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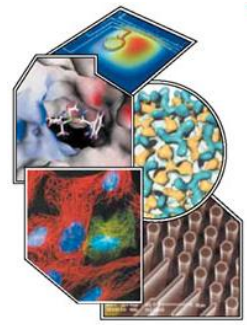
Mol3014

Nanomedicine I - bioanalysis

Øyvind Halaas,
Dept Cancer Research and Molecular Medicine,
Medical Faculty, NTNU



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Contact:

Tel 72825341 Mob 97790870

oyvind.halaas@ntnu.no

Gastrosenteret 3etg N

431.03.058

You can use ”Its learning” also during semester

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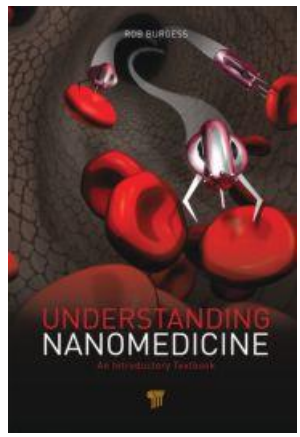
What you find when looking for nanomedicine at web

4

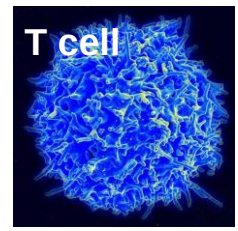
Nanomedicine:

the hype: autonomous systems for finding and repairing disease

medical nanobots seen by engineers



medical micro/nanobots seen by biologists



12μm

Not to scale

80nm

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Not just a ”hype”

Nature, July 2009:

”We need people who have developed an intuition about multiscale systems”

CAREERS NATURE|Vol 460|23 July 2009

Big opportunities in a small world

Nanomedicine has started to gather momentum in recent years, and cutting-edge jobs abound for those with the right training. **Virginia Gewin** takes a closer look.

Mauro Ferrari is on a mission to make Houston a major hub for nanomedicine. Housed at the University of Texas Health Science Center, Ferrari's lab will become the Department of Nanomedicine and Biomedical Engineering in September. According to Ferrari, it will be the first nanomedicine department at a US medical school. The nanomedicine professor, whose team is developing nanosized diagnostic devices to treat cancer and cardiovascular disease, is in an enviable position, especially given the current economic climate. Ferrari plans to recruit another 30 researchers to complete his 100-member academic research team, and he has co-founded two companies. NanoMedical Systems, in Austin, Texas, is developing a nanomaterial-based drug-delivery system, and Leonardo Biosystems in Houston is researching nanotechnology-based cancer therapeutics.

Houston is already well known for its prowess in the nanoscopic field. The city was home to the 1985 discovery of spherical carbon-based fullerenes known as 'buckyballs'. That work was later awarded the 1996 Nobel Prize in Chemistry. Yet so far, nanotech advances have been more incremental than monumental. This could be set to change as research funds start to flow, nanomedicines head to clinical trials and entrepreneurial academics aim to incorporate nanomedicine into mainstream medical care.

Governments around the world are banking on high economic returns as they invest in a field that aims to use atomic- or molecular-level techniques to repair damaged tissue or diagnose, treat or prevent disease. Academics are forging multidisciplinary teams of scientists, engineers and clinicians eager to test nanosolutions to medical problems. But there are challenges. The field needs greater numbers of highly trained students, and a sound regulatory infrastructure.

Entrepreneurial academics

Houston isn't the only budding

In the future, nanotechnology could be used to fight pathogens.

© ANDERSON/GETTY IMAGES

of a plan to grow its schools of medicine and engineering. The building is slated to open in 2010, and Swansea University administrators are searching for researchers eager to cross disciplinary boundaries. Over the next year, they will begin to fill 12 core research posts, including the centre manager, academic posts and clinicians to support the centre's mission.

The key to successful growth of a nanomedicine hub, say the organizers, is forging industry partnerships. One of Swansea University's spin-off companies — Haemair, also based in Swansea — has developed a

"We need people who have developed an intuition about multiscale systems."
— Randy Goodall

five years, many in small and medium-sized partner companies. Conlan says the centre will build on the university's strengths in engineering and physical sciences to first focus on developing nanotech devices, such as *in vivo* sensors. People trained in rheology, scanning microscopy, biochemistry, device fabrication and chemistry will be in demand as the centre develops high-tech platforms to be licensed and commercialized.

Such institutional configurations mirror a merging of nanotechnology and medical career paths. Shad Thaxton was halfway through his urology

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Definitions Nanomedicine

Nanomedicine is the medical application of nanotechnology

The US National Nanotech Initiative
Nanotechnology is the understanding and control of matter at dimensions between approximately 1 and 100 nanometres, where unique phenomena enable novel applications. Encompassing nanoscale science, engineering, and technology, nanotechnology involves imaging, measuring, modelling, and manipulating matter at this length scale. Nanomedicine is the application of nanotechnology to medicine.

The European Science Foundation
The field of nanomedicine is the science and technology of diagnosing, treating and preventing disease and traumatic injury, of relieving pain, and of preserving and improving human health, using molecular tools and molecular knowledge of the human Body

The European Technology Platform on Nanomedicine
Nanomedicine is defined as the application of nanotechnology to health. It exploits the improved and often novel physical, chemical, and biological properties of materials at the nanometric scale. Nanomedicine has potential impact on the prevention, early and reliable diagnosis and treatment of diseases

The application of nanotechnology to medical diagnostics and therapies, which encompasses the use of nanoscale sensors to detect internal signals—e.g., glucose levels—and respond by releasing insulin or other biomolecules

Modern medicine: A developing field in which nanoscale–ie, teeny-weeny–sensors would detect internal signals–eg, glucose levels, and respond by releasing insulin or other biomolecule

That branch of medicine reliant on nanotechnology in any form.

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J.S. Murday et al / Nanomedicine: Nanotechnology, Biology, and Medicine 5 (2009) 251–273

2 *J.S. Murday et al / Nanomedicine: Nanotechnology, Biology, and Medicine xx (2009) xxx–xxx*

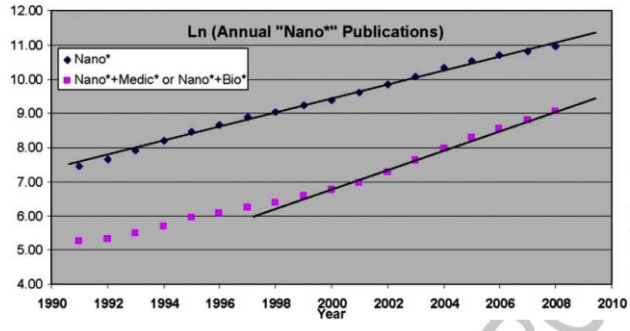

Figure 1. Publication counts derived from the Thompson ISI Web of Science database on 15 March 2009 using the indicated key words. The vertical axis is the natural logarithm of the number of publications. There is a clear change in slope for the publications associated with biology and medicine around the year 2000.

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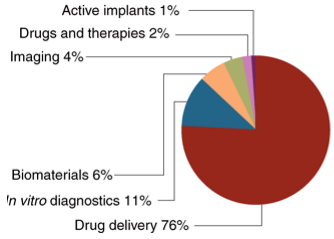
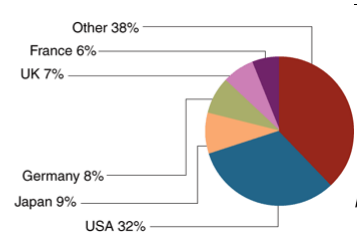
Nanomedicine world's fastest growing market

Health care market: 10.000bln$/y by 2020 (10% of world spendings)

Significant portion to nanotechnology, 1000bln$ by 2015





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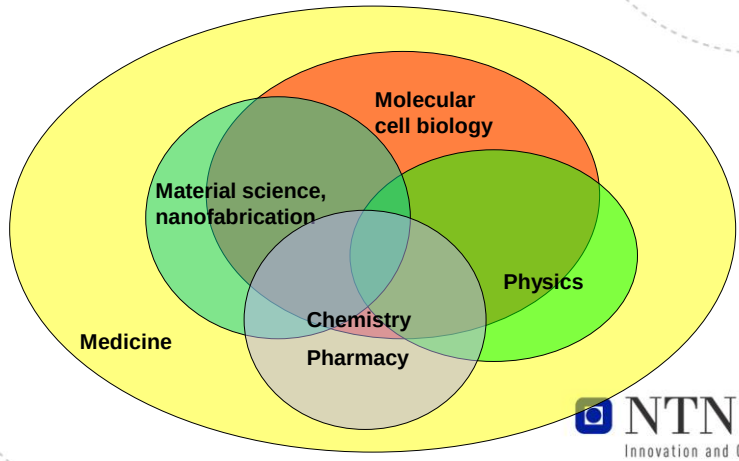
Nanomedicine: what is it

In nanomedicine we care more about medicine than about nano*



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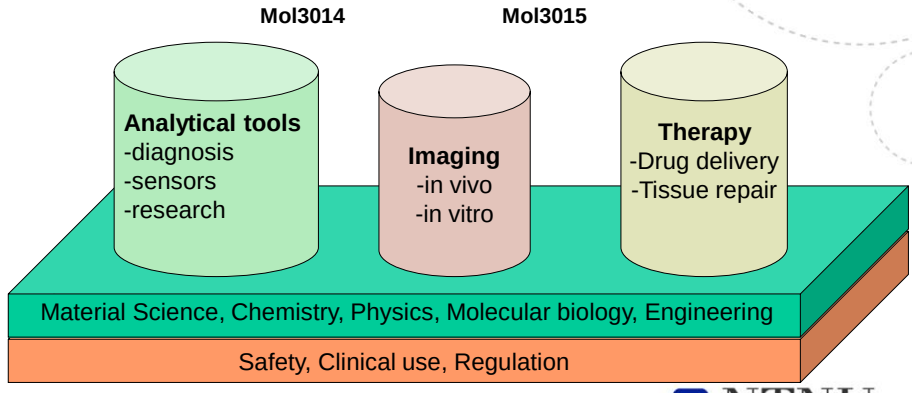
Multidisciplinary integrated approaches to novel medical practice



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Why nano?

http://learn.genetics.utah.edu/content/begin/cells/scale/

http://htwins.net/scale2/

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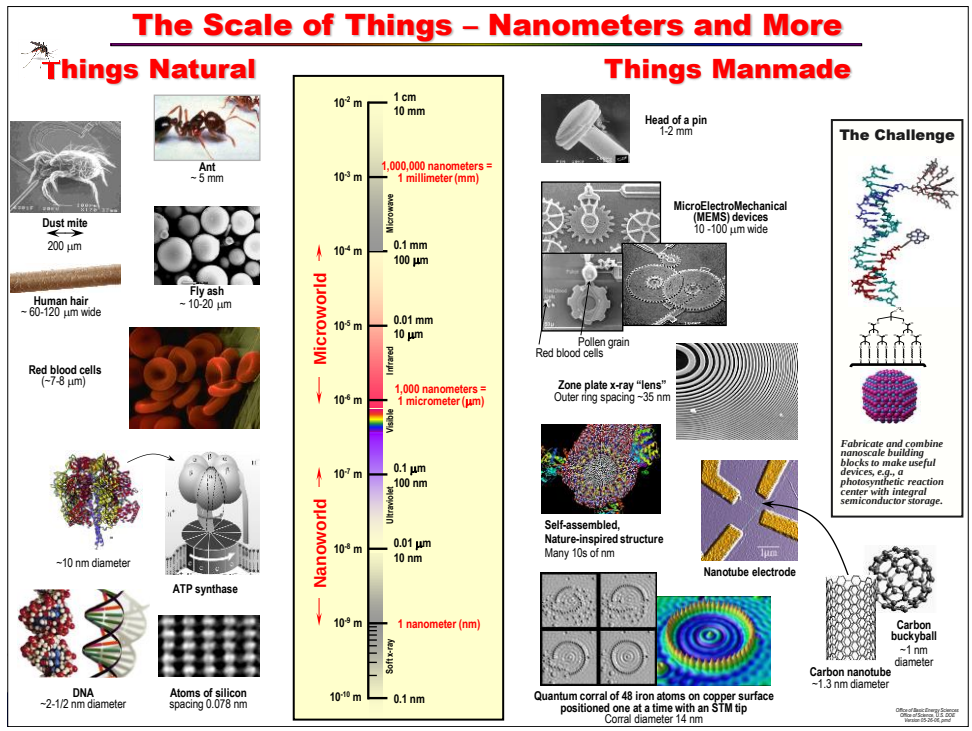

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The two sides of nanotechnology in medicine

Synthesis/ fabrication: Make things ⟷ **Characterization: Describe things**

Keywords

Lithography
Free-form fabrication
Microfabrication
Microfluidics
Microcontact printing
Nanoimprinting
3D Scaffold
Surface patterning
Surface functionalization
Layer-by-Layer

Keywords

EM
FIB-SEM
AFM
Optical microscopy
Profilometry
Dynamic light scattering
Single molecule detection

(XPS, TOFSIMS)

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Nanomedicine

Miniaturisation

- Devices
- Analytical techniques
- Biomedical materials

NANO

Molecular engineering and supramolecular chemistry

-Molecular assemblies

-Drug delivery systems

-Imaging agents

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Once we have Small Things, How can we Make Big Things?

- Top-down approaches are too expensive
  - Micro-machining
  - Photolithography
  - Electron-beam lithography
  - Focused ion beams
- Bottom-up, or so-called self assembly is needed
  - Modern synthetic chemistry enables synthesis of chemicals from molecules
  - New methods are needed

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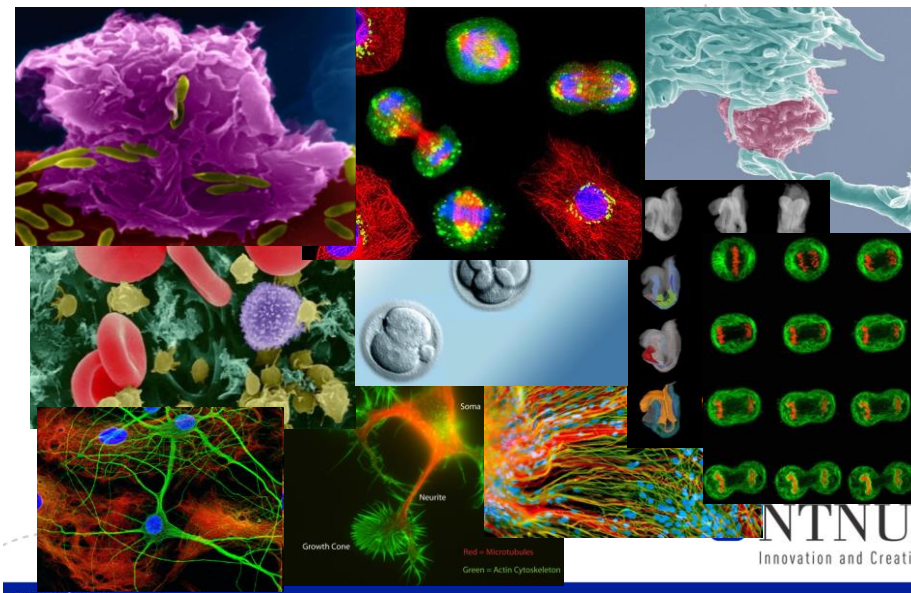
16 We are cells, and cells are dynamic assemblies of nucleotides, proteins, lipids, sugars, metabolites …..



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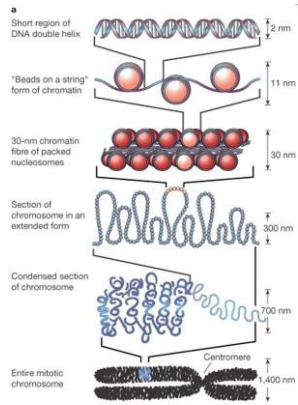
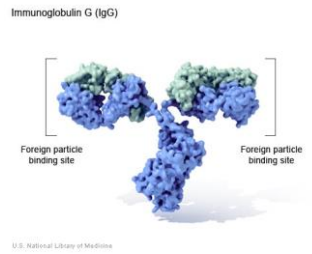
The size of building blocks of life

Length of DNA/human cell= 4 x 1m

Protein, typical size = 5-15nm





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Complex and dirty biomedicine

- some very inaccurate numbers

10000000 different species
7000000000 different people
25000 human protein-coding genes
3000000000 basepairs in human genome
100000? SNP/genome
500000 human proteins
2000 extracellular metabolites (will increase)

20000 drugs (will increase)
2000 pathogens
10000000 antibodies/person
1000000 T cells/person
70000000 different cancers

→ **Typical concentrations**
10^{18}-10^{2} molecules/ml

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Nano everywhere

Who takes this course

- **Nanotechnology**
- **Molecular Medicine**
- **Biotechnology**
- **Neuroscience**
- **Physics/biophysics**
- **Medical technology**
- **PhD**
- **Medical doctors**

One of the first courses world wide in nanomedicine

Should nanomedicine be separate courses or be incorporated into every other course?

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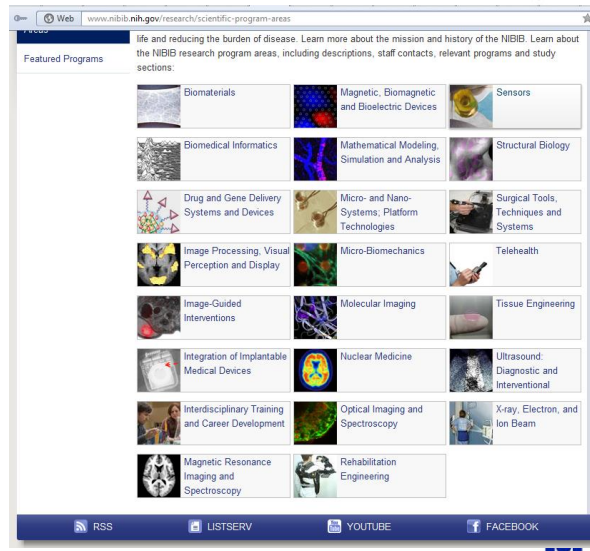
What the americans are thinking about these things



http://www.nibib.nih.gov/research/scientific-program-areas

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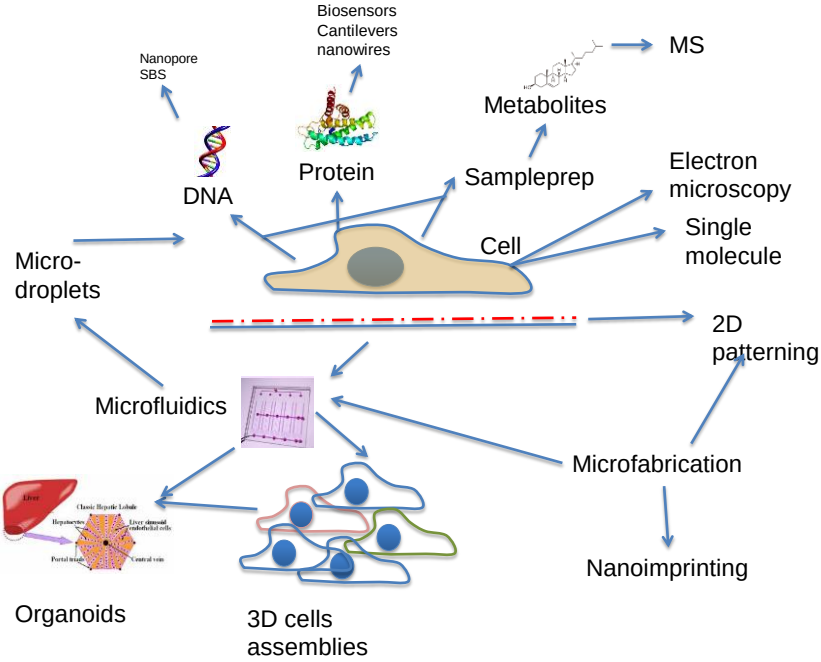
Course outline : nanotechnology for biomedicine : analysis



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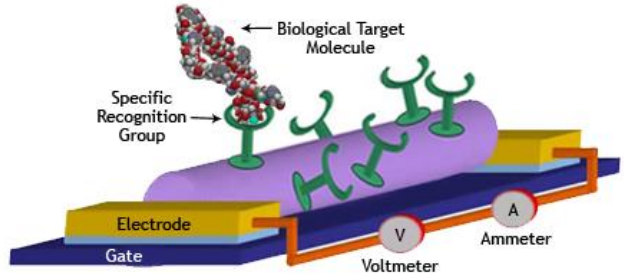
Example:
Can nanowires be used for sensing biomolecules?



Many more nanotechnologies with extreme sensitivity being tried for biosensors

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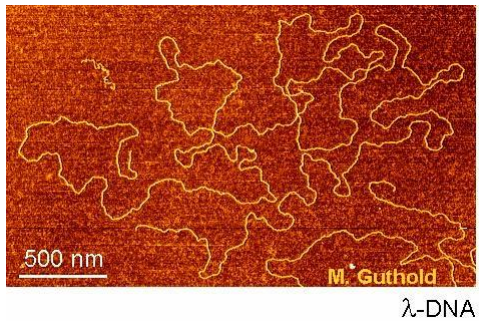
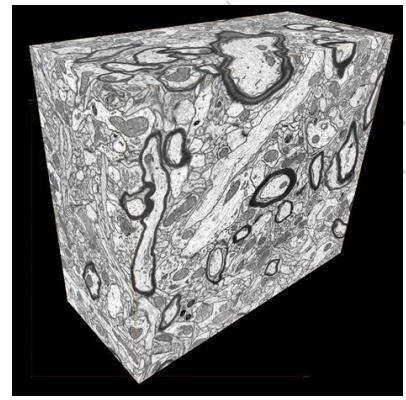
Extreme resolution of living matter

Atomic force microscopy



3D Electron microscopy



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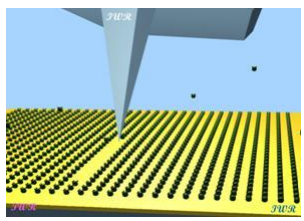
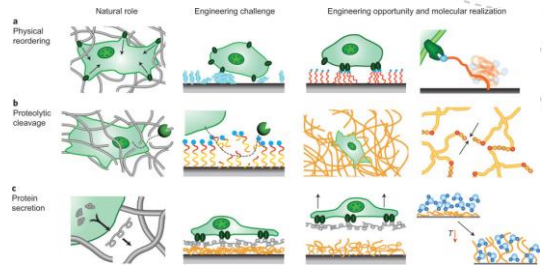
Can we instruct cells by making appropriate surroundings?





Stem cell renewal/differentiation is dependent on both soluble and structured biological cues

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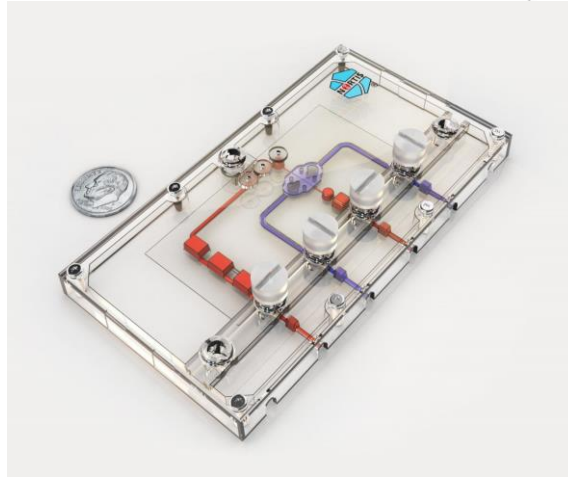
Can we recreate bodily functions outside a body?



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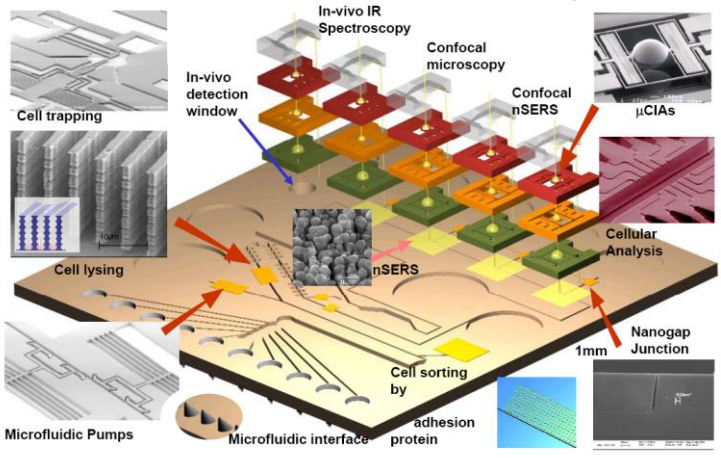
μTAS – microscale total analysis system

The biologists wet dream



http://www.microtas2013.org/program.html

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Biomedical component	«Nano»component	
	Mol3014	Mol3015
Life		Environmental nanotoxicology Nanoethics
Population		Species nanotoxicology
Organism		In vivo imaging NP Drug delivery NP Nanotoxicology
Organ	Assembly, chip	Tissue engineering
Cell	Capture, manipulation	Stem cells, immune cell
Matrices	Characterization, fabrication	Tissue engineering
Molecules		
Protein	Quantification, characterization	
Nucleic acid	Sequencing, manipulation	
Metabolite	Sample prep/sensors	

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This is NOT basic science, it is a way of thinking

Mol3014: Nanomedicine I - bioanalysis (fall)

Medical Nanotechnology. Things you want to know in order to exploit the new world of nanotechnology for biomedical analyses

Mol3015: Nanomedicine II - therapy (spring)

Nanomedicine: Things you would like to know in order to exploit the new world of nanotechnology for treatment purposes.

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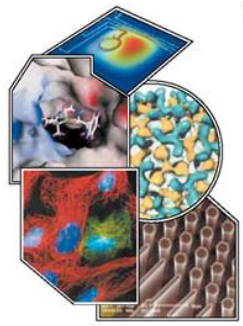
Syllabus nanomedicine at NTNU



Bioanalysis (Mol3014) (Outside of body)

- **diagnosis, research; biosensors, genome, proteome, drug screening, cell devices, in vitro imaging, microfabrication, nanocharacterization**

Therapy (Mol3015) (Inside of body)

- **drug delivery systems, nanoparticles, imaging, theranostics**
- **tissue engineering, tissue repair, gene and cell repair, stem cells, bioscaffolding, implantables**
- **biocompatibility, nanotoxicology**

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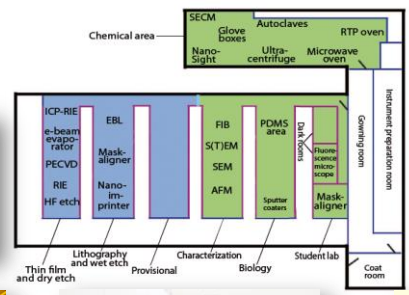
NTNU NanoLab Cleanroom

NTNU NanoLab cleanroom

- Opened in 2009
- 700m^2 divided in 2 labs
- ISO 7-5 (class 10.000-100)
- 66 tools, 5 engineers
- More than 200 users

Virtual Tour



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Nanomedicine I – bioanalysis Autumn 2015 (in LS41 unless otherwise specified)
In addition to lectures, students will chose a biomedical project and review the literature, explain existing solutions, consider new technological approaches based on nanotechnology,
and come with recommendations. Lecture days: Monday 1215-1400, Tuesdays 1015-1200

	Date	Title	h	Lecturer	Aff.	Keywords
Introductio	M2408	Introduction	2	Øyvind Halaas	IKM	What this course is about
Bioanalytical techniques	M3108					
	T0109	Single molecule analysis	2	Øyvind Halaas	IFY	AFM FCS FRET
	M0709	Protein analysis	2	Peter Køllenspe rger	IFY	DNA Nanotechnology, analysis and building blocks
	T0809	Nucleic acid analysis	2	Peter Køllenspe rger	IFY	..and proteins in Lab-on-chip settings
	M1409	Electron microscopy/FIB	2	Marianne Sandvold	IKM	Nanoscale resolution cellular imaging
	T1509	Biopatterning	2	Øyvind Halaas	IKM	How to pattern active biomolecules on surfaces and why
	M2109	Cell tools	2	Øyvind Halaas	IKM	Cells-on-chips
	T2209 LS42	Organs on chips I	2	Øyvind Halaas	IKM	Building complexity
	M2809	Organs on chips II	2	Øyvind Halaas	IKM	And more
Fabrication	M0510	Microfabrication	2	Øyvind Halaas	IKM	Making tools for biology – the hardware
	T0610	Nanoimprinting	2	Øyvind Halaas	IKM	Tools for the smallest placement of biomolecules
	T0710	Microfluidics	2	Øyvind Halaas	IFY	Small flows – special requirements
	T2010	Droplet based microfluidcs	2	Øyvind Halaas	IKM	Digital biology – one drop at the time
Semester	T1011 LS42	Paper presentation	2	Øyvind Halaas	IKM	Present your semester papers

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Semester paper

Syllabus: **Since there are no suitable books available in medical nanotechnology, the syllabus will be exclusively from lecture notes and selected papers.**

Semester paper: **Deadline is Monday 09.11.2015 at 1600. 25% of the grade will be from a semester paper on a topic chosen from the lectures, exceptionally (depending on our approval) from a chosen topic not covered in lectures. This is a good way to find an interesting master project, so consider this when you chose.**

The instructions for this paper will be:
Max 5 pages not counting references and figures:
"Chose a biomedical project preferably from lectures, review the literature, explain existing solutions, consider new technological approaches based on nanotechnology, and come with recommendations." With approximate outline;

Summary (1/4 page)
Background (What is the biomedical problem in question, ½ page)
Introduction (How is the problem addressed using current approaches ½-1 page)
Nano/microtechnological solutions (main part, describe the technicalities of the nanotech approaches to the problem in question. Use web, pubmed, nanowerk, or similar sources to find information, speak to lecturers or me. You should find more than one alternative solution and use information from more than one source. We will go through where you can find information. This section should be 2 pages)
Discusson (Identify major obstacles on why this technology hasn't been implemented yet, 1 page)
Conclusion (Recommend the solution you consider best)

Preliminary examples on projects: This is nanotechnology and not biology, emphasis must be put on analytical techniques. For those of you entering research and development, these techniques are the future.
Protein detectors (magnetic, photonic, electrical), protein-conjugation to surfaces (glass, silicon, metal), antibody nanoarrays, DNA/RNA nanoarrays, droplets-based microfluidics, AFM probe modification, cell chips, microfludic devices for biomedicine.

The paper will be scored according to relevance, creativity, feasibility and format

Exam: **Exam (please check again later)**

Course responsible.
Øyvind Halaas, Dept of Cancer Research and Molecular Medicine, DMF, NTNU.
Visiting address: Gastrocenter 3rd floor (access restricted, please make appointment)
oyvind.halaas@ntnu.no
Tel 73825341
Mob 9779087

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What we hope to learn in Mol3014

What is medical nanotechnology about?

New way of approaching biomedicine

How can we make use of nanotechnology in biomedical analysis, and what are others doing? Anecdotal accounts

More specifically: How do we identify and measure DNA, protein, cell behaviour and disease today, and what is to come…

Find requirements for bioanalytical devices (many unsolved problems for you to solve!)

Look at some fabrication processes and microfluidic devices

Important to acknowledge that this is an emerging field not having entirely identified itself.

Provide a cross-disciplinary environment where we can learn from eachother.

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Mol3015 Nanomedicine II – therapy

Tissue egineering and biocompatibility
Drug delivery systems
Nanotoxicology

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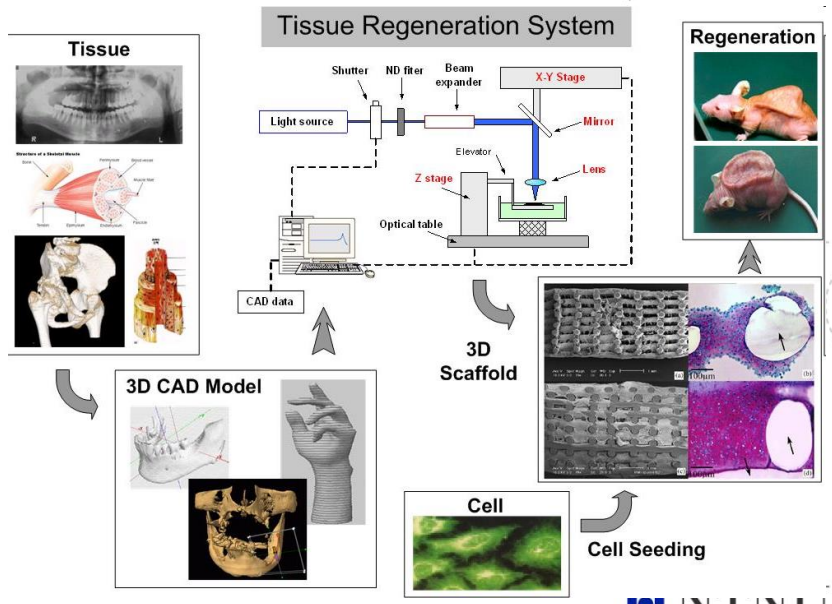

http://ims.postech.ac.kr/ims/nrl/summary_eng.php

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Multifunctional DDS

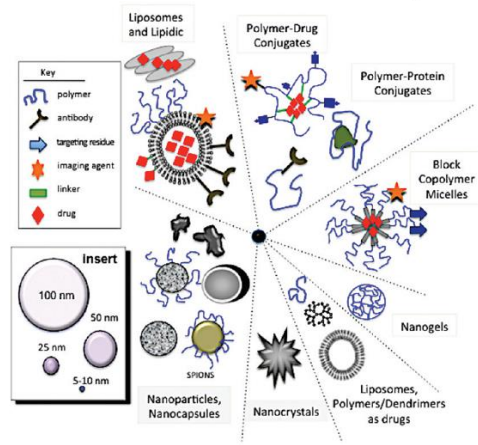

Figure 2. Schematic showing the main classes of first generation nanomedicines in clinical trial and routine clinical use. The inset gives an idea of the relative sizes of nanomedicines as the cartoons in each panel are not drawn to scale. For example, liposomes, nanocrystals, and some polymeric nanoparticles are ≥100 nm, and some polymeric nanoparticles, polymer conjugates, and dendrimers are in the range 5–25 nm.

From Duncan et al 2011

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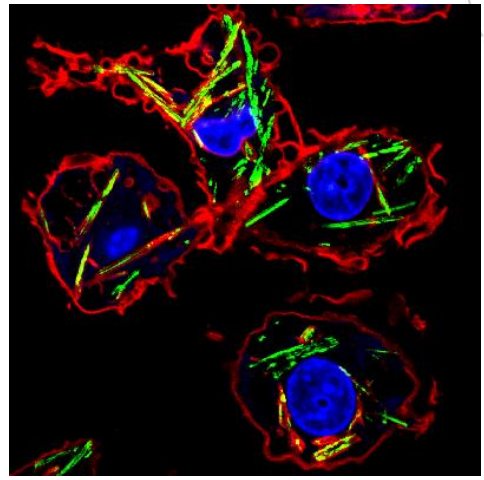
Nano/microcrystals disrupt cell integrity = chronic inflammation



Latz E et al Nat Immunol 9:2008

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Some useful links

http://www.nanowerk.com/

http://www.azonano.com/

http://www.nano.org.uk/links.htm

http://www.nanotech-now.com/

http://www.nanoforum.org/

http://www.nanotechnology.net/

Publications

List: http://www.azonano.com/journals.asp

Nature Nanotechnology

Nano Letters

Lab-on-chip http://pubs.rsc.org/en/Journals/JournalIssues/LC#Issues

Small

Langmuir

And manymany more

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Who are you?