Introduce professors
Content, Rules and locations
How to properly compile a lab notebook
Error analysis
CMI+

ADVANCED METHODS IN BIOENGINEERING LABORATORY
INTRODUCTORY LECTURE

Introduce Professors

- Georg Fantner
  - **LBNI-** Laboratory for Bio- and Nano- Instrumentation
  - Lab website, lbni.epfl.ch georg.fantner@epfl.ch
- Carlotta Guiducci
  - **CLSE**- Chair on Engineering. Laboratory of Life Sciences Electronics.
  - Lab Website: clse.epfl.ch; carlotta.guiducci@epfl.ch
- Aleksandra Radenovic
  - **LBEN -**Laboratory of Nanoscale Biology LBEN
  - Lab website: lben.epfl.ch ;aleksandra.radnovic@epfl.ch

CONTENTS, RULES AND LOCATIONS

Teaching method

- Except for an ex-cathedra introduction session, the teaching proceeds with weekly alternating sessions of laboratory practice and classroom data analysis. Both the laboratory practice and classroom data analysis sessions are supervised work in groups.
- The textbook reading and laboratory notebook filling are an independent work, with available support from the teacher and assistants during specified office hours.

Content

- The core of the course consists of 5 exercises that are meant to be performed in either 2 or 3 weeks/sessions each for a total of 11 weeks.
- The course also comprehends an introduction, instructions on
  - How to write a notebook
  - Error analysis
  - Safe laboratory behavior

to be held and discussed during the 1st week.

Objectives

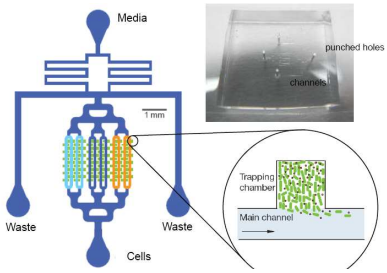
- **LAB-ON-A-CHIP** The students will learn how to design and fabricate miniature chemical and bio-chemical analysis systems, also known as Lab-on-a-Chip systems, referring to the idea of shrinking a complete chemical analysis laboratory onto a small chip.
- **BROWNIAN MOTION** The students will learn how to how to simulate and analyze Brownian motion of single particles in Matlab, use brightfield and darkfield microscopy. They will be introduced to the image data acquisition, theory and software design for image filtering and particle tracking in Matlab.
- **OPTICAL TRAPPING** In this students will learn the basics of operating a high-end optical tweezers to record mechanical transitions of single molecules.
- **SURFACE DESIGN** The students will learn some basic techniques of surface design for bioanalytics
- **SURFACE PLASMON RESONANCE** The students will learn how to plan and interpret surface bio-molecular binding experiments

Handouts, applets and additional literature

- The handouts, applets and additional material for respective exercise can be found on our moodle website
- http://moodle.epfl.ch/course/view.php?id=9661
- enrolment key is bioeng11

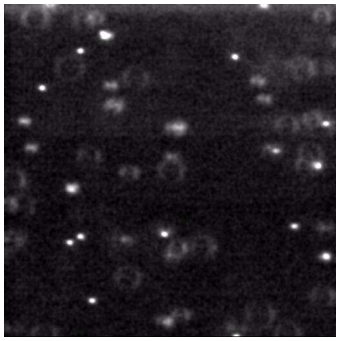
Lab-on-a-chip

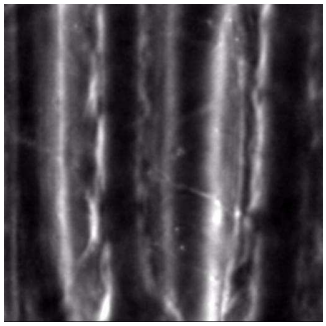
- Lab-on-a-chip (LOC) exercise will introduce students to the fundamental elements of moving fluids in LOC systems such as flows, pressure driven flow, electro-osmotic driven flow, capillary effects, surface forces.



Brownian motion

- In the first part of this exercise, the students will replicate Perrin's work with modern equipment. Next they will investigate intracellular vesicle transport inside living cells and determine if the vesicle transport is accomplished by Brownian motion or by directed transport





Optical Trapping

- Optical trapping is one of the most successful technology transfers from a physics lab to biology. The goal of this exercise is to provide hands on experience to the bioengineering students of one of the mostly used single molecule technique.

Surface design

Description:

Modern bioanalytics is based on surface detection of biomolecules. The exercise will explore a surface modification technique commonly employed in biosensor and microbiosensors.

Objectives:

- Learn how to design an experiment of biomolecular detection on arrayed surfaces
- Perform an analysis in terms of hybridization efficiency according to different conditions

Structure:

- 1st week: surface cleaning and deposition of an arrayed pattern of molecular probes (DNA oligonucleotides)
- 2nd week: hybridization with complementary sequence, data acquisition and analysis

SPR

Description:

The exercise consists in the employment of label-free biosensors for the observation of binding kinetics. Real-time biomolecular bindings will be observed for different molecules.

Objectives:

- understanding the importance of real-time measurements of biomolecular binding interactions
- Perform kinetic analysis for ligands immobilized on a sensor chip by amine coupling chemistry
  - Direct coupling
  - Ligand mediated coupling

Structure:

- 1st week: Introduction to SPR Technology and Surface preparation
- 2nd week: SPR experiment and kinetic analysis

Teaching material

- Handouts given during the course (provided on line on the moodle site http://moodle.epfl.ch/course/view.php?id=9661
  pw: bioeng11
- Reference books:
  - *Intermolecular and Surface Forces, J. Israelachvili, Academic press*
  - *Surface Plasmon resonance Based Sensors, J.Homola et al., Springer*
  - *Surface Design: Applications in Bioscience and Nanotechnology, R. Forch, H. Schonherr, A.T. Jenkins, Wiley*
  - *"Introduction to Error Analysis: The Study of Uncertainties in Physical Measurements," Taylor, John R., 1997, University Science Books,*
  - *Optical Trapping Review : K.C. Neuman & S.M. Block, "Optical trapping,"Rev. Sci. Instrum. 75 (2003).*
  - *Lab on a Chip Technology, Volume 1: Fabrication and Microfluidics, Keith E. Herold and Avraham Rasooly, Caister Academic Press, 2009*

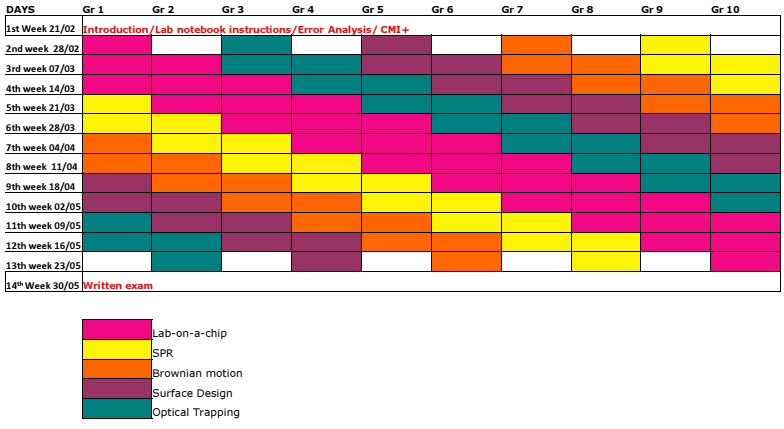
Links with other courses

- **Required background:** Biophysics I, Biothermodynamics, Biomicroscopy I, + mandatory courses of M1
- **Related Courses:** BioMEMS , Stem cell biology, MCB 1 and 2, Mechanics of Fluids, Biomicroscopy, Systems biology,, biophysics II, biothermodynamics, biomicroscopy, Image Processing, Fundamentals of Biochemical sensing systems, Biochemical engineering.

Evaluation

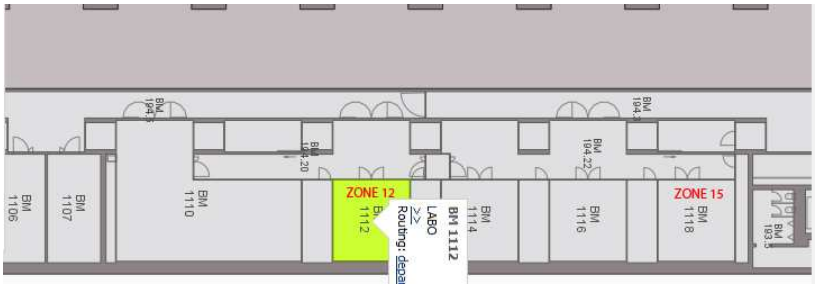
- Written exam and continuous control:
  - 2/3. Written exam on the 30th of May.
  - 1/3. Evaluation of the quality of the lab notebook and on the understanding of the exercise by the student.
- Students are asked to
  - prepare the exercise in advance by studying the handouts provided on the moodle site
  - compile properly the lab notebook (one for each student)
  - understand the exercise theoretical background and outcome of the analysis sessions.

Course Syllabus and groups distribution



Locations and dress code

- **LAB-ON-A-CHIP**
  - location: CMI+ zones 12 and 15 BM first floor, south side
  - dress code: wear pants. You will be given instruction on what to dress-LOC



Locations and dress code

- **BROWNIAN MOTION**
  - location: **TP SSV.**
  - dress code: lab coat

Locations and dress code

- **OPTICAL TRAPPING**
  - location: **TP SSV.**
  - dress code: lab coat, ***IR goggles***

Locations and dress code

- **SURFACE DESIGN**
  - location: **TP SSV**
  - dress code: lab coat. Closed shoes. Long pants

Locations and dress code

- **SURFACE PLASMON RESONANCE**
  - location: **TP SSV and CLSE BM2112**
  - dress code: lab coat. Closed shoes. Long pants.

Locations and dress code

- **ANALYSIS SESSIONS**
  - Location: ELD120

Safety

- In any laboratory, there is potential for injury if certain common-sense practices are not followed. In AMBL this is minimal, but it's still important to follow a few basic rules.

Electrical Safety

- Electrical injuries happen when large amounts of electrical power are dissipated by the body. Most often, this happens in high-current situations, which is why you always hear that "it's not the voltage, it's the current that is dangerous." Strictly speaking, both are dangerous, and it's a good idea to avoid becoming a current path.
- In AMBL, we will work with only low-power electronics, and nothing we do is likely to cause injury. However, some common-sense precautions, are in order:
- – don't connect supply voltages directly to ground
- – don't touch any current-carrying conductor with your bare hands
- These simple rules will keep you from injuring yourself and damaging circuit components. Some components will have maximum power ratings that should not be exceeded, so pay attention to these values.

Laser saftey

- 300 mW NIR diode lasers with λ=975nm (optical traps) The hazards of this Class IIIb laser come from its higher power level, and because it is invisible, making it harder to be aware of its location/direction. The beam will be largely constrained in the apparatus, and you will not need to make adjustments that might put you in the beam path. Safety goggles will be available, but not required.
- In general, other important things to keep in mind:
- Always know the path of the beam, and keep any body parts or reflective items (rings, watches, etc.) out of the beam path.
- Always read the pre-labs and know what special precautions you need to take associated with lasers or optics.
- When in doubt about doing something, don't do it before checking with the lab instructor.

Chemical Safety & Biosafety

- Though there is minimal wet work in AMBL please do not bring food or drink into the lab. The electronics will appreciate it, and we will also later be handling some bacteria and fluorescent dyes. When needed, latex gloves will be provided, as well as proper containers for disposing of chemical/biological waste and sharps. Please make sure to wash your hands with soap and water after removing gloves and before leaving the lab. Please report any spills or injuries to the lab instructor immediately

CMI+ Center of MicroNanoTechnology

- Safety
- Rules
- Access

HOW TO KEEP A GOOD LAB NOTEBOOK

Why is it Important to Keep a Good Laboratory Notebook?

- Keeping a complete and accurate record of experimental methods and data is a **vital part of science and engineering**. Your laboratory notebook is a **permanent record of what you did and what you observed in the laboratory**. Learning to keep a good notebook now will establish good habits that will serve you throughout your career. Your notebook should be like **a diary,** recording what you do, and why you did it.

- You should feel free to record your mistakes and difficulties performing the experiment - you will frequently learn more from these failures, and your attempts to correct them, than from an experiment that works perfectly the first time. It is extremely important that your notebook accurately record everything you did. A good test of your work is the following question: ***could someone else, with an equivalent technical background to your own, use your notebook to repeat your work, and obtain the same results?***

- For that matter, **could you come back six months later, read your notes, and make sense of them? If you can answer yes to these two questions, you are keeping a good notebook.**

Why is it Important to Keep a Good Laboratory Notebook?

- The laboratory notebook forms a permanent record that can be referred to while completing a disclosure report (often the first step in patent preparation) and later, provides accurate documentation of the work done. When an investigator makes an invention during the course of a research project, the dates of the conception and reduction to practice (turning an idea into a reality) become very important. Generally, a sketch and a brief written description are sufficient to establish conception. Reduction to practice is accomplished by actually constructing and successfully testing a material or device incorporating the invention.
- During prosecution of a patent application before the U.S. Patent Office, or even after issuance of a patent, the filing of another patent application may initiate an interference proceeding to determine which party was the first to invent. Each party has an opportunity tos ubmit documentary proof of his or her dates of conception and reduction to practice. A laboratory notebook may be, and in several high-profile cases has been the crucial piece of evidence in this procedure.

What your notebook is for

- Your lab notebook serves three important purposes:
- A record of important procedures for experiments you have developed during your experimentation.
- A record of the results of experiments that you have performed.
- The means to reproduce the results of your experiments by following the procedures you have developed at another time or place.
- A good notebook is not simply a list of results of experiments but allows you to develop methods that you can use for further experimentation and would allow someone else to reproduce your results and understand why you did what you did in your experiments.

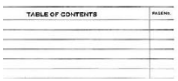
What goes into your notebook

- Page numbers – if your notebook doesn't already have them add them to the upper outside corner of each page. These are important so you can refer back to frequently used tables, procedures, or results. You can also be sure that there are no missing pages (leading to missing steps) if following a past procedure.
- A table of contents – The first few pages should be reserved for this, it allows you to quickly find the information you are looking for and makes the book a useful reference. Later on you will be able to find a particular experiment without having to read every page.
- Dates – Every entry, or at the very least every day that you record data should be dated, this allows you to more easily.
- Unusual conditions during an experiment – Sometimes things go differently than we plan and we have something unusual happen during our experiments some of the things you might want to look for and record are: Strong storms (ie. behavior of an observed animal may be atypical) Extremes in temperature or humidity (many instruments and materials are sensitive to temperature and humidity) Power failures (if your experiment requires power)

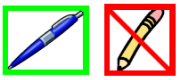
What goes into your notebook

- Something is went wrong or was unexpected (ie. you notice that the apparatus is no longer working at some point during your experiment)
- Experimenter fatigue may impair your ability to make good observations
- Reasons for decisions made during an experiment – What we did isn't always good enough, why we did what we did is just as important to record. Make sure that you record the whys and not just the whats. Contact information for people that provided you with information or supplies – They may be able to provide you with some materials in the future or to give you more information later on should you need it. It is important to give credit where it is due as well. Any information that you might need to reproduce the results of an experiment – Your notebook alone should be sufficient *for someone* to reproduce your experiment. Aim to be as complete as possible!

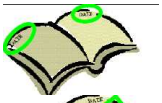
Rules for Maintaining your Laboratory Notebook



Leave several pages blank at the beginning for a **Table of Contents and update it when** you start each new experiment or topic



Always use pen and write neatly and clearly



Date **every page on the top outside corner**

Start each new topic (experiment, notes, calculation, etc.) on a right-side (odd numbered) page

Record the **TITLE and OBJECTIVES of each** experiment (or notes or calculations) at the top of the first page of the notebook dedicated to this topic.

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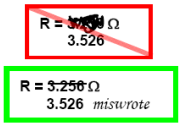
Rules for Maintaining your Laboratory Notebook



If you make a mistake, don't obliterate it! You may need to read your mistake later – perhaps you were right the first time! Use a single cross out and EXPLAIN why it was an error.

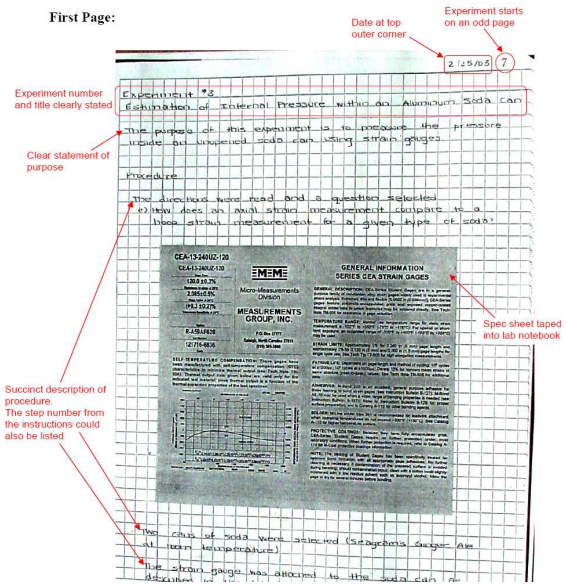
Data typed into the computer must be printed and taped into your lab notebook. Plots of data made in lab should also be printed and taped in your lab notebook.

When you record an observation in your notebook, include an explanation of what you were doing at the time. If appropriate, you may just record the step number in the instructions followed by your observation

Rules for Maintaining your Laboratory Notebook

Metric	Requirements	Worth
Pen	Write in pen, not pencil	10 %
Date	Date **every page at the top**	10 %
Right Side	Begin each experiment on odd page	10 %
Printouts	Attach printouts and plots of data as needed	10 %
Legible	Obvious care taken to make it readable, even if you have bad handwriting	10 %
Mistakes	Mistakes crossed out with one line and explained	10 %
Organized	table of contents title of experiment on 1st page objectives of experiment clear from notebook what you were doing when	20 %
Informative	all required data and information descriptive comments of your observations	20 %

Example: Complete Experiment



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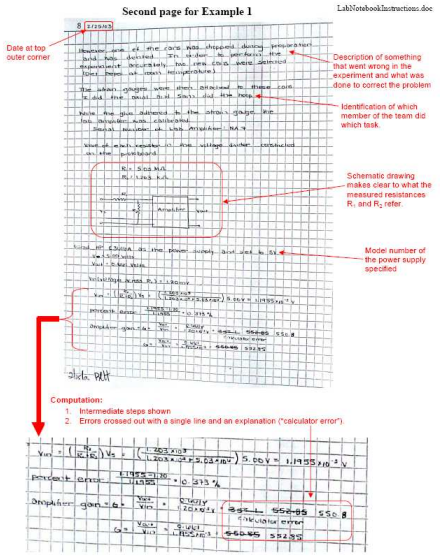
Example: Complete Experiment



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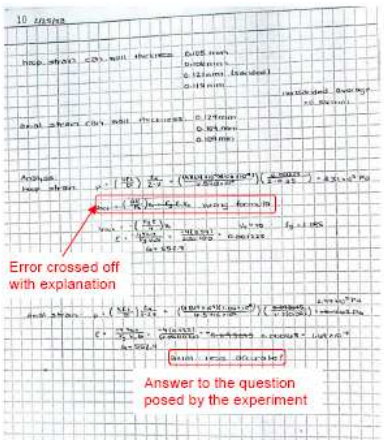
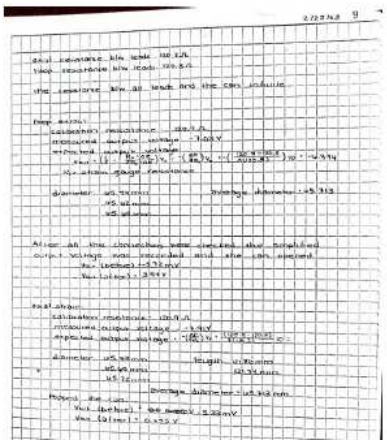
Example: Complete Experiment

Remaining pages for Example 1:





Example: Complete Experiment

- Key points in this example:

1. Neat and legible handwriting
2. Experiment title and purpose clearly stated
3. Procedure described clearly and succinctly, including errors and the steps taken to correct

them

4. Computations performed neatly showing intermediate steps
5. Errors crossed out with a single line and explained
6. All pages dated at the top and signed by lab professor on the same

1:30

INTRODUCTION TO ERROR ANALYSIS

GROUP 1

2nd week 28/02	Lab-on-a-chip. First experimental session.Location CMI+
3rd week 07/03	Lab-on-a-chip. Second experimental session. Location CMI+
4th week 14/03	Lab-on-a-chip. Analysis session. Location ELD 120
5th week 21/03	SPR. Location TP SSV
6th week 28/03	SPR. Second experimental session and Analysis session. Location BM2112
7th week 04/04	Brownian motion. Location TP SSV
8th week 11/04	Brownian motion. Analysis session. ELD 120
9th week 18/04	Surface Chemistry
10th week 02/05	Surface Chemistry. Analysis session. Location ELD 120
11th week 09/05	Optical Trapping. Location TP-SSV
12th week 16/05	Optical Trapping. Analysis session. Location ELD 120

GROUP 2

3rd week 07/03	Lab-on-a-chip. First experimental session.Location CMI+
4th week 14/03	Lab-on-a-chip. Second experimental session. Location CMI+
5th week 21/03	Lab-on-a-chip. Analysis session. Location ELD 120
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10th week 02/05	Surface Chemistry
11th week 09/05	Surface Chemistry. Analysis session. Location ELD 120
12th week 16/05	Optical Trapping. Location TP-SSV
13th week 30/05	Optical Trapping. Analysis session. Location ELD 120

GROUP 3

2nd week 28/02	Optical Trapping. Location TP-SSV
3rd week 07/03	Optical Trapping. Analysis session. Location ELD 120
4th week 14/03	Lab-on-a-chip. First experimental session.Location CMI+
5th week 21/03	Lab-on-a-chip. Second experimental session. Location CMI+
6th week 28/03	Lab-on-a-chip. Analysis session. Location ELD 120
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10th week 02/05	Brownian motion. Analysis session. ELD 120
11th week 09/05	Surface Chemistry
12th week 16/05	Surface Chemistry. Analysis session. Location ELD 120

GROUP 4

3rd week 07/03	Optical Trapping. Location TP-SSV
4th week 14/03	Optical Trapping. Analysis session. Location ELD 120
5th week 21/03	Lab-on-a-chip. First experimental session.Location CMI+
6th week 28/03	Lab-on-a-chip. Second experimental session. Location CMI+
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13th week 30/05	Surface Chemistry. Analysis session. Location ELD 120

GROUP 5

2nd week 28/02	Surface Chemistry
3rd week 07/03	Surface Chemistry. Analysis session. Location ELD 120
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GROUP 6

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11th week 09/05	SPR. Second experimental session and Analysis session. Location BM2112
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13th week 30/05	Brownian motion. Analysis session. ELD 120

GROUP 7

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GROUP 8

3rd week 07/03	Brownian motion. Location TP SSV
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12th week 16/05	SPR. Location TP SSV
13th week 30/05	SPR. Second experimental session and Analysis session. Location BM2112

GROUP 9

2nd week 28/02	SPR. Location TP SSV
3rd week 07/03	SPR. Second experimental session and Analysis session. Location BM2112
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12th week 16/05	Lab-on-a-chip. Analysis session. Location ELD 120

GROUP 10

3rd week 07/03	SPR. Location TP SSV
4th week 14/03	SPR. Second experimental session and Analysis session. Location BM2112
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