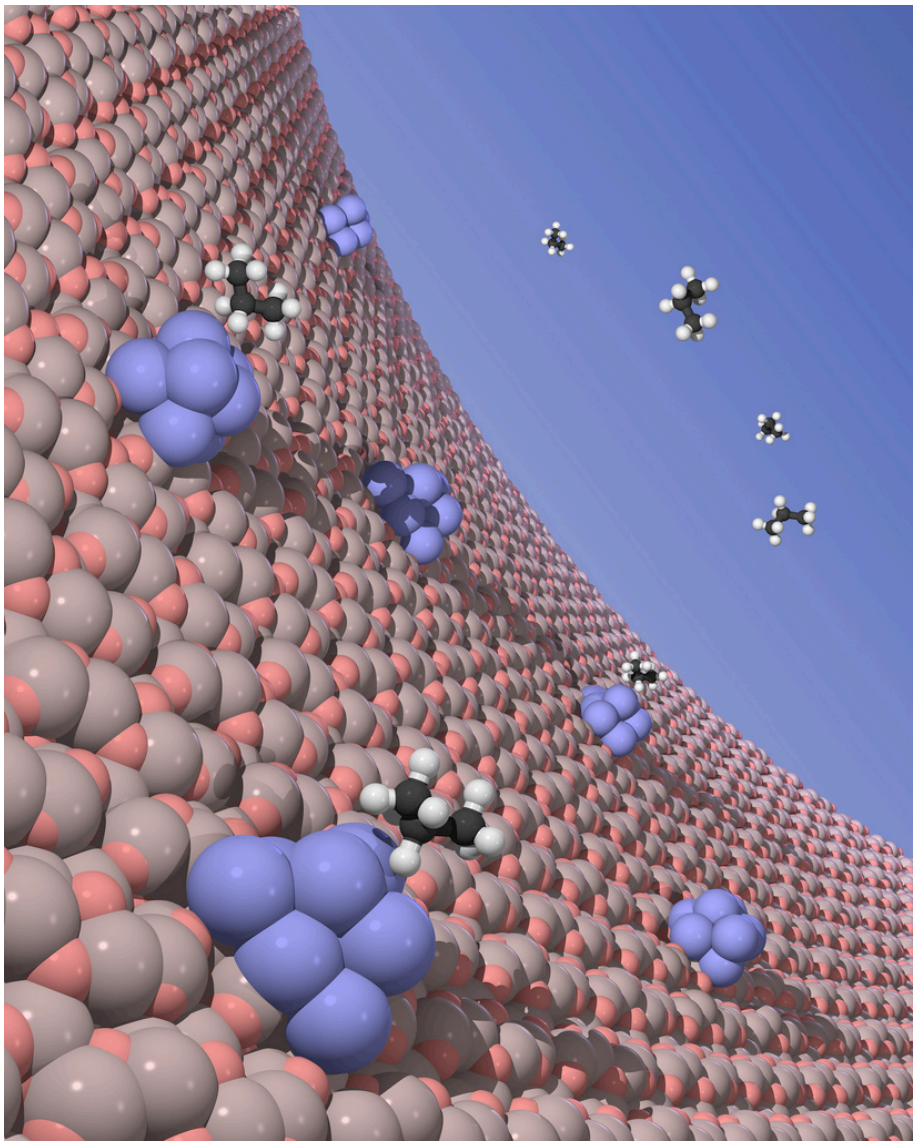
Interdisciplinary Science

PA3017

Nanoscale Frontiers



University of Leicester

Contents

Welcome

The module is designed to provide an introduction to the world of nanoscience and its applications in nanotechnology.

Nanotechnology has been the interest of both physicists and chemists alike; however, as one MIT representative once said, "biology is the nanotechnology that works". The subcellular structures that make up the cells within any organism are all constructed from macromolecular building blocks, demonstrating that complex systems and processes on the nanoscale are possible.

Bionanotechnology has taken a synthetic route using engineering approaches to create a biological mimetic system, which is controllable and predictable. For example, removing existing components of a biological system and placing it into a hybrid environment, such as in molecular motors and photosynthetic complexes.

Biomarkers are used to describe a variety of chemical markers which can be measured easily (un-invasive) in vivo, in the body. Its concentration is measured in response to dose, biological responses, and interpreted as a beneficial effect or risk. In Cell Biology, markers can be used to label specific areas within the cell, by selectively tagging specific proteins localised to certain areas of the cell

In this section you will explore basic cell biology and cell imaging techniques. using quantum dots. You will also be introduced to the flow of genetic information through the cell, whereby the DNA inherited by an organism leads to specific traits by dictating the synthesis of proteins.

Module Authors

Prof Derek Raine Dr Mervyn Roy Dr Chris Willmott

Cover Image: Platinum atoms deposited in aluminum oxide membrane by Argonne National Laboratory CC-BY-SA

http://www.flickr.com/photos/argonne/3853255001/

Problem 01

It was not quite the deadly legacy the Germans had in mind when they deployed a U-boat on a daring mission to Japan in the last desperate months of World War II……

When it set sail in December 1944, U-864 was packed with 65 tonnes of weapons-grade mercury destined to help the Japanese win back supremacy over the US in the Pacific - and divert American attention away from Europe in the process.

Neither the cargo nor the 73 men on board made it. The U-boat was torpedoed to the bottom of the North Sea floor by a British submarine.

More than 60 years on, its toxic cargo is slowly leaking into the waters off the coast of Norway, an ecological time bomb threatening marine - and potentially human - life.

Now the Norwegian government is set to act, following recommendations that the wreck be hermetically sealed to prevent any more of the mercury from escaping.

"We are worried about the long term consequences of the contamination," says Ane Eide Kjeras, spokeswoman for The Norwegian Coastal Administration.

A no-fishing zone was imposed around the wreck site after the discovery of documents listing mercury as part of the vessel's cargo. Tests were carried out on the water and silt, with alarming results.

The Norwegian coastal authorities have decided against raising the wreckage, deeming it too dangerous, and are recommending the two parts should be sealed.

Ms Kjeras said that an area of about 150m in diameter would be covered with up to 12m (40ft) of material. It is thought a special type of sand or gravel could be used. Nearly 2,000 eroding flasks of mercury will be covered as a result.

She went on: “During routine investigations of the levels Mercury contamination in coastal waters in the provinces of Hordaland and Sogn Og Fjordane abnormally high levels of the mercuric ion (Hg^{2+}) were detected. We are very concerned that this contamination will affect the local ecosystem and possibly spread into the water sources used by communities near the coast. We have investigated the levels of Hg^{2+} in rivers and streams near the west coast and no contamination has been detected, our fear is that the level of contamination is too low to be detectable by conventional means.

“What we need is a technique which doesn’t require much specialist equipment and is able to quickly detect a very small (ca. 1000 pM) concentration of contamination. The fluorescence technique isn’t sensitive enough and requires a spectrometer but we’re encouraged by progress in nanoparticle methods."

Problem 02

Magnetic nanoparticles: Suitable for cancer therapy?

Adapted from Physics & Chemistry Published: Wednesday, May 28, 2008 - 08:21

Magnetic nanoparticles (with a size of some few to several hundred nanometers) are a new, promising means of fighting cancer. The particles serve as a carrier for drugs: "loaded" with the drugs, the nanoparticles are released into the blood stream, where they move until they come under the influence of a targeting magnetic field which holds them on to the tumour – until the drug has released its active agent. Besides this pharmaceutical effect, also a physical action can be applied: an electromagnetic a.c. field heats up the accumulated particles so much that they destroy the tumour. Both therapeutic concepts have the advantage of largely avoiding undesired side effects on the healthy tissue.

These procedures have already been successfully been applied in the animal model and have, in part, already been tested on patients. Here it is important to know before application whether the particles tend to aggregate and thus might occlude blood vessels.

Information about this can be gained by magnetorelaxometry. In this procedure, the particles are shortly magnetised by a strong magnetic field in order to measure their relaxation after the switch-off of the field. Conclusions on their aggregation behaviour in these media can be drawn from measurements of suspensions of nanoparticles in the serum or in whole blood. As an example, it could be shown in this way that certain nanoparticles in the blood serum form clusters with a diameter of up to 200 nm – a clear indication of aggregation, so that these nanoparticles do not appear to be suitable for therapy.

Source: Physikalisch-Technische Bundesanstalt (PTB)
http://esciencenews.com/articles/2008/05/28/magnetic.nanoparticles.suitable.cancer.therapy

Brown chemists create cancer-detecting nanoparticles

Adapted from Physics & Chemistry Published: Tuesday, May 27, 2008 - 21:35

Magnetic resonance imaging (MRI) can be a doctor's best friend for detecting a tumor in the body without resorting to surgery. MRI scans use pulses of magnetic waves and gauge the return signals to identify different types of tissue in the body, distinguishing bone from muscle, fluids from solids, and so on. Scientists have found that magnetic nanoparticles can be especially helpful in locating cancerous cell clusters during MRI scans. Like teeny guided missiles, the nanoparticles seek out tumor cells and attach themselves to them. Once the nanoparticles bind themselves to these cancer cells, the particles operate like radio transmitters, greatly aiding the MRI's detection capability.

Now, Brown University chemist Shouheng Sun and a team of researchers have created the smallest magnetic nanoparticles to date that can be employed on such seek-and-find missions. With a thinner coating, the particles also emit a stronger signal for the MRI to detect.

The team of Brown graduate students Jin Xie, Chenjie Xu and Sheng Peng collaborated on the research, along with Professor Xiaoyuan Chen and his associates from Stanford University. They created peptide-coated iron oxide nanoparticles — particles billionths of a meter in size. The researchers injected the particles into mice and tested their ability to locate a brain tumor cell called U87MG. Sun and his collaborators concentrated specifically on the nanoparticle's size and the thickness of the peptide coating, which ensures the nanoparticle attaches to the tumor cell.

Size is important because the trick is to create a nanoparticle that is small enough to navigate through the bloodstream and reach the diseased area. Bigger particles tend to stack up, creating the circulatory system's version of a traffic jam. Sun's team developed a nanoparticle that is about 8.4 nanometers in overall diameter — some six times smaller than the size of particles currently used in medicine.

"We wanted to make (the nanoparticle) very small, so the body's immune system won't recognize it," Sun explained. "That way, you let more particles interact with and attach to the tumor cell."

Nanoparticles are important in MRI detection because they enhance what scientists refer to as the "contrast" between the background, such as water molecules in the body, and a solid mass, such as a tumor.

The coating, while integral to the nanoparticles' attachment to the tumor cell, also is crucial to establishing the "signal-to-noise" ratio that a MRI uses. The thinner the coating, the stronger the emitted signal and vice versa. Sun's team outfitted their nanoparticles with a two-nanometer thick peptide coating — 10 times thinner than the coating available in popular MRI contrast agents such as Feridex. Sun's nanoparticles are like having a 50,000-watt radio transmitter versus a 150-watt station; it's easier for the MRI to "hear" the stronger signal and to hone in on the signal's source.

Another important feature of the team's work is discovering that the RGD peptide coating binds almost seamlessly to the U87MG tumor cell. The team plans to test the particle's ability to bind with other tumor cells in further animal experiments.

Those in the medical profession following this research will want to understand the underlying physical and chemical principles of this technique for tumour detection and treatment and how safe it is. They will want an explanation of why these nanoparticles are magnetized, how the nanoparticles are stabilised, how they are able to target DNA and how they are able to produce the heat necessary to kill tumour cells.

Source: Brown University
http://esciencenews.com/articles/2008/05/27/brown.chemists.create.cancer.detecting.nanoparticles

Problem 03

NEW JOURNAL OF CANCER BIOLOGY ISSUE 1 2008

Novel Proteins in Cancer Cell Transformation

INTRODUCTION

We have identified two novel proteins as playing a role in the transformation of cells into cancer cells. The sequences of these proteins have been identified using mass spectrometry, although their functions in the cell are as yet unclear. We present data showing some initial findings.

DIFFERENTIAL TEMPORAL EXPRESSION

The temporal expression of protein A and B are different. Analysis showed protein A is up-regulated first in the cells, and protein B's expression profile showed that rises in protein B occur after the peak expression of protein A.

PROTEIN A

Figure 1 shows the Amplification of the Protein A in cancer cells: FISH analysis

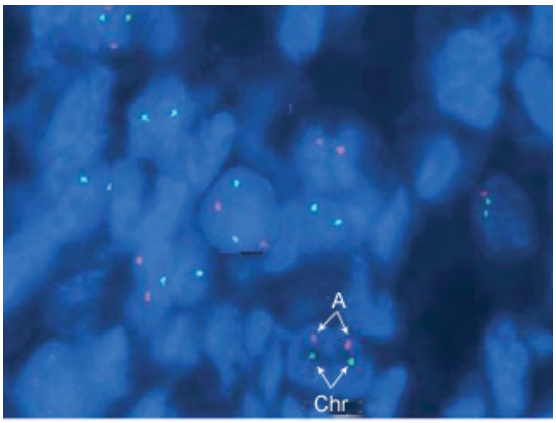


Figure 1a Normal Cell

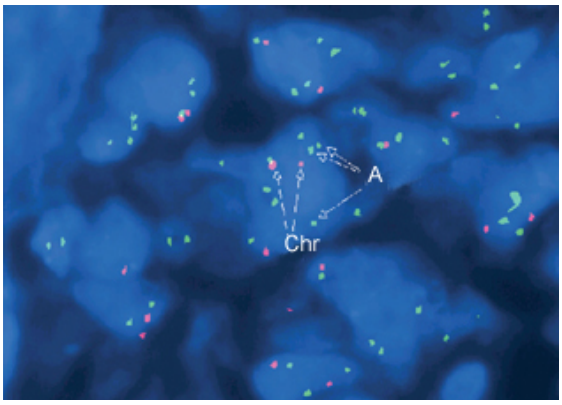


Figure 1b Tumour Cell

PROTEIN B

Figure 2 shows our results for the expression of Protein B in Cancer cells using confocal immunofluorescent microscopy. Cells, using protein B Antibody (green, left) are compared to an isotype control (right). Actin filaments have been labeled with Alexa Fluor (red). Fluorescent DNA is dyed blue.

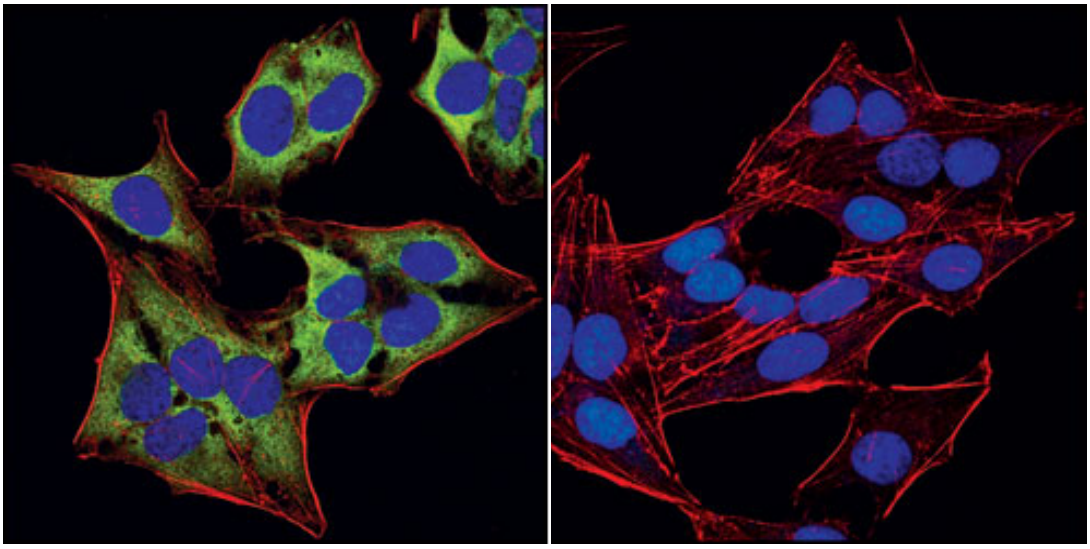
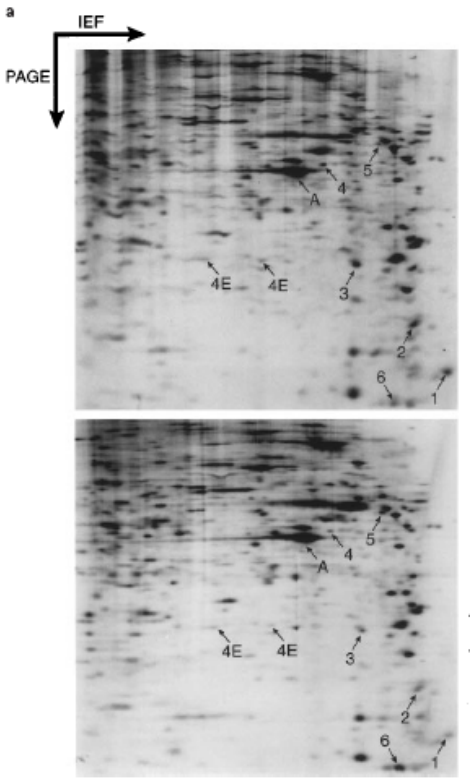


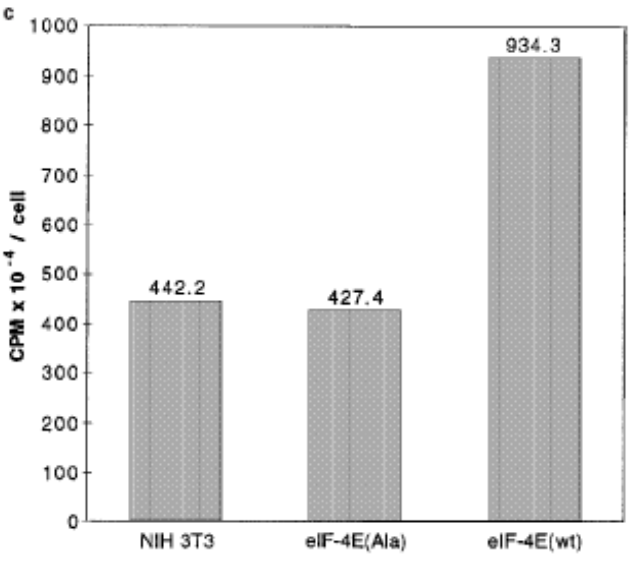
Figure 2: Expression of Protein B in Cancer cells using confocal immunofluorescent microscopy. Protein B Antibody (green, left) are compared to an isotype control (right)

UP-REGULATION OF PROTEIN B AFFECTS THE GENERAL RATE OF PROTEIN SYNTHESIS IN THE CELL.

a) 2D-gel electrophoresis of protein lysates from the cell cultures. Figure 3a (top) indicates wild-type protein B, while the bottom panel indicates results from cells with a mutated protein B.



b) Results illustrating the general rate of protein synthesis in control cells, in mutated protein B cells and in wild-type protein B cells.



Staff

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Learning Objectives

- Classical mechanics for describing particles and electrons.
- Simple quantum mechanics as applied to quantum dots.
- Interaction of light with particles.
- Origins of surface plasmon resonance.
- Use of functionalisation in species detection.
- Consideration of stabilisation factors when producing and using nanoparticles.
- Use of Rayleigh scattering as a size determining phenomenon.
- Properties of magnetism including ferromagnetism, diamagnetism and paramagnetism.
- Use of magnetic nanoparticles in cancer therapy.
- Semiconductors and Band Theory
- Describe the main types of microscopy used in cell biology and the biomarkers/dyes used in each method.
- Describe how antibodies are raised and used for cell imaging techniques.
- Understand the uses of quantum dots and how their application might be beneficial over other cell visualisation methods.
- Understand the merits and weaknesses of each method, and be able to decide which method to use in various situations.
- Understand the difference between prokaryotic and animal cells.
- Describe the structure and function of the main organelles of the eukaryotic cell.
- Explain how genetic information is transcribed and translated.

Reading List

Quantum Theory

- Tipler, P.A. (1999) *Physics for Scientists and Engineers 4th ed*. New York, W.H. Freeman and Company

NanoScience

- Schmid, G.(ed); "Nanoparticles – From Theory to Application"; Wiley-VCH, ISBN 3-527-30507-6**,**2005.
- Lee, J.-S., Han, M.-S., Mirkin, C.A.; Angew. Chem. Int. Ed. 2007, **46**, 4093-4096.
- Nolan, E.M., Lippard, S.J.; J. Mater. Chem. 2005, **15**, 2778-2783.

Magnetic Nanoparticles

- Berger, P., Adelman, N.B., Beckman, K.J., Campbell, D.J., Ellis, A.B and Lisensky, G.C.; "Preparation and Properties of an Aqueous Ferrofluid"; *J. Chem. Edu.*; 1999; **76** (7); 943.

Clinical Applications

- Jain, K.K; Nanotechnology in Clinical Laboratory Diagnostics"; *Clinical Chimica Acta*; 2005; **358**; 37.

Visualising Cells:

- Alberts et al. (2008) *Molecular Biology of the Cell*. Chapter 9 – Visualizing Cells, p579-615.
- Lodish et al. (2000) *Molecular Cell Biology*. Chapter 5 – Biomembranes and the Subcellular Organisation of Eukaryotic Cells, p138-157.
- Bruchez Jr., M., et al. (1998) Semiconductor nanocrystals as fluorescent biological labels. *Science* 281(Sept. 25):2013-2016. http://www.sciencemag.org/cgi/content/full/281/5385/2013
- *Ultrastructure of the Cell* (Electron Micrographs). Images available at: *http://www.bu.edu/histology/m/t_electr.htm*
- *Immunogold labelling in Electron microscopy* - *http://www.ebsciences.com/papers/immusem.htm*

Cell ultrastructure:

- Alberts et al. (2008). *Molecular Biology of the Cell*. Chapter 1 – Cells and Genomes, p1-42. (A detailed introduction on cells and life).
- Campbell and Reece, (2008). *Biology 8th Ed*. Chapter 6 – A tour of the Cell, p94-124.
- Lodish et al. (2000) *Molecular Cell Biology*. Chapter 5 – Biomembranes and the Subcellular Organisation of Eukaryotic Cells, p157-177.

Transcription and Translation:

- Alberts et al. (2008) *Molecular Biology of the Cell*. Chapter 4 – DNA, chromosomes and Genomes, p197-201.
- Alberts et al. (2008) *Molecular Biology of the Cell*. Chapter 6 – How Cells Read the Genome, p329-399.
- Campbell and Reece, (2008) *Biology 8th Ed*. – Chapter 17, p325-350.
- Nobel Prize Education –DNA: http://nobelprize.org/educational_games/medicine/dna/index.html
  - Select advanced information for in depth coverage on subject material. Do not cover DNA replication, as this is beyond the scope of this module.
- Virtual Cell Animation Collection: http://vcell.ndsu.nodak.edu/animations/
  - View Transcription, mRNA processing, mRNA splicing and translation animations.

Facilitation Sessions

Facilitation Session 01

Preparation:

- Read Problem 1
- Revise Quantum Mechanics from *Science of the Invisible* Module
- Revise Semiconductors from *Time and Energy* Module (see also Supplementary Material)

Detecting single ions in large volumes of solution

Class discussion regarding the issues with detecting small amounts of single ions in large volumes of contaminated solution; sensitivity and selectivity.

Preparation for the Expert Session ES01

The expert session on *Quantum Theory* will introduce quantum mechanics in the context of nanoscale particles.

Facilitation Session 02

Preparation

Read:

- MS4, a seminaphthofluorescein-based chemosensor for the ratiometric detection of Hg(II)

Link in Supplementary materials:

  - http://www.rsc.org/delivery/_ArticleLinking/DisplayArticleForFree.cfm?doi=b501615k&JournalCode=JM

- Synthesis of Novel Nanocrystals as Fluorescent Sensors for Hg^{2+} Ions

  Letter formatted in Supplementary Materials

- Colorimetric Detection of Mercuric Ion (Hg2+) in Aqueous Media using DNA-Functionalized Gold Nanoparticles**

Link in Supplementary materials

  - http://www3.interscience.wiley.com/cgi-bin/fulltext/114224240/PDFSTART

Techniques to detect low concentrations of Hg^{+}

Be prepared to discuss the size of nanoparticles; what properties does this give them compared to bulk material? How will this help in detecting small amounts of Hg^{+}?

Facilitation Session 03

Preparation

Read:

- Colorimetric Detection of Mercuric Ion (Hg2+) in Aqueous Media using DNA-Functionalized Gold Nanoparticles
  Link in Supplementary materials:
  - http://www3.interscience.wiley.com/cgi-bin/fulltext/114224240/PDFSTART

Be prepared to discuss:

- Electron confinement in nanoparticles.
- The origins of the surface plasmon resonance phenomenon.
- The physical (optical) properties that are inherent in nanoparticles
- Why use Gold over other nanoparticles for the method described?

Facilitation Session 04

Preparation:

Be prepared to discuss:

How is the Au functionalised with DNA?

What is the origin of the colour of nanoparticles?

The origins of the colour change at higher temperatures when Hg^{+} is present

Introduction to the Rayleigh scattering/ TEM imaging laboratory session

This part of the session will introduce the computer based lab session on Rayleigh scattering and TEM imaging as a means for particle size determination.

Facilitation Session 05

Preparation:

- Read problem 02
- Read the lab script for Ferrofluid synthesis.

Introduction to Problem 02

Be prepared to discuss:

- The use of magnetic nanoparticles in the treatment of cancer as both a diagnostic and therapeutic tool.

- Things that need to be considered when trying to implement the proposed treatments.

Preparation for the Ferrofluid Synthesis Laboratory Session

This part of the session is in preparation for the Ferrofluid Synthesis laboratory session.

Facilitation Session 06

Ferrofluids

Preparation:

Come to the session with your results for the Ferrofluid lab. Be prepared to discuss:

- Has visualising the type of substance used in the problem helped them understand how the technique works?
- What properties of the ferrofluid they have synthesised make its potential application useful?
- Why do the actual researchers in this field use γ-Fe_2O_3 and not the Fe_3O_4 (Fe_2O_3 and FeO) the students have synthesised?

Facilitation Session 07

Preparation:

Read Tipler: Magnetism in Matter [Section 29-5 4th ed].

Preparation for the Expert Session on Magnetism

Come to the session prepared to discuss the differences between ferromagnetism, diamagnetism and paramagnetism

Discussion of outstanding issues with Problem 01 and 02

Facilitation Session 08

Preparation

Bring draft of your reports (D01, D02) to the session.

Facilitation Session 09

Preparation

Read the problem 03

Visualising the Cell

Be prepared to discuss Visualisation of the Cell?

- Why is it necessary to use microscopy techniques for visualising cells?
- The forms of microscopy
- Why is it important to be able to visualise cells?

Facilitation Session 10

Preparation

Read :

- ***p579-584*** *on light microscopy in Alberts et al, (2008). Molecular Biology of the Cell. Chapter 9 – Visualizing cells*
- ***p604-608*** *on electron microscopy in Alberts et al, (2008). Molecular Biology of the Cell. Chapter 9 – Visualizing cells*
- *Immunogold labelling in Electron microscopy - http://www.ebsciences.com/papers/immusem.htm*

Light microscopy and Electron microscopy

A directed class discussion.

Facilitation Session 11

Preparation

Read:

- ***p586-595*** *on fluorescence microscopy and protein dynamics in Alberts et al, 2008. Molecular Biology of the Cell. Chapter 9 – Visualizing cells*
- "NanoLights! Camera! Action! Tiny semiconductor crystals reveal cellular activity like never before" (Supplementary Materials)

Be prepared to discuss

Fluorescence Microscopy

- What is fluorescence microscopy?
- How do you raise and conjugate antibodies to fluorescent biomarkers?
- Do you know what the structure of an antibody is?

Quantum Dots

- What are your opinions on this technology?
- How can it be used in place of or in conjunction with the other methods of cell imaging?

Facilitation Session 12

Preparation

Read:

- ***p94-124*** *Campbell and Reece, 2008. Biology 8th edition. Chapter 6 – A tour of the Cell*
- ***p157-177*** *Lodish et al, 2000. Molecular Cell Biology. Chapter 5 – Biomembranes and the Subcellular Organisation of Eukaryotic Cells*

Cell diagram

Class discussion in cell structure and contents.

Facilitation Session 13

Review of progress

Be prepared to discuss the following points:

- What organelles are important in this process i.e. transcription and translation?
- How would you determine if protein A and B are involved?
- How would you confirm protein A's localisation in the nucleus
- What could protein A be? i.e. knowing it localises in the nucleus – what could it be?
- What proteins are important in protein synthesis

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Facilitation Session 14

Preparation

Read:

- ***p325-336*** *on genetic flow and transcription in Campbell and Reece, 2008, Biology 8th ed, Chapter 17, From Gene to Protein*
- ***p329-366*** *on Transcription in Alberts et al, 2008, Molecular Biology of the Cell 5th ed. Chapter 6 – How cells read the genome: from DNA to Protein*

Transcription

Be prepared to discuss:

- What organelle is important in transcription?
- What types of proteins regulate gene expression?
- How do they think protein A was overexpressed?
- How is the mRNA transcript processed before translation; why is this step important?
- Students should realise that one of the proteins in the problem is a transcription factor. Ask how they could use an antibody to determine this – as it is localised in the nucleus, is this enough to confirm its role?

Facilitation Session 15

Preparation

Read:

- ***p337-348*** *on Translation in Campbell and Reece, 2008, Biology 8th ed. Chapter 17- From Gene to Protein.*
- ***p367-400*** *on Translation in Alberts et al, 2008, Molecular Biology of the Cell 5th ed. Chapter 6 – How cells read the genome: from DNA to Protein.*

Translation

Be prepared to discuss:

- What are the key events during translation?
- Where in the cell does it occur?
- How does tRNA and ribosomes interact with the mRNA?
- What is the genetic code?
- What is the difference between mRNA, tRNA and rRNA – does all mRNA in the cell get translated?
- How can you visualise ribosomes?
- What proteins are involved in translation – could protein B be one of these – how would they confirm this
- How is the accuracy of translation assured?
- What proteins are important in control of this process?
- What is the consequence of damaged proteins remaining uncorrected?
- Why is transcription and translation important? Can the students describe any situation where T&T are vitally important?
- How has understanding of transcription and translation helped in development of genetic engineering?

Facilitation Session 16

Preparation:

Bring your draft reports

This session will contain a review in the form of exercises on transcription and translation and a puzzle on the genetic code.

Be prepared to discuss:

- Where does RNA polymerase work?
- What is it's role?
- Are DNA and mRNA double stranded or single stranded?
- Which DNA strand is copied during transcription, what are each of these strands called (i.e. which is the leading and template strand?).
- What leaves the nucleus after transcription?
- Does the mRNA get processed before translation?
- What proteins/molecules are important in translation, where does translation occur?
- What is the structure of a eukaryotic Ribosome?
- What other proteins are required for the ribosome to be fully active?
- What post-translational modifications occur to the translated protein?

Deliverables

Please name your deliverables in accordance with the standard naming convention (see the handbook for details). A sample filename is provided for you to cut and paste - please complete with submission date and username/group letter as appropriate.

All deliverables to be submitted to the iScience centre

Please note that although deliverable deadlines (except for CLEs) are at the end of the module, you are strongly urged not to leave all work on the deliverables until the final weekend! In particular, if you would like formative feedback on your works-in-progress from your facilitator and/or experts, please provide them with draft copies in good time.

DELIVERABLES	TYPE	FILENAME	DUE	WEIGHTING
CLE01: Nanoparticles – part I	I	PA3017_I_CLE01_*username*_*date*.pdf	Week 2, Day 1	30%
CLE02: Nanoparticles – part II	I	PA3017_I_CLE02_*username*_*date*.pdf	Week 3, Day 1	
CLE03: Cell Imaging and Biomarkers	I	PA3017_I_CLE03_*username*_*date*.pdf	Week 4, Day 1	
CLE04: Transcription and Translation	I	PA3017_I_CLE04_*username*_*date*.pdf	Week 5, Day 1	
D01: Traces of Mercury	G	PA3017_D01_TracesOfMercury_*username_date*.pdf	Week 5, Day 1	20%
D02: Magnetic Nanoparticles	G	PA3017_D02_MagneticNanoparticles_*username_date*.pdf	Week 5, Day 1	20%
D03: Proteins	G	PA3017_D03_Proteins_*username_date*.pdf	Week 5, Day 1	30%

The Deliverables D01, D02 and D03 should be in the form of reports of around 2000 - 3000 words at an appropriate scientific level. You should determine your audience for the reports from the problem statements.

Core Learning Exercise 01: Nanoparticles – Part I

1. The term nanoparticle is generally used to describe clusters of atoms in which size range? **[1]**

2. An electron exists in a 0.1nm one-dimensional box of infinite depth. Calculate the wavelength corresponding to a transition from the ground state energy to the fourth energy level? **[2]**

3. What is meant by the term 'Surface Plasmon Resonance' in the context of metal nanoparticles? **[2]**

4. Draw a simple diagram which shows the interaction of light with a noble metal nanoparticle and the resulting displacement of the conduction electrons. **[2]**

5. A nanoparticle exists in a 5nm one dimensional box. The energy of the first excited state is 1.214×10^{-21} J. What is the mass of the particle? **[1]**

6. List 5 common applications of metal nanoparticles. Please relate each application to the relevant physical property. **[5]**

7. Suggest 3 general mechanisms by which metal nanoparticles may be functionalized by biomaterials. **[3]**

8. Why do metal nanoparticles need to be stabilized? **[1]**

9. What are the two primary mechanisms for the stabilization of MNPs? Give two common examples for gold nanoparticles. **[4]**

10. Changing the ion concentration of a suspension containing Au nanoparticles in a citrate solution alters the colour of the solution. Explain this observation. **[3]**

11. What is meant by the term electric double layer and zeta potential in the context of metal nanoparticles? (Draw a labelled diagram to explain electrical double layer). **[4]**

12. How can Zeta potential be measured? **[2]**

13. What is the name of the point at which zeta potential is zero? **[1]**

14. Why do metal nanoparticles make ideal catalysts? (list at least 2 factors) **[2]**

15. In the Angewandte Chemie article what is meant by 'Complementary DNA'? **[2]**

16. Why is the DNA 'thiolated'? **[1]**

17. Name three factors which affect the stability of metal nanoparticles. **[3]**

Core Learning Exercise 02: Nanoparticles – Part II

1. Why is the magnetic behaviour of magnetic nanoparticles size-dependent? **[2]**

2. What is meant by the terms *ferromagnetic, paramagnetic and diamagnetic?* **[3]**

3. What is meant by the terms *domain, domain wall, exchange coupling and Curie temperature?* **[4]**

4. Compare the domain structure of macroscopic ferromagnetic materials with ferromagnetic nanoparticles. **[2]**

5. What is magnetic susceptibility? **[1]**

6. What is meant by magnetic anisotropy? **[1]**

7. What is the difference between extrinsic and intrinsic semiconductors? **[2]**

8. What is the type of semiconductor resulting from

   a. Si is doped with As atoms? **[1]**

   b. Si is doped with Ga atoms? **[1]**

9. State two common applications of semiconductors. **[2]**

10. There are 10^{10} free electrons per centimeter cubed in Si at ordinary temperatures. If one atom out of every million is replaced by Ga, how many holes per cm^3 are there in the valence band? (ρ_{Si} = 2.33 g/cm^3; M_r [Si] = 28.1 g/mol) **[3]**

Core Learning Exercise 03: Cell Imaging and Biomarkers

1. a. Explain the difference between magnification and resolution. **[2]**

   b. What is the limit of resolution of a light microscope in air? How does using immersion oil help? The shortest wavelength of visible light is λ = 450nm (blue). The maximum angular aperture for objective lenses 70°.
   [3]

$$D = \frac{0.61 \times \lambda}{N \times \sin\theta}$$

$$D = \frac{0.61 \times 450}{1 \times 0.94} = 292nm$$

$$D = \frac{0.61 \times 450}{1.5 \times 0.94} = 194nm$$

2. Draw the pathway of light through the schematic illustration of a compound light microscope below. Label each component and describe their function.
   [12]

3. Describe the five main types of light microscopy. **[10]**

4. What are the advantages and disadvantages of using a compound light microscope?
   [6]

5. Draw and label a diagrammatic representation of a fluorescent microscope. Why are the functions of these two filters? **[4]**

6. Is this statement true? Explain why or why not.
   "A fluorescent molecule, having absorbed a single photon of light at one wavelength, always emits it at a longer wavelength." **[2]**

7. Explain in your own word the principles of indirect immunofluorescence microscopy.
   [2]

8. What are the main differences between a monoclonal antibody and a polyclonal antibody?
   [4]

9. Determine whether each of the following statements is TRUE or FALSE and give a brief explanation for your answer.

   a. Objectives with a small numerical aperture (NA) can resolve very small objects.
   [2]

   b. Antibodies can be used to determine the activation state on an enzyme.
   [2]

   c. In a FRET assay Cyan Fluorescent Protein (CFP) can be the donor molecule and Yellow Fluorescent Protein (YFP) can be the acceptor molecule.
   [2]

10. a. Explain in your own words how GFP can be used to determine the intracellular localisation of a protein. **[4]**

    b. List 2 advantages and 2 disadvantages of using a GFP-fusion protein over immunofluorescent microscopy. **[4]**

11. What are quantum dots? How have they been developed to use in cell imaging? Why are they seen as advantageous to organic fluorescent probes such as Cy3 and Alexa dyes? **[3]**

12. What is FRET and why is it a useful technique? **[3]**

13. How are the components of an electron microscope different to a light microscope? **[2]**

14. Can living tissue be observed in a transmission electron microscope? What special preparation is required for specimens to be visualised in EM? **[3]**

15. How can specific molecules be visualised in the cell, using EM? What cellular structures are in particular better observed under an EM? **[2]**

16. What is scanning electron microscopy? **[2]**

17. The practical resolving power of a modern electron microscope is around 0.1nm. The major reason for this constraint is the small numerical aperture (nsinθ), which is limited by θ (half the angular width of rays collected at the objective lens). Assuming that the wavelength (λ) of the electron is 0.004nm and that the refractive index (n) is 1.0, calculate the value for θ. How does that value compare with a θ of 60o, which is typical for light microscopes? **[2]**

$$D = \frac{0.61 \times \lambda}{N \times \sin\theta}$$

18. Label the cellular structures in the prokaryote cell in your CLE pack and describe the function of each structure. **[18]**

19. Label the cellular structures in the eukaryotic animal cell in your CLE pack and describe the function of each structure. **[28]**

20. What are the major differences in prokaryotic and eukaryotic cells? **[16]**

21. Describe the role of the centrosome in an animal cell. **[3]**

22. List three functions of microtubules. **[3]**

Core Learning Exercise 04: Transcription and Translation

1. A full rotation of the DNA helix is 3.4nm in length and contains 10.4 base pairs. The human genome contains ~3 billion base pairs. Approximately how long is it? **[1]**

2. Draw a ribose and a deoxyribose sugar side-by-side and highlight what makes them different. Identify the carbon atoms in your diagrams by their position number. **[3]**

3. What is the difference between a nucleotide and a nucleoside? Give an example of each together with its molecular structure. **[3]**

4. What does the term "antiparallel" mean when applied to a DNA double helix? Why is this term necessary? **[2]**

5. There are five Nitrogen bases in nucleic acids. Name them and group them according to their structure. Which base is only found in RNA and what base does it substitute? **[3]**

6. Which of the following statements are true and which false? Explain your answer in each case.

   a. Deoxyribose is a sugar in which the hydroxyl at the 2' position of the carbon ring of ribose is replaced by H **[2]**

   b. A and T are purine bases **[2]**

   c. A and T are base pairs **[2]**

   d. Any purine can be linked to any pyramidine by hydrogen bonds **[2]**

7. Look at the following DNA template strand. Work out the complementary mRNA sequence, the tRNA anticodons, and the appropriate amino acid sequence using The Genetic Code". **[3]**

   DNA sequence: **A G C T T A C C G T G G**
   mRNA sequence:
   tRNA anticodon:
   Amino Acid Sequence:

8. What are the three main kinds of ribonucleic acid and what is the specific job of each type? **[3]**

9. Draw a diagram of the structure of a typical amino acid. How many amino acids are there? What makes each one different? **[3]**

10. What are the sites in a eukaryotic cell in which transcription and translation take place? How does this affect the two processes? **[2]**

11. Which of the following are true and which false? Explain your answer in each case.

a. Introns are coding regions of DNA **[2]**

b. Post-translational modification of RNA removes intron sequences **[2]**

c. All coding sequences give rise to proteins **[2]**

12. What makes RNA polymerase start transcribing a gene at the correct place on the DNA? What is a promoter, and were is it located? **[5]**

13. Which of the following statements are true? Explain your answer in each case.

    a. The consequences of errors in transcription are less than those of errors in DNA replication. **[3]**

    b. Since introns are largely genetic 'junk' they do not have to be removed precisely from the primary transcript during RNA splicing **[2]**

    c. Wobble pairing occurs between the first position in the codon and the third position in the anticodon. **[3]**

    d. Protein enzymes are thought to greatly outnumber ribozymes in modern cells because they catalyse a much greater variety of reactions at much faster rates than ribozymes. **[3]**

14. Phosphates are attached to the CTD (C-terminal domain) of RNA polymerase II during transcription. What are the various roles of RNA polymerase II CTD phosphorylation? **[3]**

15. What modifications are made post-transcription to the pre-mRNA strand? What is the importance of these modifications? **[7]**

16. What is the first codon in every protein and what is the corresponding amino acid? **[1]**

17. What signals the end of translation? **[1]**

18. Why is each amino acid usually coded for by several different codons; wouldn't one codon be sufficient? **[1]**

19. How are peptide bonds between amino acids formed (give the chemical diagram AND the facilitating enzyme in translation). **[2]**

20. What are the "A" and "P" sites? Are they fixed points on the mRNA? **[2]**

21. Draw a basic diagram of a eukaryotic ribosome with an mRNA strand bound. Label the appropriate domains and give their functions. **[4]**

22. The elongation factor EF-Tu introduces two short delays between codon-anticodon base pairing and formation of the peptide bond. These delays increase the accuracy of protein synthesis. Describe these delays and explain how they improve the fidelity of translation. **[6]**

23. Draw the two dimensional structure of a tRNA molecule, with appropriate labelling. What is the function of this molecule? **[3]**

23. Name the enzymes important in the two processes transcription and translation. What is the function of each enzyme? **[10]**

Deliverable 01: Traces of Mercury

A group report on Problem 1 around 2000 words. The subject and style of the report, and the audience for it, is up to the group to decide on the basis of the identification of the problem. Your facilitator will be available to provide advice and feedback on any draft material.

Deliverable 02: Magnetic nanoparticles

A group report on Problem 2 around 2000 words. The subject and style of the report, and the audience for it, is up to the group to decide on the basis of the identification of the problem. Your facilitator will be available to provide advice and feedback on any draft material.

Deliverable 03: Proteins

A group report on Problem 3 of around 3000 words. The subject and style of the report, and the audience for it, is up to the group to decide on the basis of the identification of the problem. Your facilitator will be available to provide advice and feedback on any draft material.

Supplementary Material

Contact your facilitator for the supplementary material.

Meta tags

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Owner: University of Leicester

Title: Interdisciplinary Science Nanoscale Frontiers Student Document

Classification: PA3017 / Nanoscale Frontiers

Keywords: Nanoscience; Biology; Chemistry; Physics; sfsoer; ukoer

Description: In this module you will explore basic cell biology and cell imaging techniques. using quantum dots. You will also be introduced to the flow of genetic information through the cell, whereby the DNA inherited by an organism leads to specific traits by dictating the synthesis of proteins.

Language: English

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Additional Information

This module pack is the open student version of the teaching material. An expanded module pack for facilitators and additional information can be obtained by contacting the Centre for Interdisciplinary Science at the University of Leicester. http://www.le.ac.uk/iscience

This pack is the Version 1.0 release of the module.