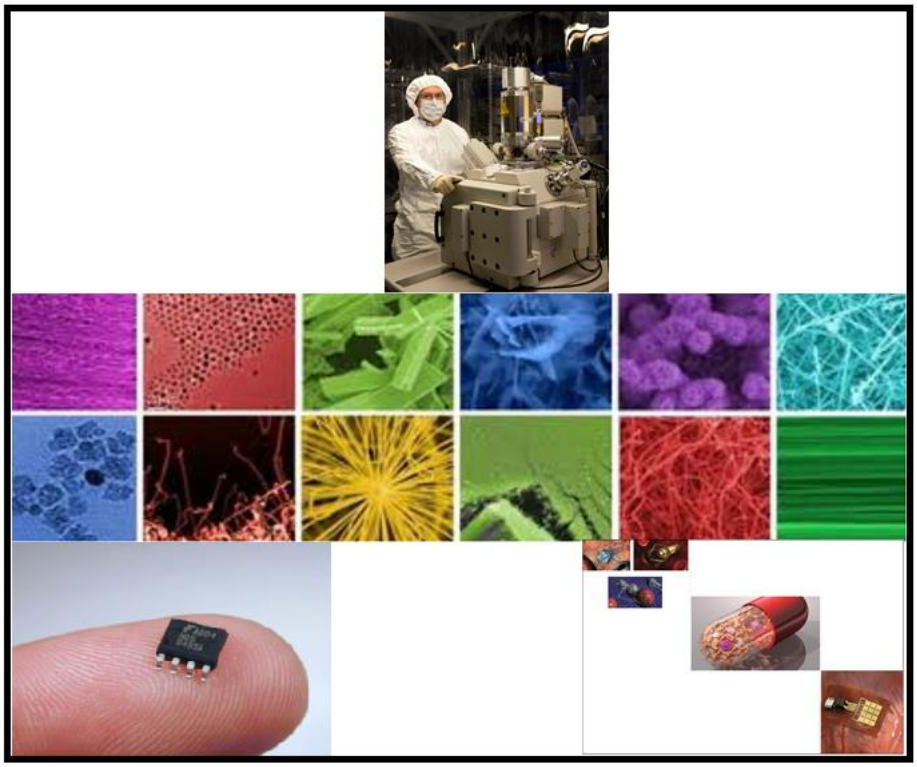
When you are writing your assignment, think about:

- What is good about nanoscale? and why is it important to us?

Notes & Questions

Tutorial 1

Tutorial 2 – Applications (Part I)



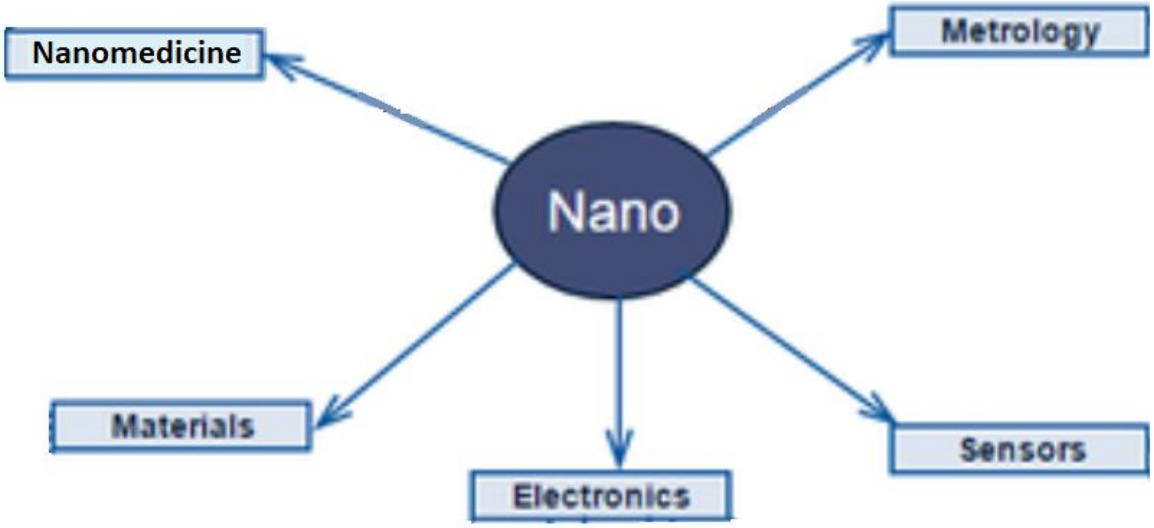
What is the Purpose of Tutorial 2?

- To understand different types of nanotechnology.
- What are the applications in Metrology? (Example)

Before we begin ...

On a post-it, write down different types of nanotechnology that you have heard about and think about example of applications you know for each type.

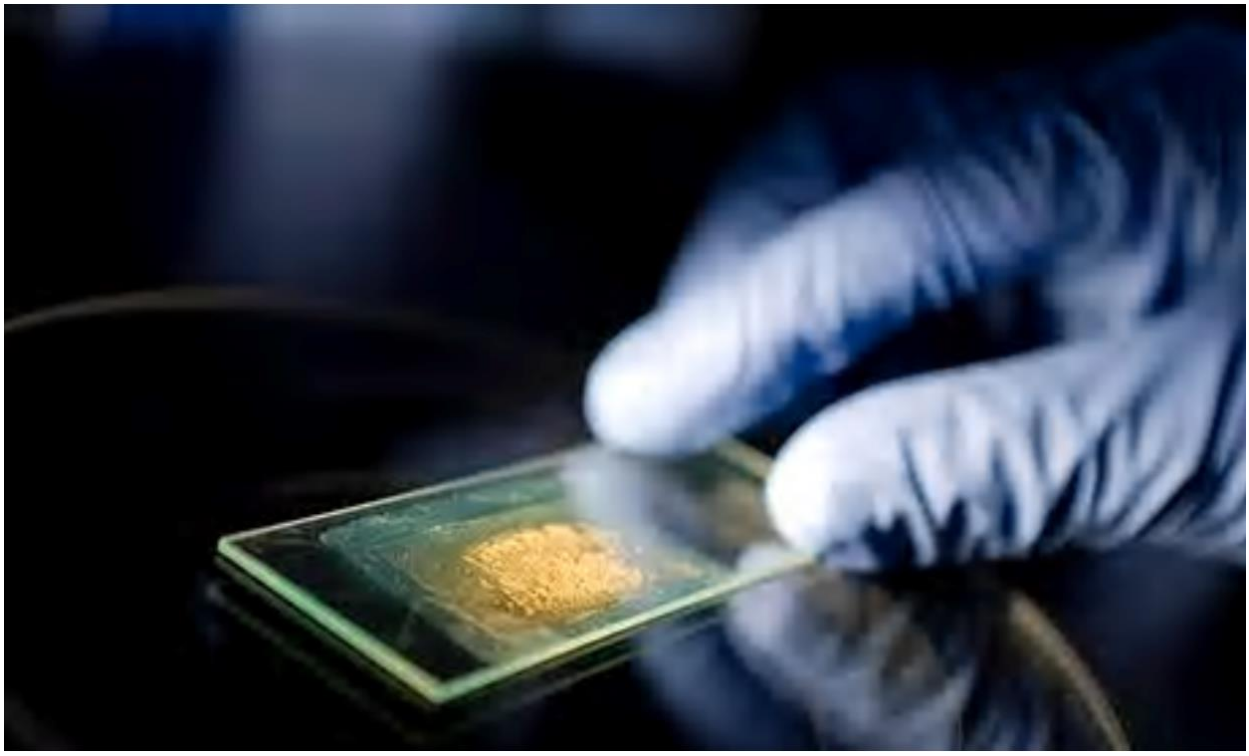
2.1 Different types of Nanotechnology



Task 1) Sort card

Can you match the given examples of nanotechnology to its appropriate type?

2.2 Metrology: Forensics



Task 2) Reading

Please read the following fictional case scenario carefully and answer the questions on your worksheet.

If Sherlock Holmes was a nanomaterial scientist, his partner might have replied: Forensic Nanotechnology: a scientific whodunit.

Yes, nanoparticles are a big deal in forensic science. If you have ever watched the TV series crime scene investigation, you know the science can help us to catch criminals. As it turns out, one particular area of science – nanotechnology – is a big player in crime solving game.

Nanotechnology can help identify, fingerprints, source of ink, and even residue from gunshots.

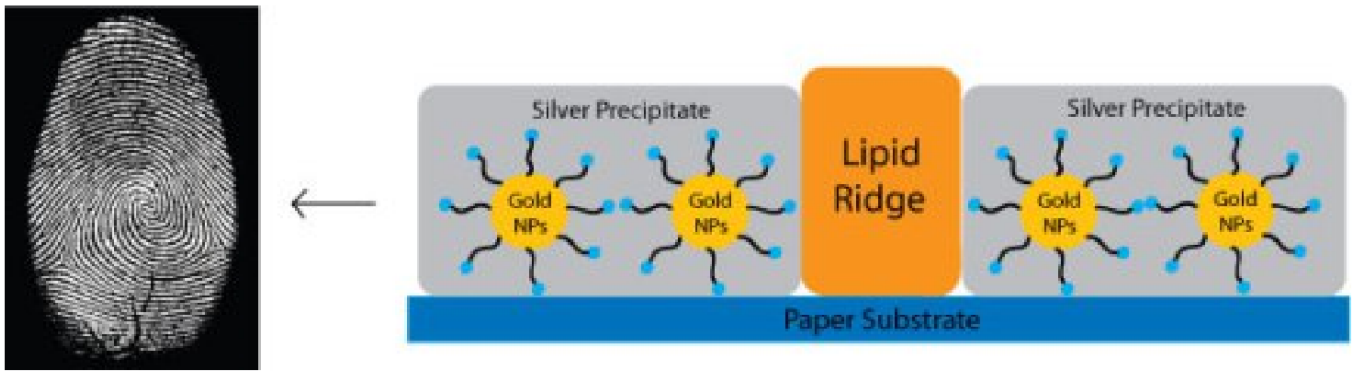
Fictional case scenario

To show us this, I'm introducing a fictional character named Dr. Nanock Holmes, who is an expert at using non-fictional nano-forensics to reveal the truth.

Upon invitation from detectives, Dr. Nanock Holmes arrived at a grisly scene on a second-floor apartment in the center of Nanoville. A single man was deceased on the floor. The man had a gun in his right hand, with his finger on the trigger. A sad farewell letter was sitting on a desk nearby, with a pen resting on top of it. All initial evidence pointed to a suicide. However, Dr. Nanock Holmes was not convinced.

He retrieved the farewell letter, the pen and the deceased man's long-sleeved shirt and headed back to his lab. The first thing Dr. Holmes checks for are fingerprints on the letter. As a solid way to identify suspects, fingerprint analysis has been one of the most common and important techniques to solve crimes. When your finger touches anything, the raised grooves on your fingers leave traces of your sweat secreted from your eccrine glands.

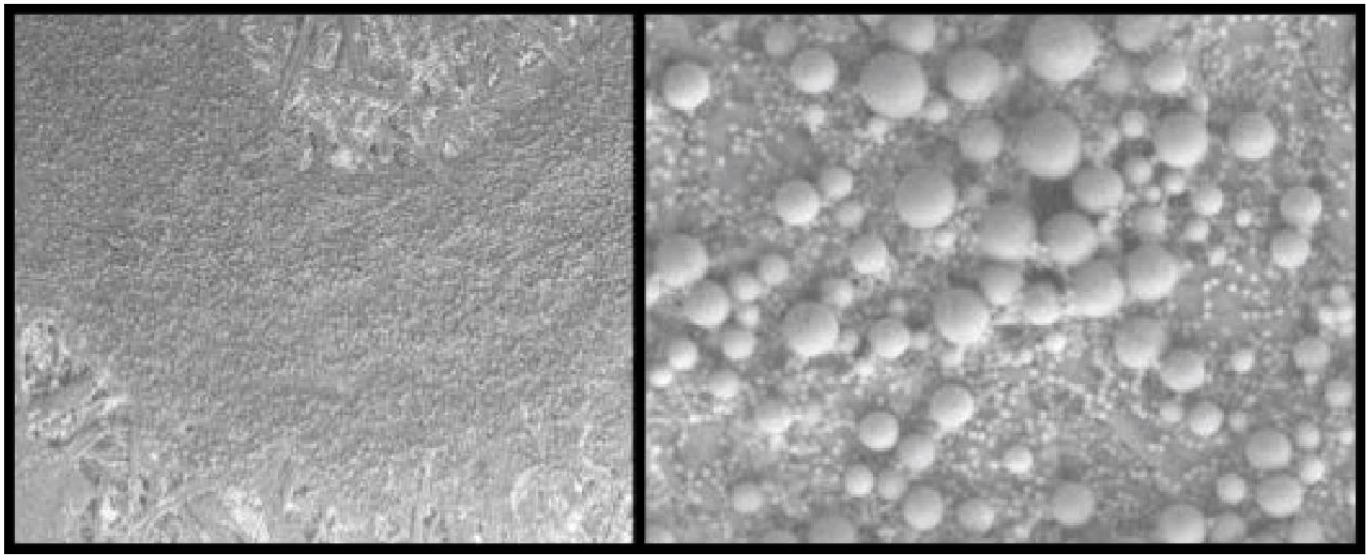
Traditional fingerprint analysis uses fine powders and a brush to reveal fingerprints on glasses and other flat materials. However, developing fingerprints on porous materials, like paper, is particularly difficult. Fortunately, Dr. Nanock Holmes knew that an Israeli research group had published a way to use nanoparticles to do just this. Applying this procedure, Holmes applied gold nanoparticles to the paper. Those nanoparticles were specially coated to stick to paper but not fingerprint residue. However, the fingerprint is still invisible at this point. In order to make the fingerprint visible, Holmes next applied a "developer solution" containing silver (similar to how photographs can be developed). The silver was deposited only on the non-fingerprint region of the paper, where the gold nanoparticles had become attached. This resulted in an "inverse fingerprint."



So what did Dr. Holmes find?

Well, a fingerprint was revealed—but it didn't belong to the poor dead man. Looks like things are getting interesting. What else can Holmes, the nanomaterial scientist do?

The answer is ink analysis. Currently, the most common types of ink that contain nano-sized particles are gel inks and ink jet inks. There are two main ways to analyze ink. Besides a composition analysis to know what kinds of chemicals exist in the ink, scientists can also look at the morphology, which means the shape and size of nanoparticles in ink. Scanning electron microscopy (SEM) can help us to image the nanoparticles. Below are two SEM images of a gel ink at 100X magnification (left) and at 1000X magnification (right).



After getting the analytical profile of the ink, the profile will be compared with those of a standard reference collection. When the composition of the ink sample and the size and shape of the nanoparticles inside it match those of the known reference collection, one can infer who the manufacturer of the ink is, where it is sold, when the ink first became commercially available, and in what pens the ink is used.

Interesting! Now Dr. Holmes has finished the morphology analysis of the ink on the letter and the gel ink from the pen which was found uncapped on the farewell letter on the desk. It sure seems like that pen was the one used to write the will.

Bang! Nanoparticles tell the truth.

Holmes' analysis revealed that these two inks are definitely from two different manufacturers, indicating that the farewell letter was not written using the pen on the desk. What do you think? It sure seems like someone forged the farewell letter with a different pen.

Think that the work for the nanomaterial scientist is done? Nope!

Don't forget we have another piece of evidence—the long-sleeve shirt. Gun-shot residue analysis is always a critical step in forensic investigations involving shooting. Upon firing a gun, both burned and unburned powder form a cloud that may cause a roughly circular pattern around the bullet hole upon contact. The gun-shot residue commonly spreads up to 36 inches away from the bullet hole, and this gun-shot residue contains nanoparticles! By looking at the shape, size and element composition of nanoparticles in gun-shot residue, one can determine from what distance the gun was shot and also what kind of gun was used.

Had it been suicide, scientist should have also found nanoparticles on the sleeves of the dead man. Guess what? Dr. Holmes doesn't find anything. There are nearly identical nanoparticles on the gun and around the wound, but none on the man's sleeves. That means the dead man could not have been the one who fired the gun. It is likely that someone else shot him and then put the gun in his hand, making it seem like a suicide.

Now we see: everything Dr. Nanock Holmes has done to reveal the truth made use of nanoparticles. In the analysis of fingerprints, inks, gun-shot residues, and much more (like explosives residues), nanoparticles are helping us reveal what conventional investigation methods cannot. Maybe one day, more and more people like Dr. Nanock Holmes will be around us, and they would say in confidence: "Hey, you know my methods, so don't you dare to commit a crime—'cause nanoparticles will tell us the truth![3]

[3] Source: http://sustainable-nano.com/2013/08/27/forensic-nanotechnology-a-scientific-whodunit/

Homework 2

Nanomedicine: Drug Delivery

This homework assignment for the second tutorial is to assess your knowledge and skills that will be relevant to the final assignment.

Please read the article on nanomedicine carefully and answer the following questions:

Question 1) What are the current applications of nanomedicine? (Give example)

Question 2) What is drug delivery? and what are the different types of it?

NIH Public Access
Author Manuscript
Nano Lett. Author manuscript; available in PMC 2011 September 8.

Published in final edited form as:
Nano Lett. 2010 September 8; 10(9): 3223–3230. doi:10.1021/nl102184c.

Nanotechnology in Drug Delivery and Tissue Engineering: From Discovery to Applications

Jinjun Shi[†,§], **Alexander R. Votruba**[§], **Omid C. Farokhzad**[†,§], and **Robert Langer**[†,‡,*]
[†]MIT-Harvard Center for Cancer Nanotechnology Excellence, Cambridge, Massachusetts, 02139

[‡]Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts, 02139

[§]Laboratory of Nanomedicine and Biomaterials, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, 02115

Abstract

The application of nanotechnology in medicine, referred to as nanomedicine, is offering numerous exciting possibilities in healthcare. Herein, we discuss two important aspects of nanomedicine—drug delivery and tissue engineering—highlighting the advances we have recently experienced, the challenges we are currently facing, and what we are likely to witness in the near future.

Keywords

Nanotechnology; nanomedicine; drug delivery; tissue engineering

In pharmaceutical industries, a new molecular entity (NME) that demonstrates potent biological activity but poor water solubility, or a very short circulating half-life, will likely face significant development challenges or be deemed undevelopable. On the other hand, less active but pharmaceutically optimal compounds may become more suitable candidates for development. In either case, there is always a degree of compromise and such trade-offs may inevitably result in the production of less-ideal drugs. However, with the emerging trends and recent advances in nanotechnology, it has become increasingly possible to address some of the shortcomings associated with potential NMEs. By using nanoscale delivery vehicles, the pharmacological properties (e.g. solubility and circulating half-life) of such NMEs can be drastically improved—essentially leading to the discovery of optimally safe and effective drug candidates. This is just one example that demonstrates the degree to which nanotechnology may revolutionize the rules and possibilities of drug discovery and change the landscape of pharmaceutical industries. Indeed, current nanotechnology-based therapeutic products have been validated through the improvement of previously approved drugs, and many novel classes of nanotherapeutics are now underway.[1-3]

Drug discovery is only one of the many areas in healthcare that nanotechnology is now benefiting. The current and promising applications of nanomedicine include, but are not limited to, drug delivery, *in vitro* diagnostics, *in vivo* imaging, therapy techniques, biomaterials, and tissue engineering. Summarized in Box 1 are some important opportunities that nanotechnology may afford in each research area. Some of these opportunities are becoming realities or are actually being used today, while others are generating promise in

*To whom correspondence should be addressed. rlanger@mit.edu.

Conflict of Interest. O.C.F. and R.L. have financial interest in BIND Biosciences and Selecta Biosciences.

NIH-PA Author Manuscript
NIH-PA Author Manuscript
NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

their early phases of development and are expected to experience vigorous growth in the foreseeable future. As recognition of the importance of this exciting field, it is expected that the global market of nanoscale applications in the medical field could grow to $70 - $160 billion by 2015.[4,5] In this perspective, we discuss the applications of nanomedicine with specific focus on drug delivery and tissue engineering.

Box 1

Nanoscale Applications in Medicine

Drug delivery

Nanoscale delivery vehicles can (1) enhance the therapeutic efficacy and minimize adversities associated with available drugs; (2) enable new classes of therapeutics; and (3) encourage the re-investigation of pharmaceutically suboptimal but biologically active new molecular entities that were previously considered undevelopable.

In vitro diagnostics

Nanotechnology-based sensors (e.g. nanowires, nanotubes, nanoparticles, cantilevers, and micro-/nanoarrays) can enable fast and high throughput detection of disease biomarkers with higher sensitivity and lower sample consumption. Nanotechnology also offers hope for the early detection of viruses, bacteria, and circulating tumor cells, as well as for single cell analysis.

In vivo imaging

Targeted imaging nanoprobes (e.g. magnetic nanoparticles, quantum dots, and carbon nanotubes) could provide a faster, less invasive, and more accurate way to diagnose diseases (e.g. cancer) at their earliest stages and monitor disease progression. Some other possible opportunities include reporting *in vivo* efficacy of therapeutics, tracking nanocarrier biodistribution in the body, and helping surgeons to locate tumors and their margins, identify important adjacent structures, and map sentinel lymph nodes.

Therapy techniques

Certain nanomaterials have unique therapeutic properties that differ from conventional drugs, and can, therefore, be directly used to treat diseases. For example, hafnium oxide- and gold-based nanoparticles can greatly enhance X-ray therapy; gold nanoshells/ nanorods, carbon nanotubes, magnetic nanoparticles can induce hypothermia to kill cancer cells; and nanocrystalline silver is being used as an antimicrobial agent.

Biomaterials

Biocompatible nanomaterials that have optimal mechanical properties can be used as medical implants (e.g. dental restoratives and bone substitutes)[†]. Nanocoatings or nanostructured surfaces can also improve the biocompatibility and adhesion of biomaterials.

Tissue engineering

Nanotechnology can enable the design and fabrication of biocompatible scaffolds at the nanoscale and control the spatiotemporal release of biological factors—resembling native extracellular matrix—to direct cell behaviors, and eventually lead to the creation of implantable tissues.

([†]It can also be categorized as hard-tissue engineering.)

NIH-PA Author Manuscript NIH-PA Author Manuscript NIH-PA Author Manuscript

Drug Delivery

Since liposomes were first described in the 1960s and proposed as carriers of proteins and drugs for disease treatment,6 nanotechnology has made a significant impact on the development of drug delivery systems. A variety of organic/inorganic nanomaterials and devices have been used as delivery vehicles to develop effective therapeutic modalities (Figure 1). So far, there are over two dozen nanotechnology-based therapeutic products approved by Food and Drug Administration (FDA) for clinical use, and more are in clinical trials.1-3 Of these products, the majority are composed of a non-targeted delivery system (e.g. liposomes and polymers) and a drug, and are therefore considered first generation nanotherapeutics.7

Compared to conventional drug delivery, the first generation nanosystems provide a number of advantages. In particular, they can enhance the therapeutic activity by prolonging drug half-life, improving solubility of hydrophobic drugs, reducing potential immunogenicity, and/or releasing drugs in a sustained or stimuli-triggered fashion. Thus, the toxic side effects of drugs can be reduced, as well as the administration frequency. In addition, nanoscale particles can passively accumulate in specific tissues (e.g. tumors) through the enhanced permeability and retention (EPR) effect.8 Beyond these clinically efficacious nanosystems, nanotechnology has been utilized to enable new therapies and to develop next generation nanosystems for "smart" drug delivery. Below are several areas, from our perspective, that will generate medical breakthroughs in the near future, and some of them could inspire the derivation of the next "Killer Applications".

New therapeutics delivery

Gene therapy and RNA interference (RNAi), the two most recent and notable therapies, hold great promise as treatment and prevention methods for various diseases.9-10 However, the systemic administration of new therapeutics (e.g. DNA and siRNA) is affected by several barriers such as enzymatic degradation, uptake by reticuloendothelial system, kidney filtration, and limited intracellular entry. Cationic nonviral nanocarriers have, therefore, been widely used to encapsulate and make these new therapeutics more efficient. Unfortunately, a substantial number of these materials can produce severe problems associated with toxicity, immune or inflammatory responses, and serum instability, making them unsuitable for clinical applications. Consequently, safe and effective delivery materials have become the bottleneck for the widespread use of gene therapy and RNAi.

Recent and exciting developments are now paving the way for the clinical application of these new therapeutics. For example, high throughput screening platform technologies have been described and proof-of-concept has been demonstrated by identifying cationic polymers and lipid-like-materials suitable for systemic gene and RNAi delivery.11-12 Rational design approaches, on the other hand, are also showing great potential in creating successful delivery materials (e.g. DLin-KC2-DMA13 and cyclodextrin-containing polymer14). Nevertheless, it would be favorable to use previously FDA-approved materials for new therapeutics delivery, as they have specific benefits such as safety and sustained release. One such material being studied is poly(lactic-co-glycolic acid) (PLGA), a specific polymer that can be applied to form nanoparticles densely loaded with siRNA for sustained gene silencing.15 Beyond assuring the safety and efficiency of delivery materials, more progress is needed to screen other factors, including the physicochemical properties of nanocarriers, targeting ligands, and formulation methods—all of which can affect the delivery of new therapeutics *in vivo*.

NIH-PA Author Manuscript NIH-PA Author Manuscript NIH-PA Author Manuscript

Targeted delivery

It is widely believed that active targeting, through the modification of nanoparticles with ligands, has the potential to enhance the therapeutic efficacy and reduce the side effects relative to conventional therapeutics.16 The ability to actively target specific cells rather than tissues also allows ligand-conjugated nanocarriers to outperform first generation, non-targeted nanosystems. While the necessity of targeted delivery depends on various factors (e.g. delivery vehicles, drugs, and diseases), a myriad of important benefits have been demonstrated.3,16-19

In cancer therapy, the presence of targeting ligands can greatly enhance the retention and cellular uptake of nanoparticles *via* receptor-mediated endocytosis—even although tumor accumulation is largely determined by the physicochemical properties of nanoparticles.16,17 This can then lead to higher intracellular drug concentration and increase therapeutic activity, which is particularly important for bioactive macromolecules (e.g. DNA and siRNA) that require intracellular delivery for bioactivity.16 In the case of endothelial targeting for cardiovascular diseases or immunological tissue targeting, nanoparticle localization is guided by ligand-receptor interactions rather than EPR.18 Similarly, ligand-mediated targeting is of importance for the transcytosis of nanodrugs across tight epithelial and endothelial barriers (e.g. blood-brain barrier).19 Additionally, targeted delivery has been applied, in some instances, to combat multidrug resistance (MDR).3 It is also envisioned that long-circulating targeted nanoparitcles may be able to locate and fight migrating cancer cells.

Despite three targeted nanoparticle systems now in phase I/II clinical trials,3 the clinical translation of targeted delivery is not as smooth as we expect. One possible barrier stems from the complexity behind manufacturing viable targeted nanoparticles. Targeted nanoparticle fabrication usually requires multiple steps—biomaterial assembly, ligand coupling/insertion, and purification—and could cause batch-to-batch variation and quality concern. The recent development of single-step synthesis of targeted nanoparticles by self-assembling pre-functionalized biomaterials provides a simple and scalable manufacturing strategy.14,20 Another important consideration is targeting ligands. Among others, some variables that must be considered include ligand biocompatibility, cell specificity, binding affinity, mass production, and purity.21 For example, to achieve maximal specificity, the ideal ligand would be able to recognize the most over-expressed receptors on target cells relative to healthy ones. Other factors that could also affect cell targeting include ligand surface density and arrangement, as well as spacer type and length dividing ligand molecules and nanoparticles.22 Nevertheless, with advances in ligand engineering and screening, and nanoparticle optimization, targeted delivery will become a mainstay in the next generation of drug therapy.

Co-delivery

Combination therapy has shown several potential advantages (e.g. synergistic effects and reversal of drug resistance) and may prove more effective than single drug therapy.23 However, due to the distinct pharmacokinetic profiles of individual drugs, the synergistic drug ratio optimized *in vitro* will undoubtedly change after the conventional administration of drug 'cocktails'—an outcome that could in turn lead to insufficient therapeutic results *in vivo*. To this end, lipid- and/or polymer-based nanoscale systems, previously developed for single drug delivery, have been applied to facilitate co-delivery. For some drug combinations, we can successfully tune the relative dosage of various drugs in single particle levels, and simultaneously deliver them to target sites with a maintained drug ratio.24 For other combinations, we need to develop novel delivery vehicles with desired functionalities that enable co-encapsulation of hydrophobic and hydrophilic drugs, active

NIH-PA Author Manuscript NIH-PA Author Manuscript NIH-PA Author Manuscript

targeting, and/or temporally controlled release.25,26 Such features are especially essential for the co-delivery of drugs and nucleic acids, which requires intracellular delivery in order to elicit bioactivity.27,28 For example, in the case of co-delivering chemotherapy and RNAi therapy to treat multidrug resistant cancers, the ideal nanoparticle would be expected to first release siRNA to reduce the expression of MDR transporters, followed by the release of anticancer drugs.

Another exciting advancement in co-delivery is the ability to combine targeted imaging and therapeutic agents within the same particle—allowing us to visualize sites of targeted drug delivery and deliver therapeutics simultaneously ("theranostics").29 This technology is innovative in concept and holds significant promise for making large medical impacts within the next few decades. It could provide us with critical information on intracellular targets, ensure that therapeutic agents are efficiently reaching their target sites, and enable the effective early detection and treatment of diseases. Current research is primarily focused on the design of such multifunctional nanosystems and proof-of-concept tests,30-33 but more systematic *in vivo* studies are needed.

Future research in this arena will also likely help us trace the absorption, distribution, metabolism and excretion of nanoparticles *in vivo*. It is important that we understand the pharmacokinetics of a given drug delivery system in order to improve upon formulations, estimate clinical doses, and guarantee safety.34 Currently, radionuclide labeling is the only technique that can be used to provide *in situ* quantitative information; but radio emitters may be too unstable to conjugate with nanomaterials. With the help of recently developed *in vivo* imaging probes like magnetic nanoparticles,7 quantum dots,35 gold nanoparticles,36 and carbon nanotubes,37 more imaging modalities may become available to track the distribution of nanotherapeutics in the body.

MEM/NEM devices for drug delivery

Parallel to the development of particulate delivery systems, the field of micro-/nanoelectromechanical (MEM/NEM) device-based drug delivery has also made significant headway over the past decade. In particular, implantable microchips containing nanosized reservoirs have been developed to deliver drugs for long time periods in a precisely controlled manner; microneedles are being tested in painless transdermal drug delivery; and the incorporation of nanofeatures (e.g. nanopores, nanochannels, and nanoparticles) in microfabricated systems are perfecting drug delivery and immunoisolation techniques.38-41 Intriguingly, these devices can be further modified to deliver new therapeutics, achieve targeted delivery, and co-deliver multiple agents.41,42 Substantial efforts are also being put into creating intelligent devices that could potentially sense when and how much dose is needed and then automatically release it from reservoirs.42 To do this, one feat that must be met is the continuous and stable monitoring of physical and biochemical conditions, *in situ*. The recent development of nanotechnology-based sensors (e.g. nanowire and nanotube) may offer new ways to address this concern, and could even facilitate device miniaturization.43

In addition to drug delivery, micro- and nanofabricated devices have shown potential in developing nanocarriers with controlled physicochemical properties (e.g. size, shape, and surface chemistries). By using perfluoropolyether molds, fabricated by traditional top-down approaches, polymeric particles at the submicron scale can be replicated with variable shapes and controllable surface chemistries.44 Compared to bulk synthesis, microfluidic devices have also recently been used for nanoprecipitation synthesis of smaller and more homogeneous PLGA-PEG nanoparticles.45 Nonetheless, micro- and nanotechnologies, which can be universally used to control the biophysicochemical properties of various nanosystems, are still in great demand.

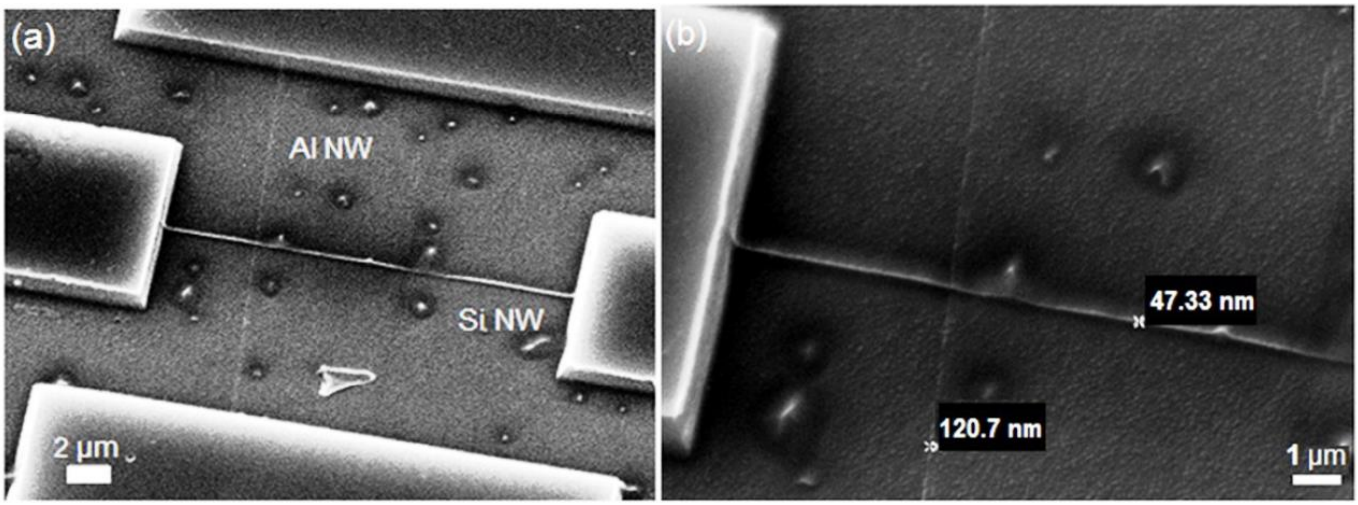
NIH-PA Author Manus

Beyond the aforementioned opportunities and challenges, the following are also essential for the development of next generation drug delivery systems: (1) detailed physicochemical characterization of nanosystems (which will require sophisticated and state-of-art techniques); (2) restriction of undesired uptake by non-target organs (e.g. liver and spleen); (3) improvement of stimuli-triggered or programmable drug release systems (e.g. pH, temperature, light, enzyme, ultrasound, magnetic field, and electric current); (4) furthering the means by which we can understand the biological principles of disease and its microenvironment, the biological barriers that hinder drug delivery, and endosomal trafficking pathways; and (5) identification of biological markers attributable to diseased cells. With continual advancement in these areas, we can expect that the field of drug delivery will benefit greatly from the emergence of finely engineered nanomaterials and devices.

Notes & Questions

Tutorial 2

Tutorial 3 – Applications (Part II)



What is the Purpose of Tutorial 3?

- Si NW - based Chemical Sensors: Example of the applications in Electronics and Sensors
- What are the issues of current Si NW - based Chemical Sensors?
- How to solve these issues?! (Aims and Research Goals)

Before we begin ...

On a post-it, write down the examples of applications you know in electronics.

On a different post-it, write down the examples of applications you know in sensors.

<u>Challenge</u>: Can you name any application using both type of technologies?!

3.1 Electronics and Sensors: Si NW Chemical Sensors and their Issues

Task 1) Reading

Read the following section about Si-NW based chemical and biological sensors, and find out 3 issues with these sensors:

In early works in this field, the use of Si NWs as a basis for nanoscale sensors was demonstrated by Lieber and Cui in 2001 [14]. Following their initial work on the growth of high quality Si NWs using CVD, Lieber and Cui fabricated Si NW-based sensors to detect different chemical and biological species down to single molecules and 10 pM sensitivity [6, 13, 14]. Since then, numerous other groups have investigated nanometre-scale chemical and biological sensors using Si NWs [13]. State-of-the-art Si NW-based chemical sensors may be classified into two types, based on their operating principles. These are conduction-detection sensors (Fig.1.1(a)) [6–9], and mass-detection sensors (Fig.1.1(b)) [15].

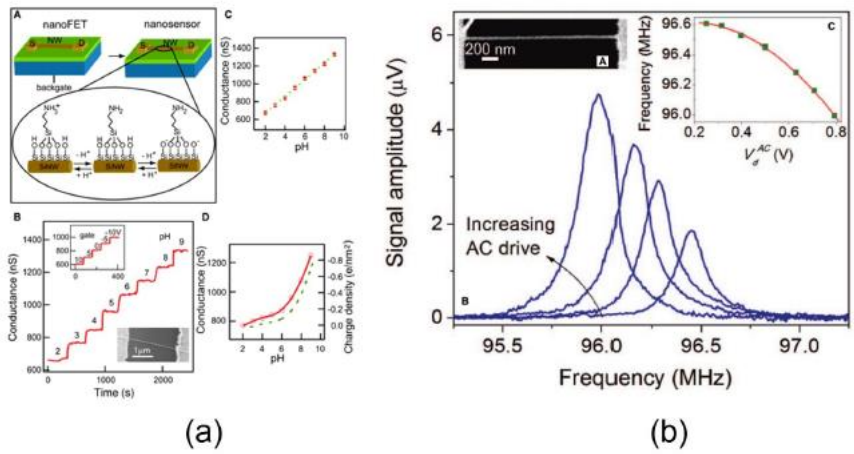


Figure 1.1: *(a) Conduction-detection sensors [6–9] vs. (b) mass-detection sensors [15]: (a) Si NW pH sensor: (A) The schematic diagram of a NW FET converted into NW nanosensors; (B) Conductance of an APTES-modified Si NW vs. time; (C) Conductance vs. pH; (D) Conductance of unmodified Si NW vs. pH [6]. (b) (A) SEM image of a 40 nm thick and 1.8 μm long Si NW and a DC resistance of 80 kΩ; (B) The DC voltage is fixed at* $V_d^{DC} = 0.2\,V$ *and the AC drive is set at* $V_d^{AC} = 0.50, 0.63, 0.71,$ *and* $0.79\,V$ *for the curves, respectively; (C) The resonance frequency vs.* V_d^{AC} *[15].*

In both types, the surface of the NWs is functionalised with particular silane-coupling agents as linker molecules [6], in order to make either an H-terminated Si surface or a native-oxide-covered Si surface active to the targeted molecules. A high-quality surface functionalisation layer is essential, primarily for sensor selectivity but also for sensors sensitivity. However, while various functionalisation methods [16–18] have been examined for Si NWs, based on both liquid-phase and vapour-phase surface processes, it is unclear if any of the existing techniques can cover the NW surface uniformly at the nanoscale. Technically-challenging and often costly surface functionalisation is a crucial issue, creating a bottleneck in realising reliable, cost-effective Si NW-based chemical sensors.

A second issue in present Si NW-based chemical sensors is that adsorbed chemical molecules cannot be identified directly from the detected change in the conductance or resonant frequency. Other chemical interactions may also be possible, reducing sensor selectivity. Existing sensors monitor only the concentration of particular chemical molecules selectively bonded onto the functionalised surface.

A third issue in present Si NW-based chemical sensors is the lack of simple techniques to make the sensor reusable. Joule heating caused by forcing a high current density through the NW has been proposed to remove the adsorbed molecules on the NW surface, but this process inevitably ablates the functionalisation layer covering the NW surface as well. Therefore, sensors after this refresh operation require re-functionalisation, making the device impractical for commercial application.

3.2 Aims and Research Goals

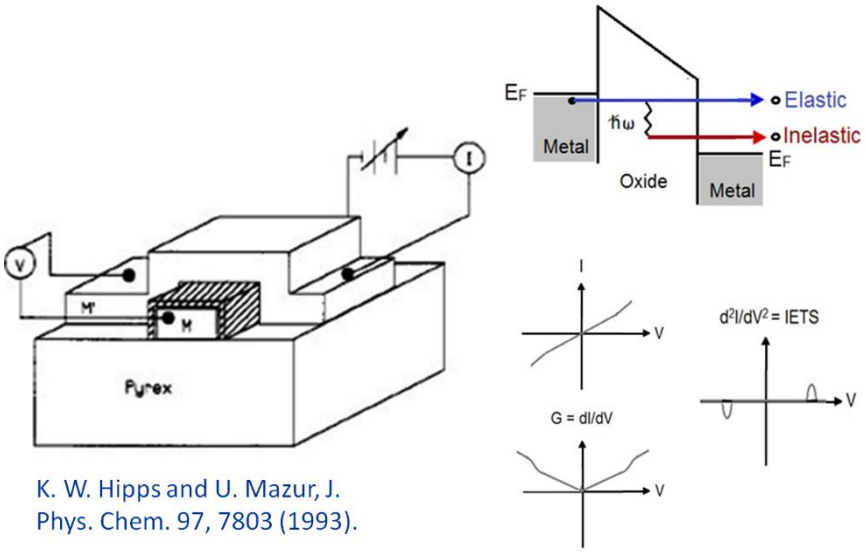
• Fabricate a functionalisation-free silicon-based chemical molecule detector: using molecular phonon spectrum or IETS technique

• Use of Semiconductor / Insulator / Metal Tunnel junction instead of Metal / Insulator / Metal Tunnel junction allows: identification of a variety of harmful gas molecules at very low concentration, by measuring the elastic and inelastic tunnelling current components

• Nanoscale: Increase sensitivity (from ~ 10^{13} Molecules to ~ 500 molecules)
+
IETS measurements at room temperature (300K)

• Reusable device and therefore very cost effective

What is IETS?!



K. W. Hipps and U. Mazur, J. Phys. Chem. 97, 7803 (1993).

Task 2) Writing

Summarise what you have learned about IETS:

Homework 3

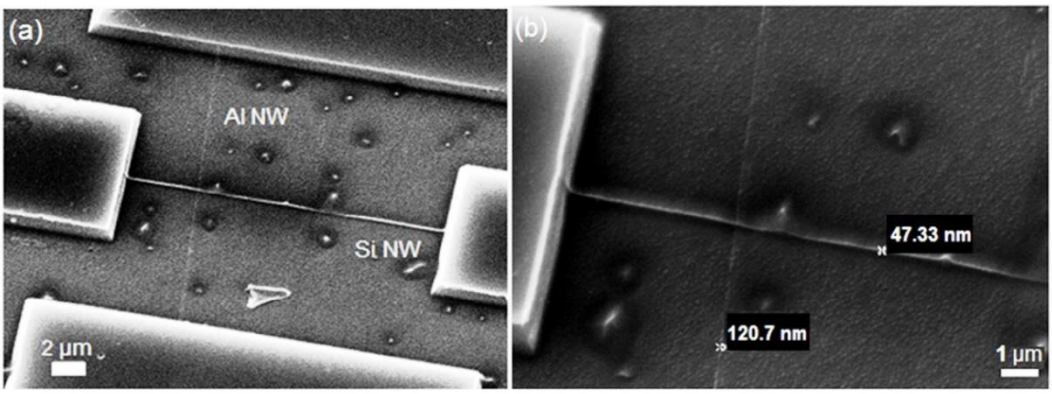
This homework assignment for the third tutorial is to assess your knowledge and skills that will be relevant to the final assignment.

Please research on one of the applications of nanotechnology in materials, and then write about the problems that can be potentially solved by this application. (500 Words)

Notes & Questions

Tutorial 3

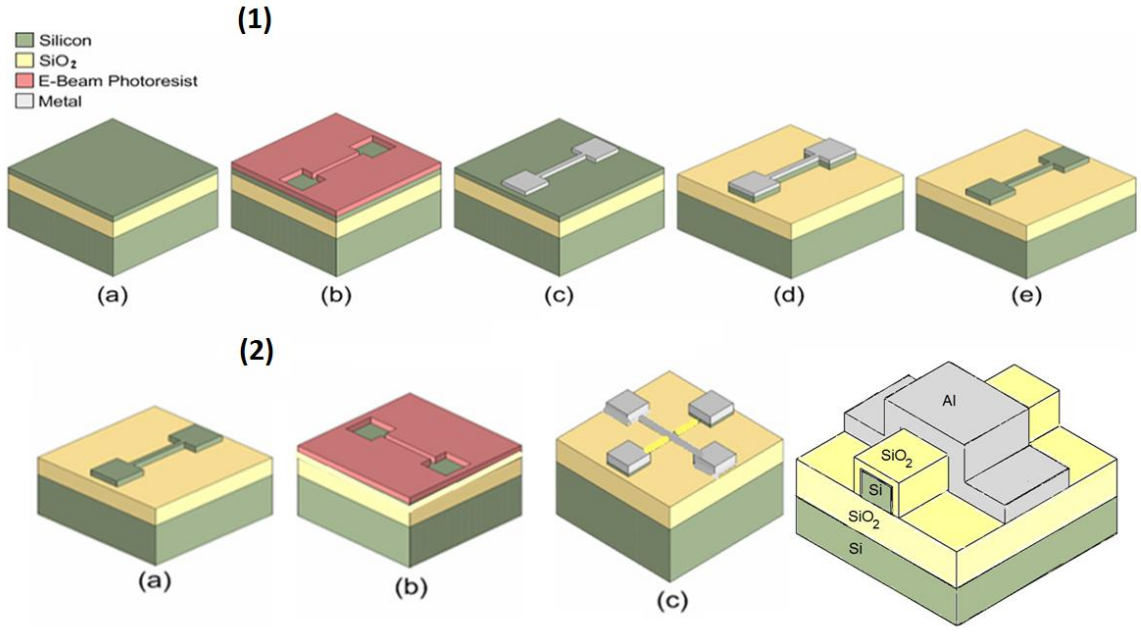
Tutorial 4 – My PhD Project

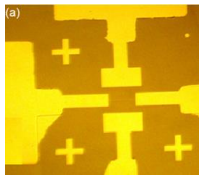


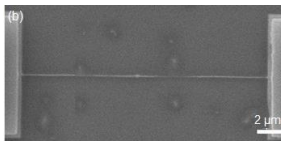
What is the Purpose of Tutorial 4?

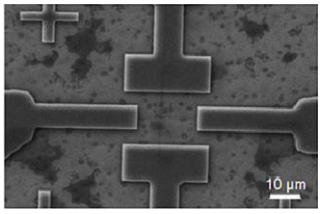
- Fabrication of Si NW / SiO_2 / Al NW Tunnel junction
- Measurements and Results
- How to design a scientific poster?

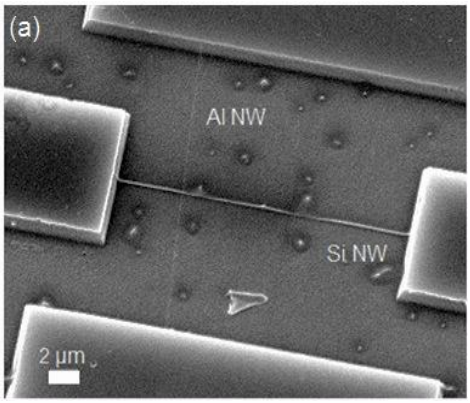
4.1 Fabrication of Si NW / SiO_2 / Al NW Tunnel junction

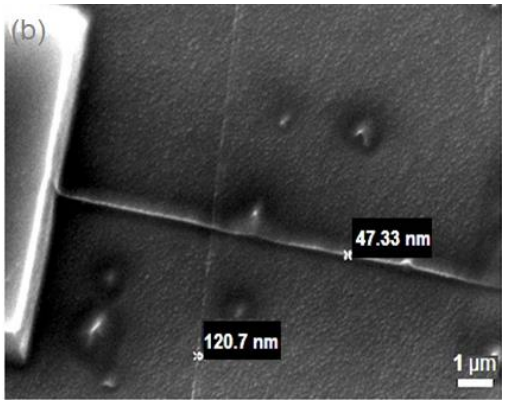










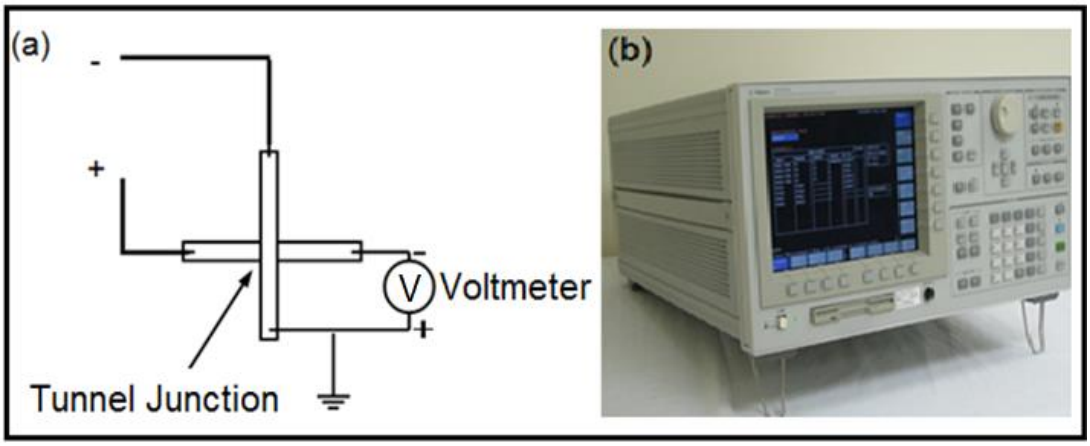


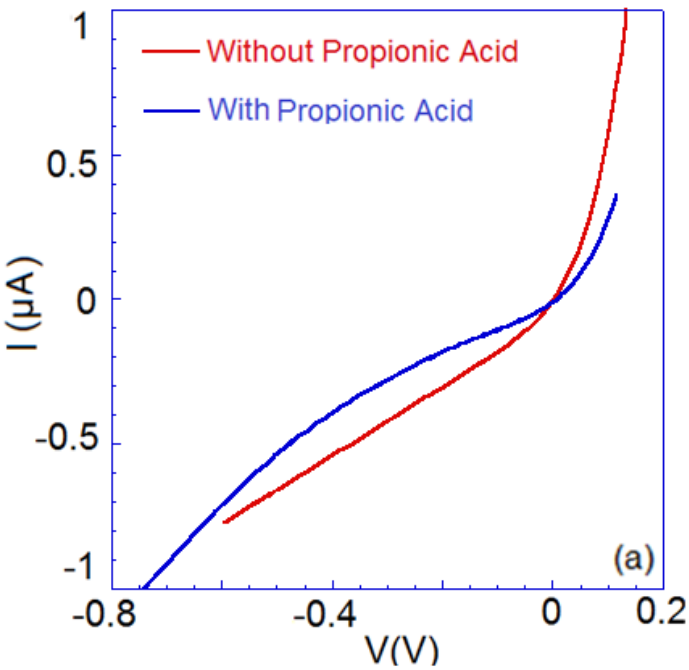
Task 1) Description

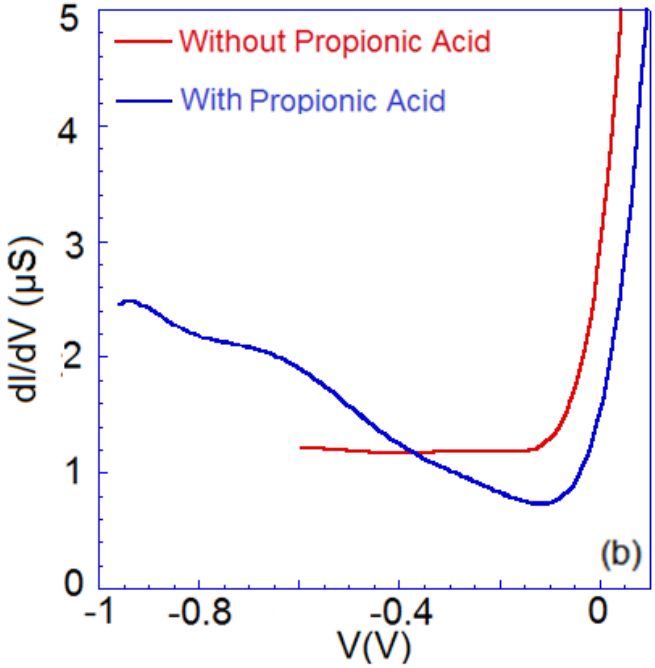
Write a short description for each fabrication step:

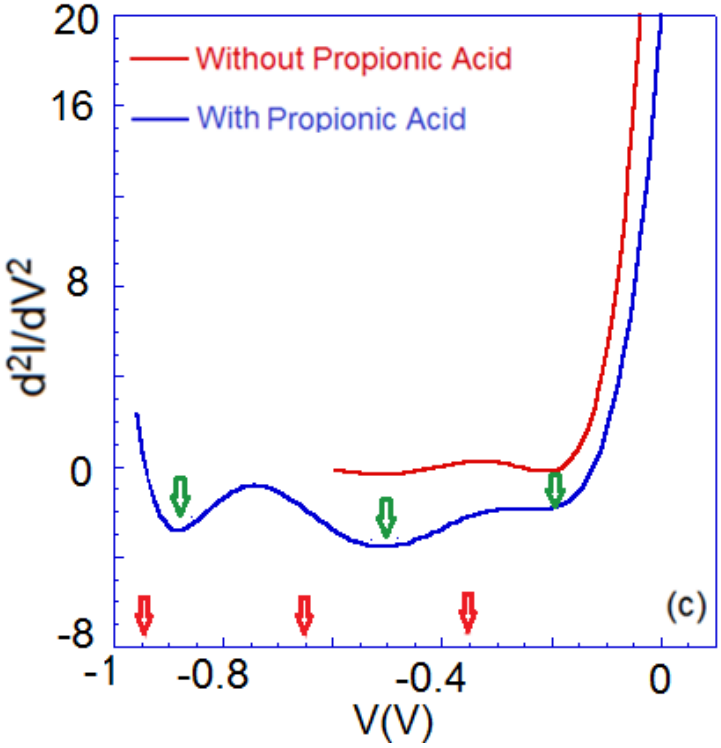
<u>**Challenge**</u>: Can you figure out whether Si NW made by bottom-up technique or top-down technique?!

4.2 Measurements and Results



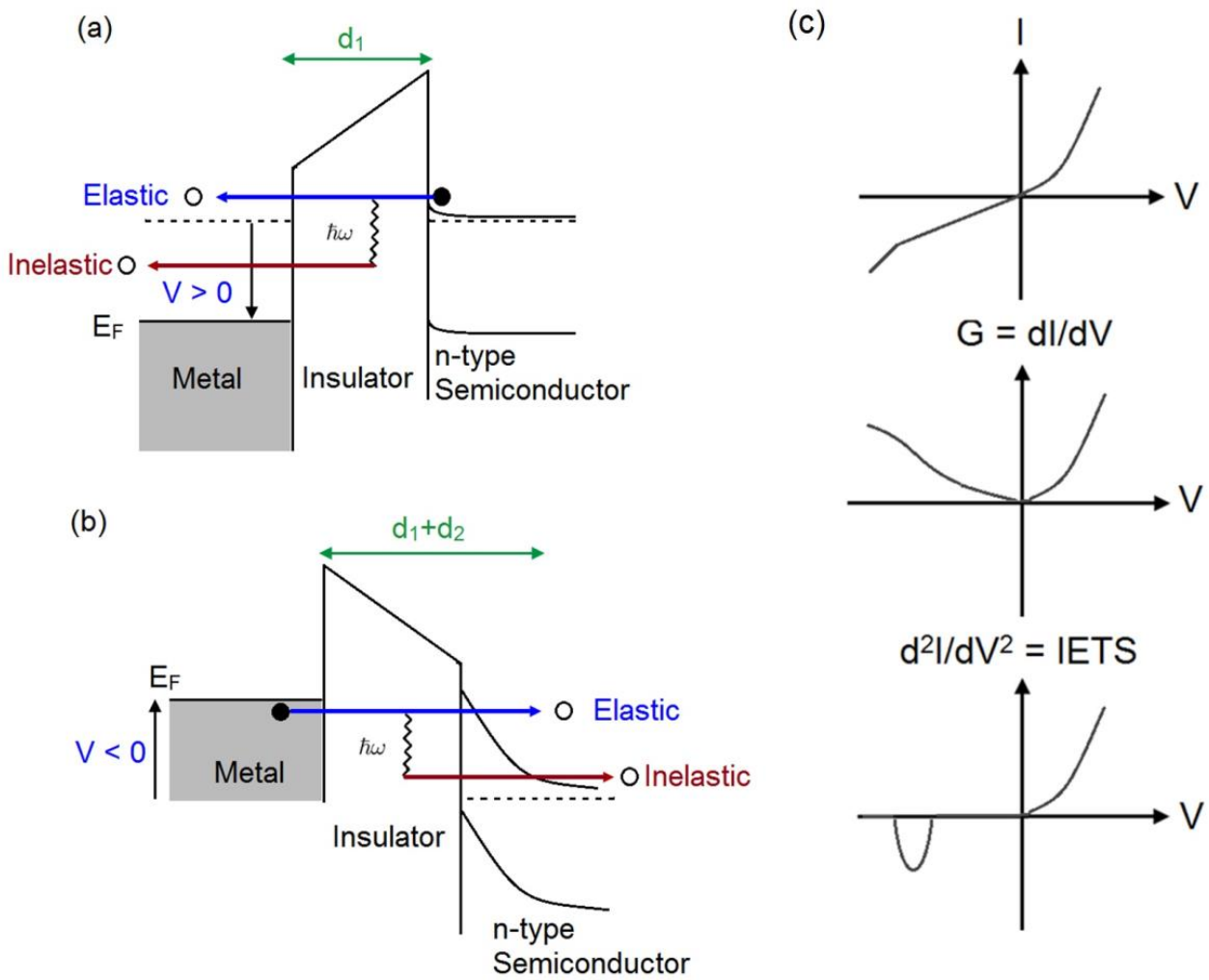




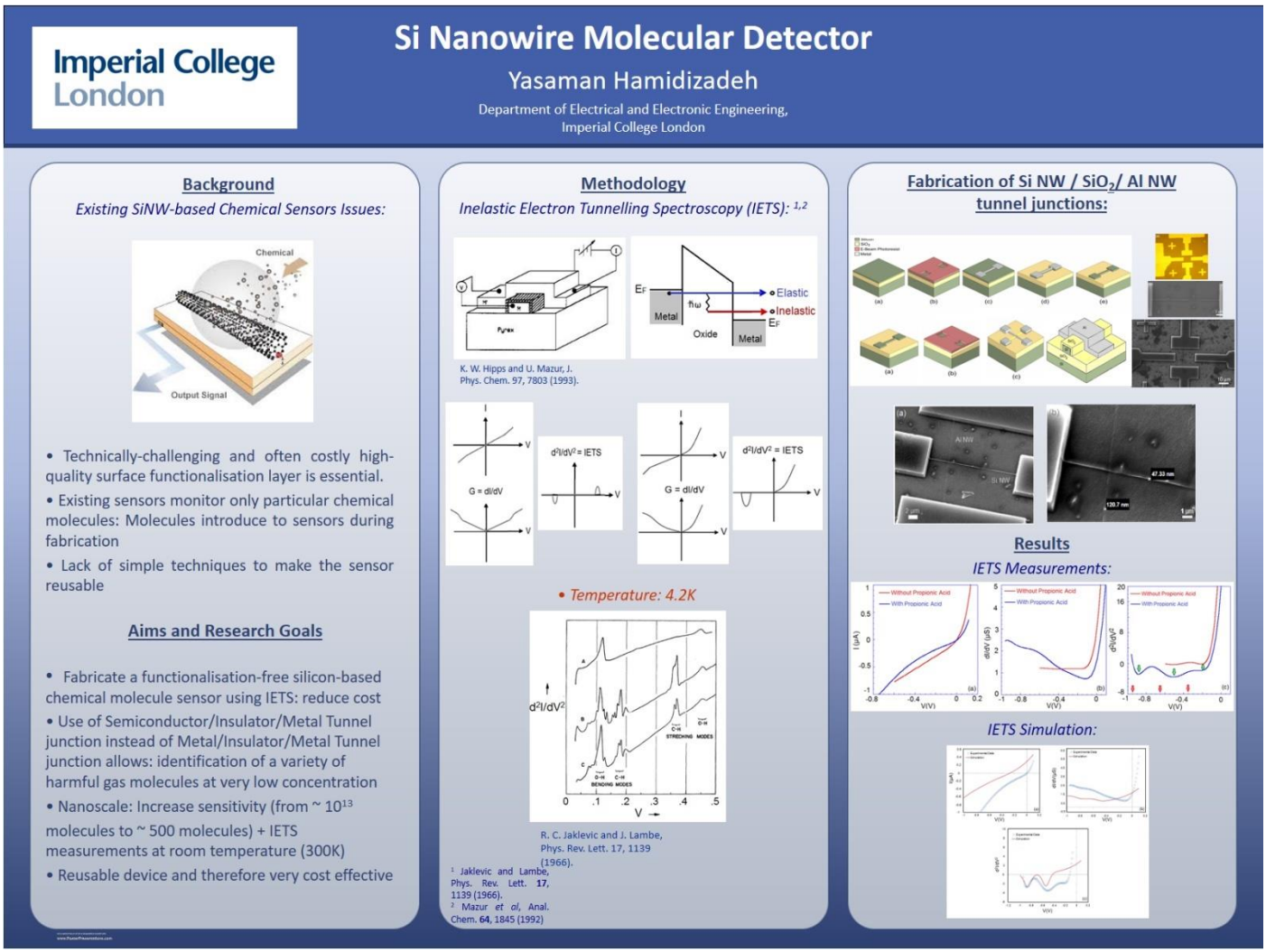


Task 2) Think – Pair - Share

Why do you think these graphs looks different from traditional Metal / Insulator / Metal tunnel junctions?!



4.3 How to design a scientific poster



Homework 4

This homework assignment is to assess your knowledge and understanding retained after Tutorial 4 about designing a poster.

Write a short paragraph about:

- What do you think are the important features of a good poster?!
- How much details you need to put in a poster?
- What are the main sections of a poster?!

Notes & Questions

Tutorial 4

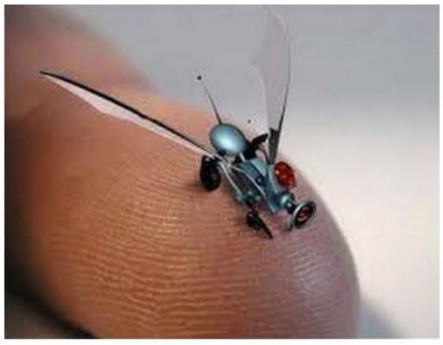
Tutorial 5 – Future & Risks

What is the Purpose of Tutorial 5?

- Get familiar with the examples of technology that nano can bring us in near future
- What are current risks of nanotechnology?
- What are the future risks of nanotechnology?

Before we begin ...

5.1 Future



5.2 Risks

Ready or not, here it comes. In the next 20 years, nanotechnology will touch the life of nearly every person on the planet. The potential benefits are mind boggling and brain enhancing. But like many of the great advancements in the earth's history, it is not without risk.

Here are some of the risks posed to society by nanotechnology[4]:

5.2.1 Now!!

Risk	Example
Nanopollutants	Nanopollutants are nanoparticles small enough to enter our lungs or be adsorbed by your skin. Nanopollutants can be natural or man-made. Nanoparticles are used in some of the products found on the shelves today, like anti-aging cosmetics and sun-cream. The highest risk is to the works in nanotechnology research and manufacturing processes

[4] Source: www.futureforall.org/nanotechnology/risks.htm

5.2.2 Future!!

Risk	In how many years	Example
Privacy Invasion	5-15 years	virtually undetectable surveillance devices could dramatically increase spying on governments, corporations and private citizens
Economic Upheaval	10-20 years	Molecular manufacturing in the assembly of products one molecule at a time. It could make the same products you see today, but far more precisely and at a very low cost. It is unclear whether this would bring room or bust to the global economy
Nanotech weapons	10-20 years	Untraceable weapons made with nanotechnology could be smaller than an insect with the intelligence of a supercomputer. Possible nano and bio technology arms race
Gray Go	+30 years	Free range, self-replicating robots that consume all living matter. However, unlikely, experts say this scenario is theoretically possible, but not for some time

Final Assignment

Your task is to research and choose an application on one of the following types of nanotechnology that you think has specific impact on our lives:

- Nanomedicines
- Nanomaterials
- Nanoelectronics
- Consumer nanotechnology

And **design a scientific poster**.

Note: On your poster allocate the last section to Future of Nanotechnology: what would you design if you were a nanoscience expert.

Notes & Questions

Tutorial 5

Tutorial 6 – Feedback tutorial

What is the Purpose of Tutorial 6?

- To receive feedback on final assignments.
- To share examples of best practice with the other pupils in your group.
- To write targets for improvement in school lessons.
- To reflect on the programme including what was enjoyed and what was challenging.

Final assignment feedback

What I did well…	What I could have improved on…
•	•
•	•
•	•

My target for future work is…

Reflecting on Uni Pathways

What did you most enjoy about Uni Pathways?
•   •   •

What did you find challenging about the programme?	How did you overcome these challenges?
• • •	• • •

Appendix 1 – Referencing correctly

When you get to university, you will need to include references in the assignments that you write, so we would like you to start getting into the habit of referencing in your Brilliant Club assignment. This is really important, because it will help you to avoid plagiarism. Plagiarism is when you take someone else's work or ideas and pass them off as your own. Whether plagiarism is deliberate or accidental, the consequences can be severe. In order to avoid losing marks in your final assignment, or even failing, you must be careful to reference your sources correctly.

What is a reference?

A reference is just a note in your assignment which says if you have referred to or been influenced by another source such as book, website or article. For example, if you use the internet to research a particular subject, and you want to include a specific piece of information from this website, you will need to reference it.

Why should I reference?

Referencing is important in your work for the following reasons:

- It gives credit to the authors of any sources you have referred to or been influenced by.
- It supports the arguments you make in your assignments.
- It demonstrates the variety of sources you have used.
- It helps to prevent you losing marks, or failing, due to plagiarism.

When should I use a reference?

You should use a reference when you:

- Quote directly from another source.
- Summarise or rephrase another piece of work.
- Include a specific statistic or fact from a source.

How do I reference?

There are a number of different ways of referencing, and these often vary depending on what subject you are studying. The most important to thing is to be consistent. This means that you need to stick to the same system throughout your whole assignment. Here is a basic system of referencing that you can use, which consists of the following two parts:

1. **A marker in your assignment**: After you have used a reference in your assignment (you have read something and included it in your work as a quote, or re-written it your own words) you should mark this is in your text with a number, e.g. [1]. The next time you use a reference you should use the next number, e.g. [2].
2. **Bibliography**: This is just a list of the references you have used in your assignment. In the bibliography, you list your references by the numbers you have used, and include as much information as you have about the reference. The list below gives what should be included for different sources.

    a. **Websites** – Author (if possible), title of the web page, website address, [date you accessed it, in square brackets].

    E.g. Dan Snow, 'How did so many soldiers survive the trenches?', http://www.bbc.co.uk/guides/z3kgjxs#zg2dtfr [11 July 2014].

    b. **Books** – Author, date published, title of book (in italics), pages where the information came from.

    E.g. S. Dubner and S. Levitt, (2006) *Freakonomics*, 7-9.

    c. **Articles** – Author, 'title of the article' (with quotation marks), *where the article comes from* (newspaper, journal etc.), date of the article.

    E.g. Maev Kennedy, 'The lights to go out across the UK to mark First World War's centenary', Guardian, 10 July 2014.

Appendix 2 – Using the VLE

VLE username	
VLE password	

Please remember the following key details...

- You are able log into the VLE either through the link on our website (**www.thebrilliantclub.org**) or going directly to the VLE site at (https://portal.thebrilliantclub.org/sign-in).
- Please update your profile with your full name and email address- this will allow you to retrieve forgotten passwords or usernames
- If you forget your log-in details you can request them to be emailed to you by clicking the link on the VLE home page. (If you are still having problems you can email: **schools@thebrilliantclub.org**)

What is the VLE?

The VLE is a virtual learning environment for all pupils on Uni Pathways it is used for:

- messaging your tutor
- submitting homework
- submitting your final assignment
- accessing resources for your tutorials
- finding out more information about university and careers

How should I use the VLE?

The VLE is a professional academic environment in which pupils are able to message their PhD Tutor. Here are a few things to consider:

- Ensure you keep a professional tone in the messages you send to your tutors.
- Ensure you always reply to your tutors in a timely manner.
- Thank your tutor for the effort they are putting in to give you your feedback etc.
- Submit all homework to your tutor on time.

IMPORTANT: Final assignment

- When you submit your final assignment, please remember that you need to do so through the **'My Activities'** tab and not as an attachment to a message.

Notes

Notes

Notes

Course Title

Key Stage 4 Programme

researchersinschools.org