Lab on Chip Module

The team

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Design requirements & assumptions

Mark Bentum 2014

- Request for deepening module EE
- BIOS design team composed (Jan, Mathieu, Wouter, Loes, Paul, Wesley (BKO))
- Directly the team found they preferred a multidisciplinary module with other programs participating
  - In line with BIOS expertise
- Green light for EE-BME from Mark Bentum, Ramses Wessel
- Positive reactions Ben Betlem (ST), Herbert Wormeester (AT), Katia Haijkens (BME)
  - CREATE?, TN?, ATLAS?
- Start with module design document

Design – first considerations

Starting point:

- Multidisciplinairy projects
- Multidisciplinairy project teams

- Formulate educational targets
- How to reach those targets? – teaching methods
- Need to know the starting knowledge of the students from the various programs

Global aims

- Get the experience of working in a *multidisciplinary* development team
- Make the full *design circle* (design, build, and measure) for a real-life measurement problem using Lab on a Chip technology
- Become acquainted with state-of-the-art prototyping techniques such as polymer casting and molding, 3D printing, photolithography and paper fluidics
- Learn the basic theory for Lab on a Chip
- Learn how to properly perform a measurement and how to interpret measurement data

Subjects

- Knowledge: fluidics, mass transport, fabrication, sensing, cell handling, signal analysis
- Skills: lab skills, design tools, prototyping, culturing, device characterization
- Project: Design, build and test your own chip
  - Multidisciplinary groups formed on first day
    - Diagnostic test + educational background
  - Groups choose their project from pitches

Intended learning outcomes

The student is able to

- List, explain and apply concepts (fluid handling, micro-organism handling, …)
- Apply lab & fabrication skills and report the process in a lab journal
- Create a project design
- Develop a project plan, incl. schedule and task division
- Produce a report on the complete project
- Present the outcomes of the project
- Explain evaluate and discuss on the project

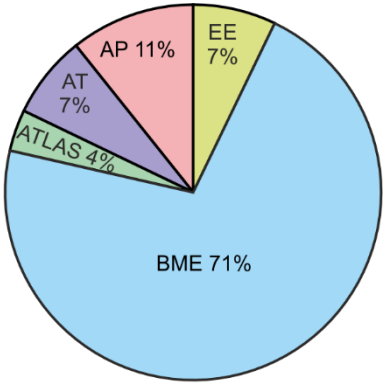
Hotly discussed

- How to cope with different starting knowledge of EE, AT, BME,…?
- Teaching method…: classical lecture/tutorial or PBL?
  - Students of different background can teach each other…? How..?
  - Wouter

Presently

- Successful module running with about 25 students each year
- Teaching staff + Hans van den Berg (also our PBL coach) is writing a paper for Journal of Chemical Education

Multi- / interdisciplinary aspect



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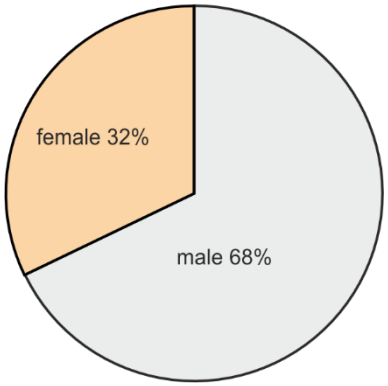
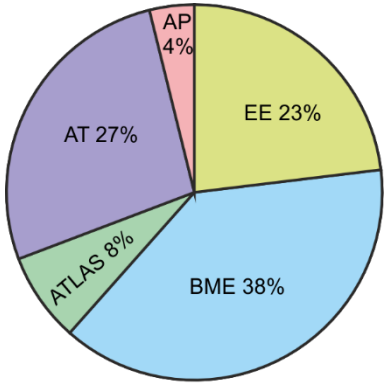


(B)

2015/2016
N=28



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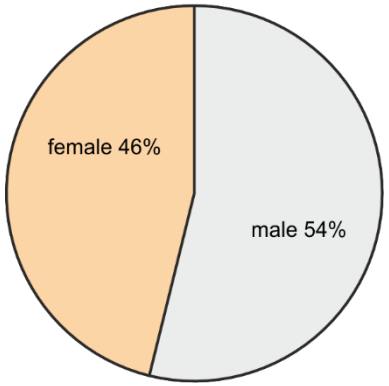

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2016/2017
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Motivation for PBL

Teaching methods

as used in the Lab-on-a-Chip module

Problem-based Learning

Project

Practical lab

Diagnostic tests

Teaching methods

Problem-based learning

What is the problem based learning?

Problem-based learning (**PBL**) is a student-centered pedagogy in which students learn about a subject through the experience of solving an open-ended **problem** found in trigger material.

en.wikipedia.org/wiki/Problem-based_learning

In a series of 11 problem-based learning session the students will activate their preexisting knowledge or acquire new knowledge on a range of subjects that are particularly relevant for labs on a chip.

PBL was pioneered by McMaster Universiteit in Hamilton, Ontario, Canada.

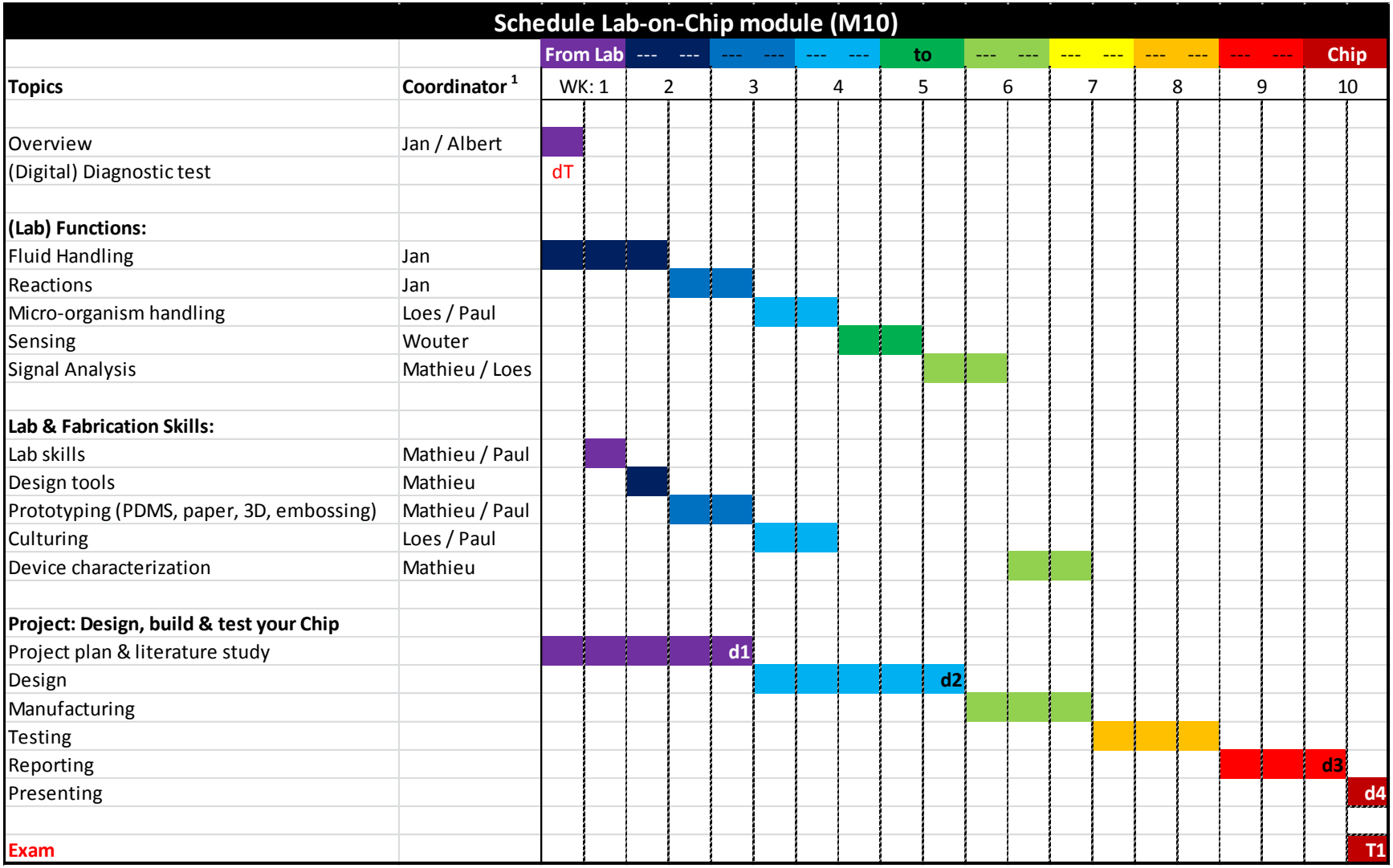
Barrows, Howard S. (1996). "Problem-based learning in medicine and beyond: A brief overview", New Directions for Teaching and Learning. ***1996*** *(68): 3–12*

Design

Initial design ideas

- Organise module in functions categories (basically topics)
- Organise module in skills sessions
- PBL sessions of 1 day
- Project throughout the module

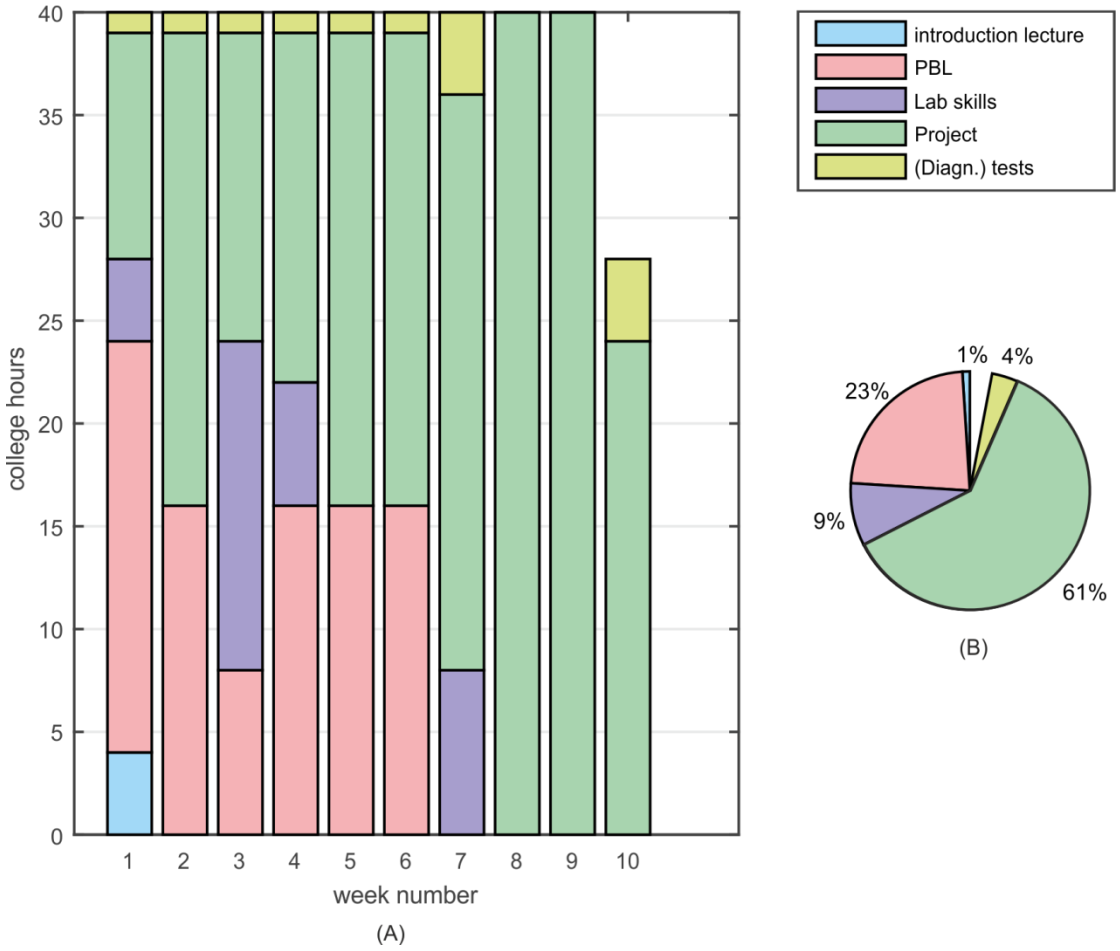
Original design



Actual timetable

MA:	14-11-2016	21-11-2016	28-11-2016	5-12-2016	12-12-2016	19-12-2016	26-12-2016	2-1-2017	9-1-2017	16-1-2017	23-1-2017	30-1-2017
Monday	Introduction lecture Project kick-off DT0: voorkennis Practice PBL [all tutors and coaches]	Project	PBL microfabrication [Mathieu + Jan, Wouter; Hai + Miguel]	PBL cell layer in LOC [Loes + Paul, Anne; Martijn + Hugo]	PBL river water [Wouter + Mathieu, Jan; Miguel + Hai]	Project	2e Kerst	Brugdag	Project	Project	Project	Project Final report
Tuesday	PBL pumping in microfluidic channel [Jan + Loes, Mathieu; Josh + Vasilis]	PBL meas. Methods 1 [extern + loes, Jan; Anke + Hugo]	Lab skills: design tools (middag clewin etc.; ochtend comsol) [mathieu + Floris]	PBL cell staining [Loes + Paul, Anne; Martijn + Hugo]	Project	PBL optical sensing [Wouter + Mathieu, Jan; Anke + Jasper]	Brugdag	Brugdag	Project: litho	Project	Project	Project
Wednesday	PBL mixing for cell culture [Jan + Mathieu, Wouter; Josh + Vasilis]	PBL mass-transp.1; protein detection [jan + Wouter, Loes; Hai + Miguel]	Project	L.S.: culturing [paul, Martijn]	Project deadline project plan	Project	Brugdag	Brugdag	Project	Project	Project	Project **Presentations**
Thursday	Kick-off lab skills DT1a: lab safety E1: make and meas. dil. Series [paul + martijn] Project	PBL mass-transp.2.; EOF pump [Jan + Wouter, Mathieu; Josh + Miguel]	Lab skills: fabricating devices (roulatie schema) [Johan, Josh, Stefan, Jeroen, Vasilis, Miguel, Hai]	L.S.: staining [paul + martijn]	Project Design finished (official deadline)	PBL meas. Methods 2 [extern + mathieu, Jan; Hugo + Anke]	Brugdag	Brugdag	Project Project meeting	Project	Project Project meeting	
Friday	Project Project meeting DT1b: fluid handling Project	Project Project meeting DT2: reactions & mm1 Project	Project Project meeting DT3: microfab. Project	L.S.: uitloop staining [paul+mart.] DT4: culturing **Project pitch presentations**	Project Project meeting Final design (unofficial deadl.)	Project Project meeting DT5: Sensing & mm2 Project	Brugdag	Brugdag	Project **Exam**	Project Project meeting Examen inkijkmoment	Project: Device characterization?	**Repeat Exam**

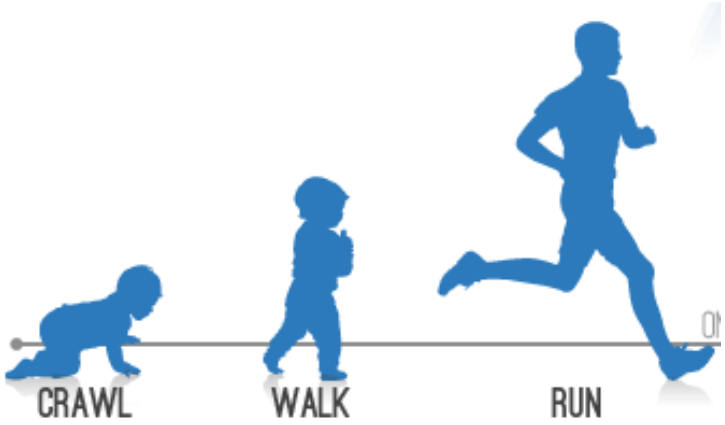
Time division



Problem-based Learning (PBL)

what and why?

- The basic knowledge is offered via PBL.
- Complex, multi-faceted, and realistic problems.
- Develop knowledge, problem solving skills, self-directed learning, collaboration skills, and to motivate.
- The teacher is "facilitator of learning“, coach.
- Like professionals learn on the job, students are supposed to learn while doing PBL



- The whole point is **not to solve** the problem, but to use it to learn.

In this module, students will tackle 11 problems in total:

Problem-based Learning (PBL)

an overview of the problems

0.	**Practice: Why miniaturizing lab functions on a chip?**
1.	**Fluid transport 1 Liquid transport**
2.	**Fluid transport 2 Mixer/cell culture chip**
3.	**Measurement methods – 1**
4.	**Mass transport 1 Protein sensing**
5.	**Mass transport 2 Channel with sensor**
6.	**Microfabrication**
7.	**Micro-organism handling – 1**
8.	**Micro-organism handling – 2**
9.	**Electrochemical sensing - River water**
10.	**Optical sensing - Tea party**
11.	**Measurement methods – 2**

Each problem takes one whole day:

Scheduled PBL time

Example: week 1 of the module

Weekly roster

Module 10 Lab on a Chip – week 1					
	Monday 14/11	**Tuesday 15/11**	**Wednesday 16/11**	**Thursday 17/11**	**Friday 18/11**
1e | 8:45-9:30	**Introduction lecture** *CR 2N* Jan en Albert	**PBL pumping** *RA2234 (& RA2337)* Josh + Vasilis	**PBL mixing for cell cult.** *RA2231 (& RA2237)* Josh + Vasilis	**Kick-off lab skills** *CR 2N* Paul	**Project** Vasilis, Josh, Hugo Anke, Miguel, Yusuf
2e | 9:45-10:30	**DT0 start test**			**DT1a lab safety** Paul	
3e | 10:45-11:30	**Kick off PBL + Project** *CR 3B* Wouter, Mathieu, Jan Paul			**EXP1 Dilution series** *CR 4028* Paul + Martijn	Project
4e | 11:45-12:30					**Project meeting**
5e | lunch				Lunch teachers and SAs *CR2510*	
6e | 13:45-14:30	**PBL exercise** *RA2334: Jan, Loes, Josh, Vasilis, Anke, Hugo* *RA2336:Wouter, Paul, Mathieu, Miguel, Hai, Martijn*	**PBL pumping** *RA2234 (& RA2337)* Josh + Vasilis	**PBL mixing for cell cult.** *RA2231 (& RA2237)* Josh + Vasilis	**EXP1 Dilution series** *CR 4028* Paul + Martijn	**DT1b fluid handling** Jan
7e | 14:45-15:30				Project	**Project** Vasilis, Josh, Hugo Anke, Miguel, Yusuf
8e | 15:45-16:30		**PBL pumping | pres** *RA2237*: Josh + Jan *RA2334:* Vasilis + Loes	**PBL mixing for cell cult. | pres** *RA2231:* Josh + Mathieu *RA2237:* Vasilis + Jan		
9e | 16:45-17:30		Backup: Mathieu	Backup: Wouter		

Problem-based Learning (PBL)

overview of the one PBL-day

time	function	details	remarks
08:45 - 08:55	**Kick-off**	• get the students in class	by one of us
08:55 – 10:30	**Action Plan**	• Analyze the problem • Define an action plan	working unsupervised
10:45 – 12:30	**Execution of work**	• Studying literature • Solving the problem	working under the guidance of SA's
13:45 – 15:30	**Execution of work**	• Solving the problem • Preparation of presentation	working unsupervised
15:45 – 17:30	**Presentation and discussion**	• 3 teams per class • 4 students in each team • Cruel fate selects the presenter	PBL coach (one of us) and SA are present Confirmation for the good teams (steep) learning for the mediocre teams

There is a predefined strategy:

Problem-based Learning:

following a predefined strategy

For every PBL session, you will work on a **big, ill-defined** problem, following a predefined **strategy**:

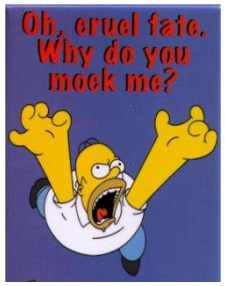
1) What is the problem? Formulate in your own words;
2) What do we want to present?
3) What do we already know?
4) What are the new concepts?
5) What should we study?
6) Working plan, containing all tasks to be performed;
7) Division of work

From: 'De Zevensprong', Universiteit Maastricht

Problem-based Learning:

some additional facts

- PBL in a ***team*** of four students.
- We choose the fellow students in a team based on multidisciplinarity
- The teacher coaches a ***group*** consisting of ***three*** teams during the PBL presentation session.
- For each PBL, the results of the team are presented (the presenter is selected randomly (cruel fate) from the team members) to the other students in the session (8th and 9th hour).
- Tutors are available at scheduled times (3rd and 4th hour) to give assistance in solving PBL problems.
- 1 full day to work on each problem.
- PBL work is graded every session, based on the presentation. The grade is an indication of the team's progress, and contributes for a small % (5%) to the final grade of the module.



Skills sessions design

- Work in smaller groups in the lab
- Focus on practical work
- Aim is real hands-on experience

Skills sessions by topic

Content	Practical implementation
1: basic lab skills & safety	Make and measure a dilution series
2a: Design tools & software	Design your own mixer
2b: Rapid prototyping	Fabricate lab on chips, using PDMS, 3D printing, SU8, Micromilling
3a: Cell seeding & culturing	Culture HUVEC cells in a PDMS chip
3b: Cell staining	Fluorescent staining of the HUVECs in the chip
4: Characterization	Use SEM, AFM, Microscope to do device characterization

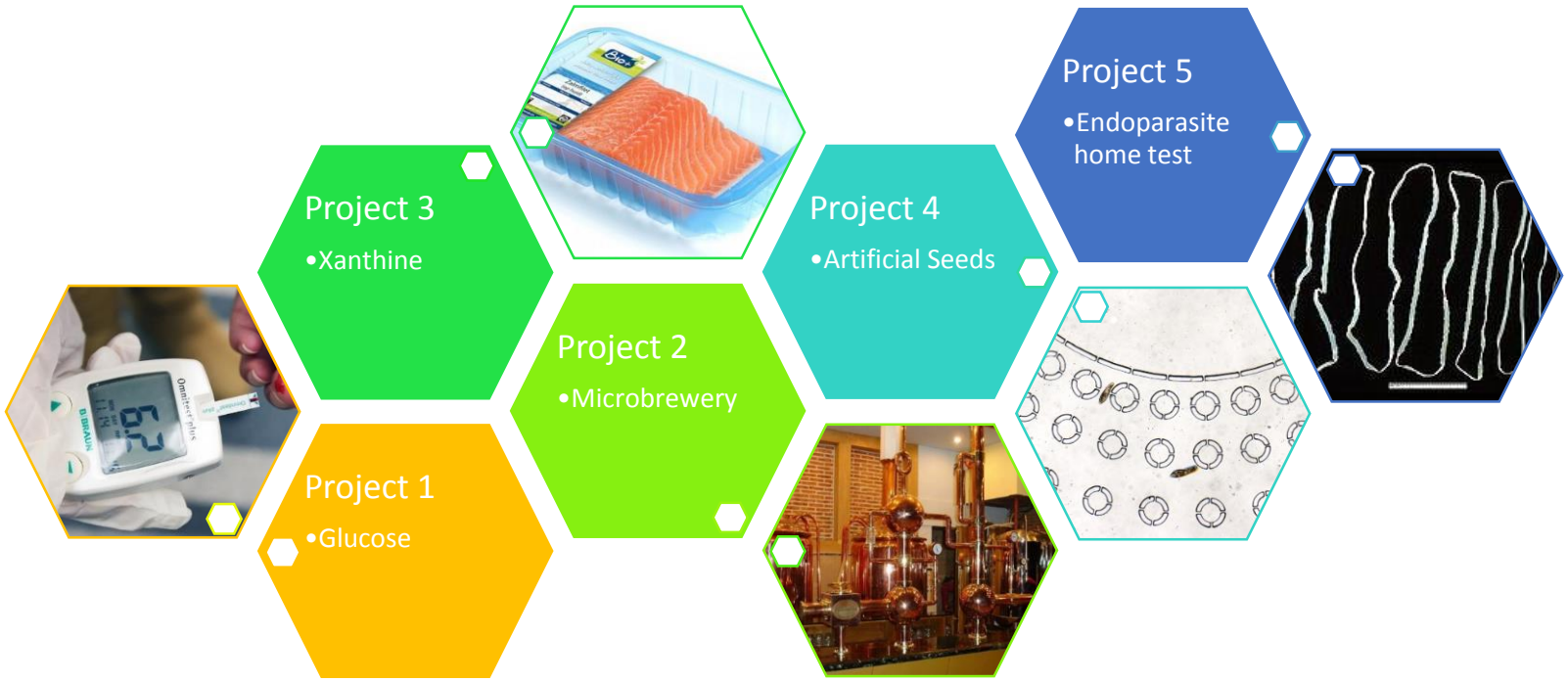
Deliverable is typically a lab journal (or process flow document)

Project organisation

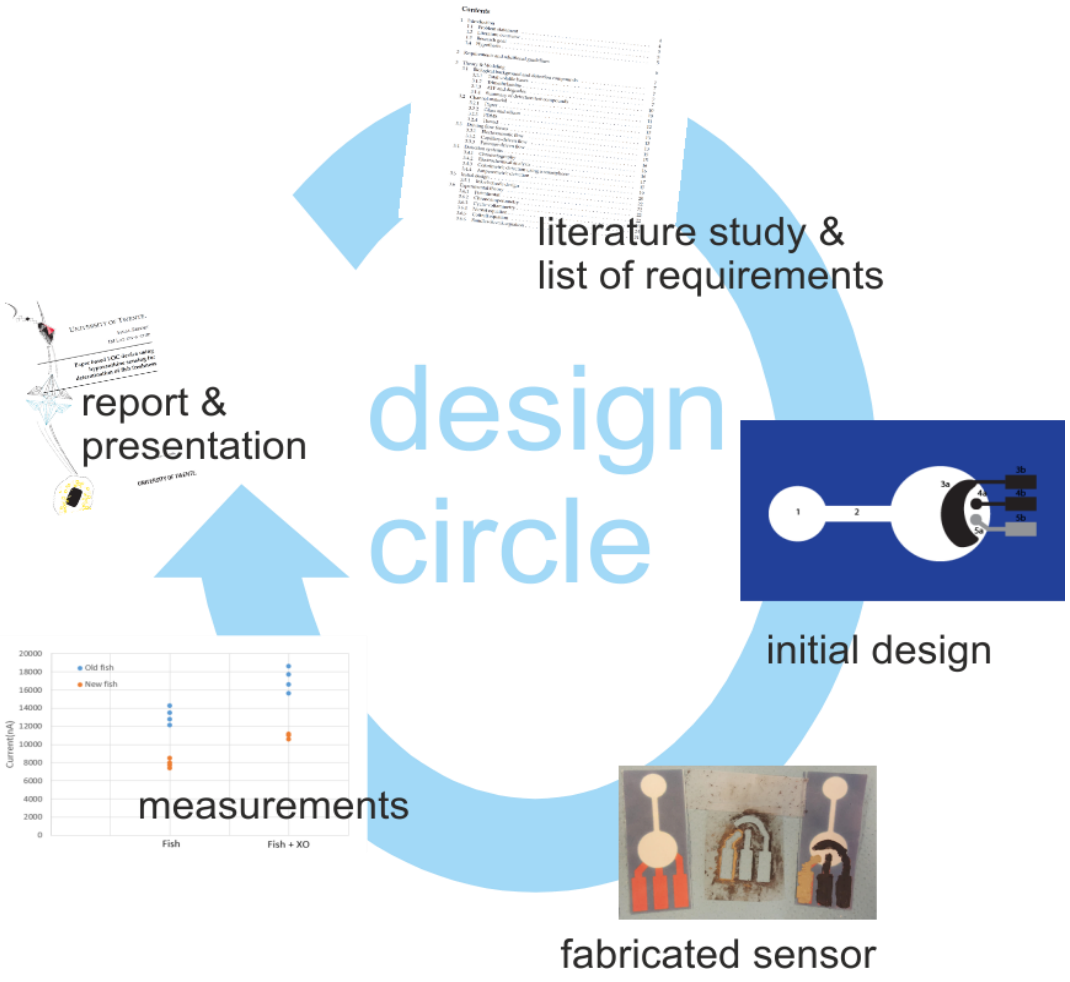
- Teams consist of 4 to 5 students
- We make the teams, based on background, score on the entry-level diagnostic test, ability to properly use Osiris, etc..
- We pitch our projects, teams choose a topic in order of preference
- We decide which team is going to do which project

- Each team gets a daily supervisor (PhD student), and a process supervisor
- Weekly meetings with process supervisor
- Deliverables are:
  - project plan & an individual project plan pitch
  - design and process flow
  - final report & presentation

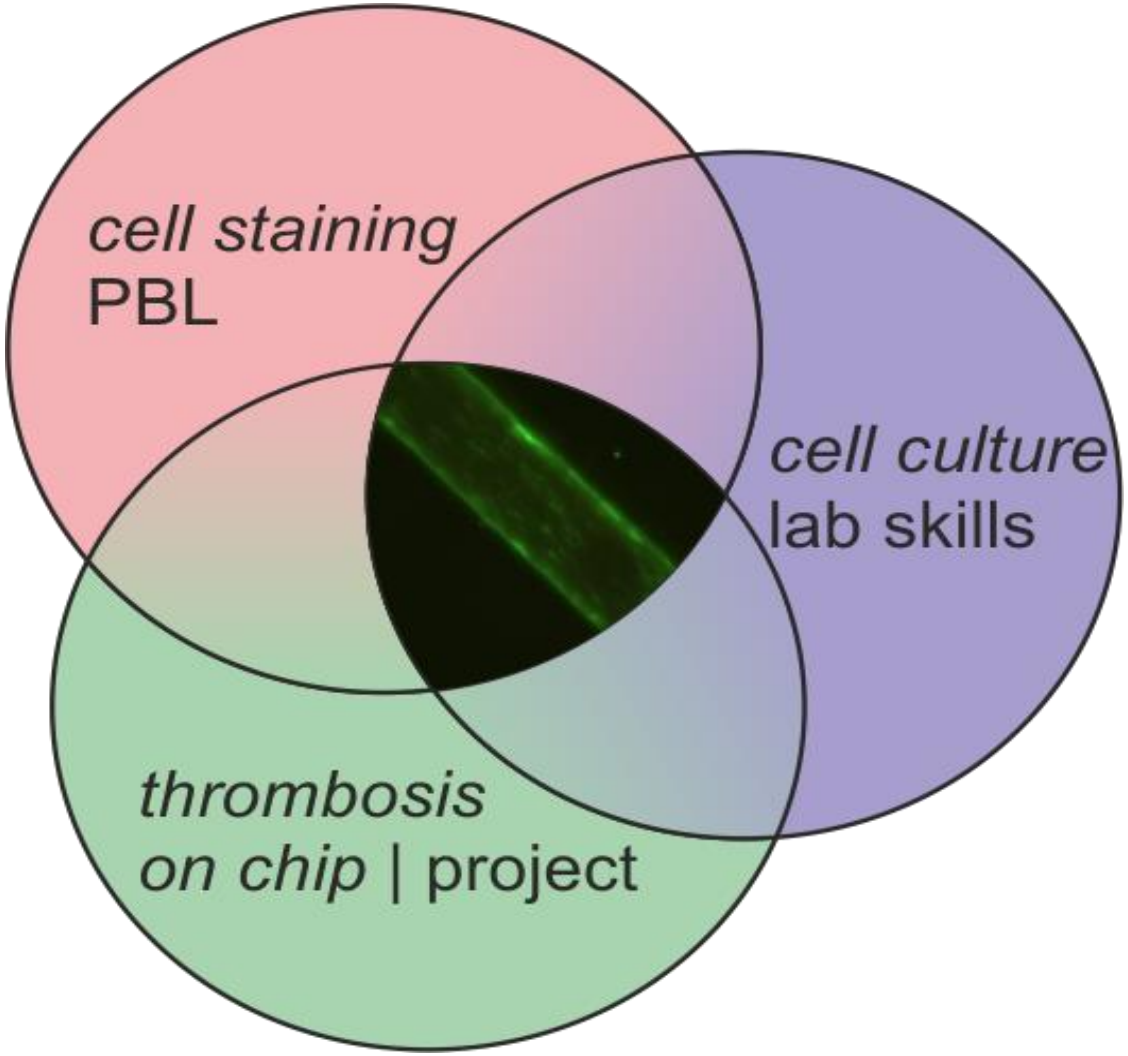
Projects


Project 3
•Xanthine
Project 5
•Endoparasite home test
Project 4
•Artificial Seeds
Project 2
•Microbrewery
Project 1
•Glucose

Full design circle



Synergy in learning formats



Power of repetition

- Example Péclet PBL, mixer assignment and testing, as well as project.

Examples & experiences

Problem-based Learning:

one example

River water – electrochemical sensing

Learning aims:

- understanding electrochemical detection methods: potentiometry, conductometry and amperometry;
- choosing the preferred method for a given situation.

Problem statement

Recently, I overheard this coffee-break discussion (obviously you (and me) want to know the answer to every question asked):

Josh: “Interesting, all these available electrochemical sensors.”
Carol: “Huh? oh, yea, right. Which operational principles are there anyway?”
Josh: “You tell me. Would be great to test river water quality.”
Carol: “Hmm, ok, Mr. Environmentalist, which kind of sensor would you choose then?”
Josh: “Depends on whether the river flows or not.”
Carol: “Ah, yes, rivers tend to flow, true… One principle down, two to go, right?”
Josh: “Not entirely, dear Carol, that depends on whether you want to know specifically what ions are in the river, or just whether the river water is like fresh water or salty.”

(…. *another half page of text*)

Literature:

Hand-out ‘Measurements of chemical quantities (Olthuis)’; (on BlackBoard)
Excerpt of the thesis of M.J.J. van Megen, section 2.1 and 2.2. (on BlackBoard)
http://www.fontyssensorwiki.nl/doku.php?id=theory:electrochemistry:electrochemistry
Background information: A. J. Bard and L. R. Faulkner. Electrochemical Methods: Fundamentals and Applications. Wiley, 2nd edition, 2001.

PBL versus lectures

some observations

PBL

+ active learning
+ student involvement required and (almost) guaranteed
+ creative thinking required
+ (better) prepared for real-life problems
+ soft skills built-in
- student complains (‘ hard work, no complete answers, we want lectures, what do we need to learn?’)
- PBL coaching is hard, requires several (new) skills, can be confronting *(but very rewarding too)*
- PBL doesn’t scale economically with student numbers
- repetitively practicing skills is hardly possible; roof-tiling learning aims helps

Lectures

+ can be motivating, enjoyable
+ easy to cover all learning aims (by the teacher(!))
+ are cheap
- all +’s at PBL with an extra negation

PBL

some additional observations

Writing proper PBL problems is an art:

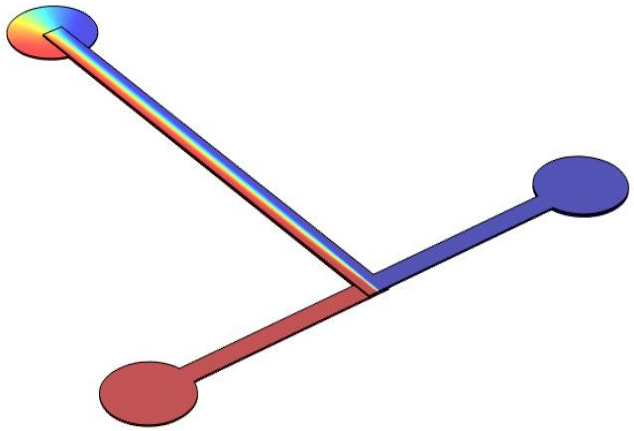
- ill-defined and open, but no riddles
- not too long (and not too short)
- all the learning aims should be targeted

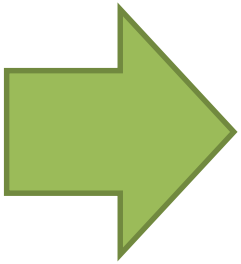
Good, appropriate reading material is essential (also for exam preparation)

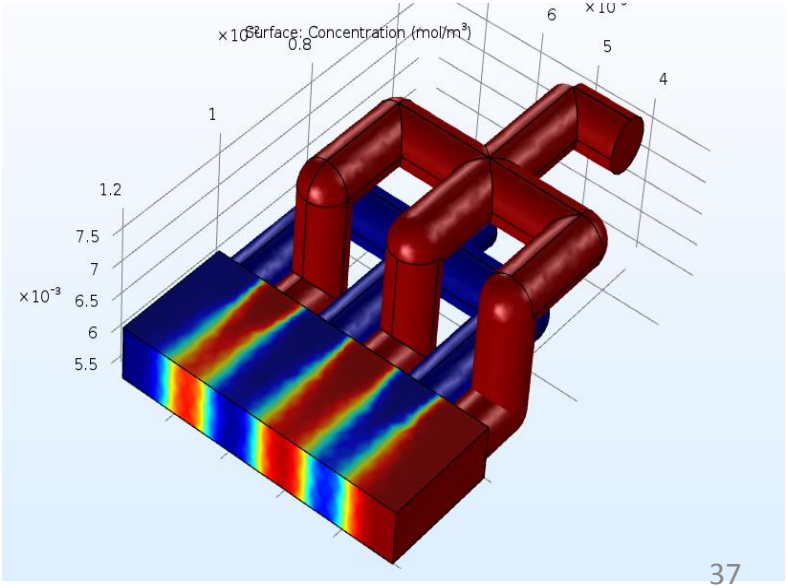
Teachers and SA's must be trained (especially in the art of coaching, observing and asking guiding questions

Skills example: design session

- Goal: design your own mixer that can be fabricated by rapid prototyping

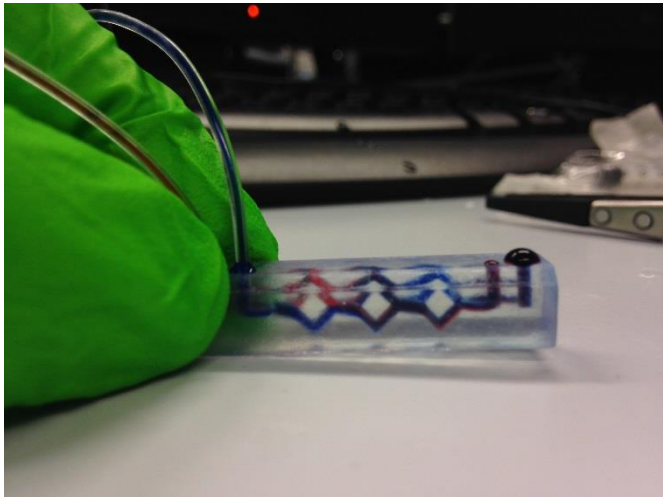


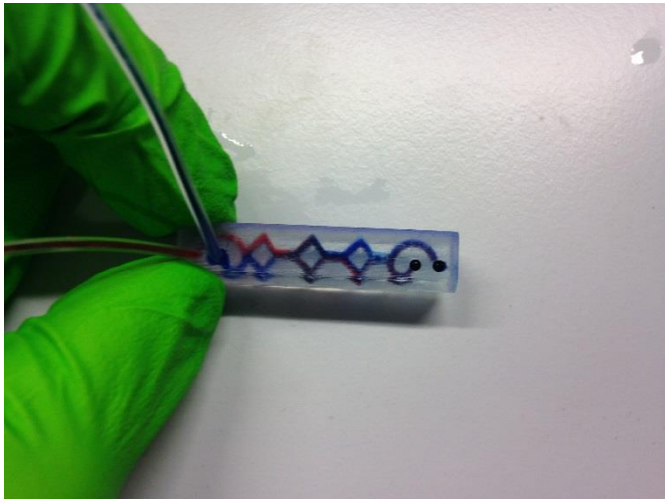




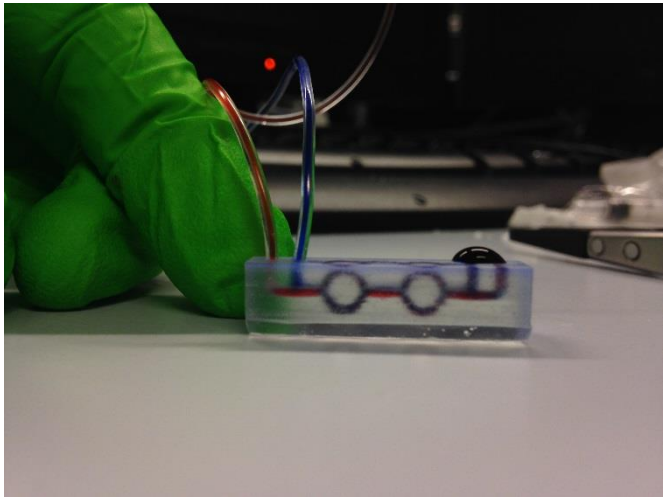
Skills example: Rapid prototyping

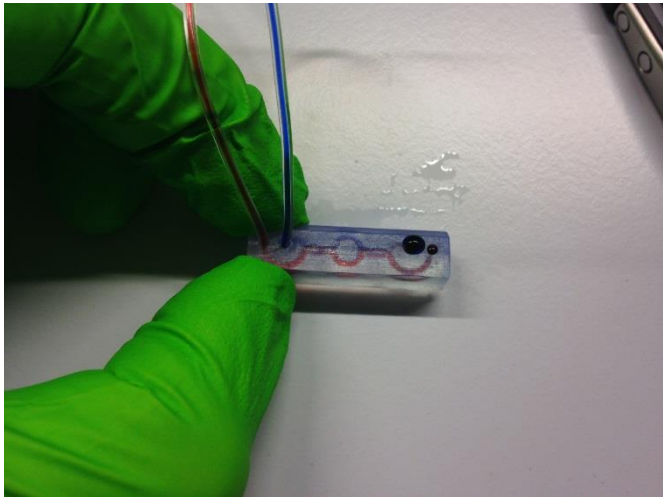
Mixer





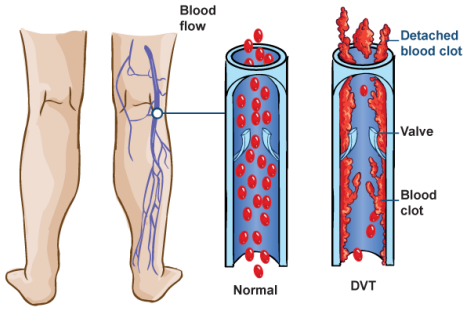
Non-Mixer



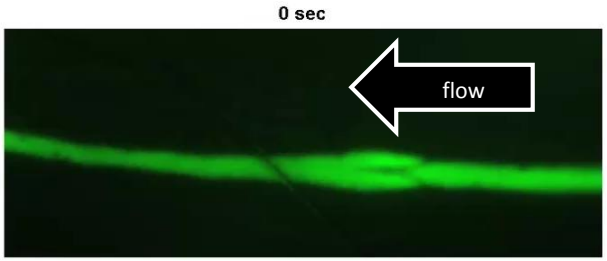


Pictures from: Josh Loessbergh-Zahl and Vasillis Papadimitriou

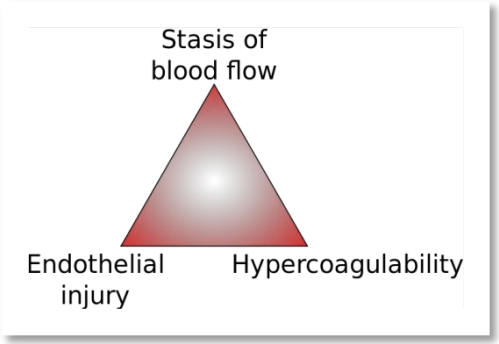
Project example: Organs-on-chips
Deep vein thrombosis



- Clots in the large veins
- 1 in 1000 persons per year
- Mostly in elderly
  - Cost for society in billions and rising
  - Risk of life-threatening pulmonary thrombo-embolism



- Clots form near venous valves
- Virchow's triad of clotting
  - Blood flow pattern
  - Vessel wall
  - Blood clotting factors



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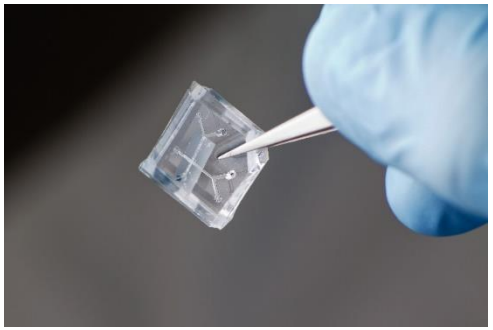
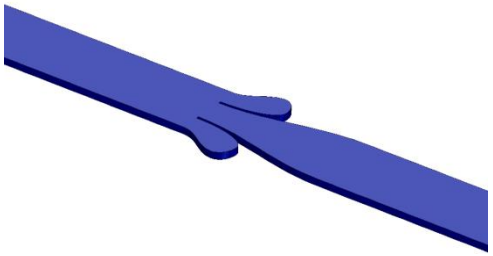




- Living, microfluidic laboratory models of human organs and diseases
- Mimic complex diseases

- Can we realistically mimic deep vein thrombosis in a microfluidic chip?

Assessment

Intended learning outcomes

Intended learning outcomes	Test
The student is able to	
List, explain and apply concepts categorized into six functions: fluid handling, mass transport and reactions, micro-organism handling, sensing, measurement methods and microfabrication	Problem-based learning assignments
Apply lab & fabrication skills (lab skills, prototyping and culturing) and report the process in a lab journal	Lab and fabrications skills
Create a project design with a process flow for lab on a chip device.	Design tools and project design
Develop a project plan: formulate a hypothesis, list of project goals and device specifications. Plan the project schedule and task division.	Project plan
Produce a report with analysis, evaluation, discussion and conclusion on the complete project.	Project report
Present the outcomes of the project.	Project presentation
Explain evaluate and discuss on the project.	Final exam

Assessment plan

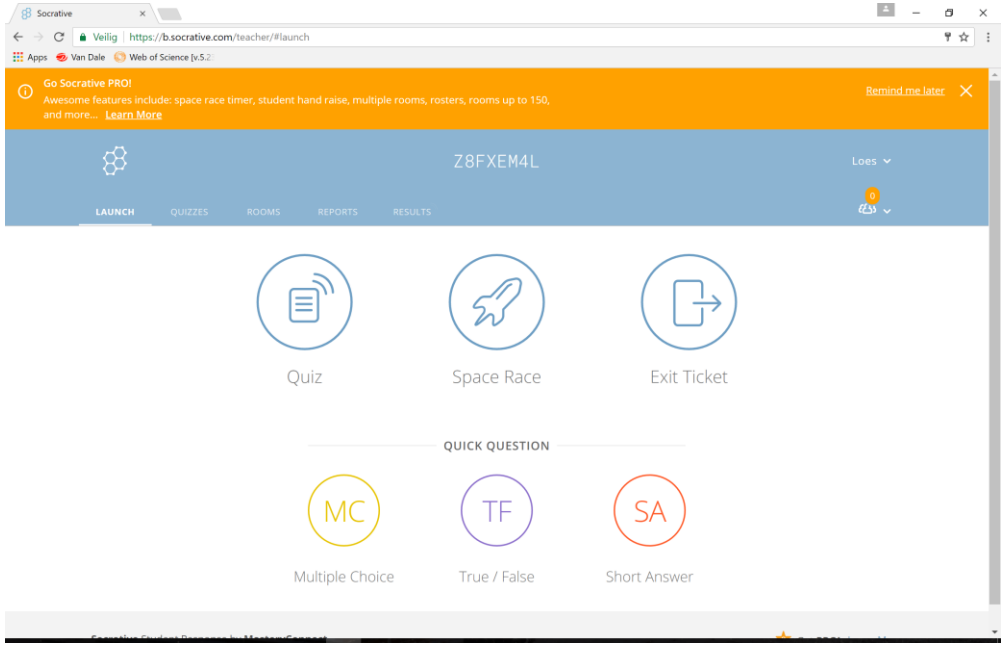
Test		Assessment method		% of total score
Diagnostic test	dT0-dT6	Multiple choice questions, digital	Individual	0%
PBL exercises	P1-P11	Presentation	One randomly chosen person presents, grade is for whole project group	5%
Lab and fabrication skills	e1-e3, p.f.	Lab journal, written digital	Groups of two	5%
Project plan	D1a	Project plan document, written digital	Project group	10%
	D1b	Project plan presentation, oral	Individual	5%
Project design	D2	Project design document (with process flow), written digital	Project group	5%
Project report	D3	Project report, written digital	Project group*	20%
Project presentation	D4	Final project presentation, oral	Project group	10%
Final exam	T1	Open and multiple choice questions, written	Individual*	40%

* minimum mark 5.5 (on a scale from 1.0-10.0)

PBL | 5%

- Presentation
  - Directly at end PBL
  - One presenter randomly chosen

- Diagnostic test
  - Individually
  - End of the week | Socrative



- Form
  - 1 teacher and student assistent

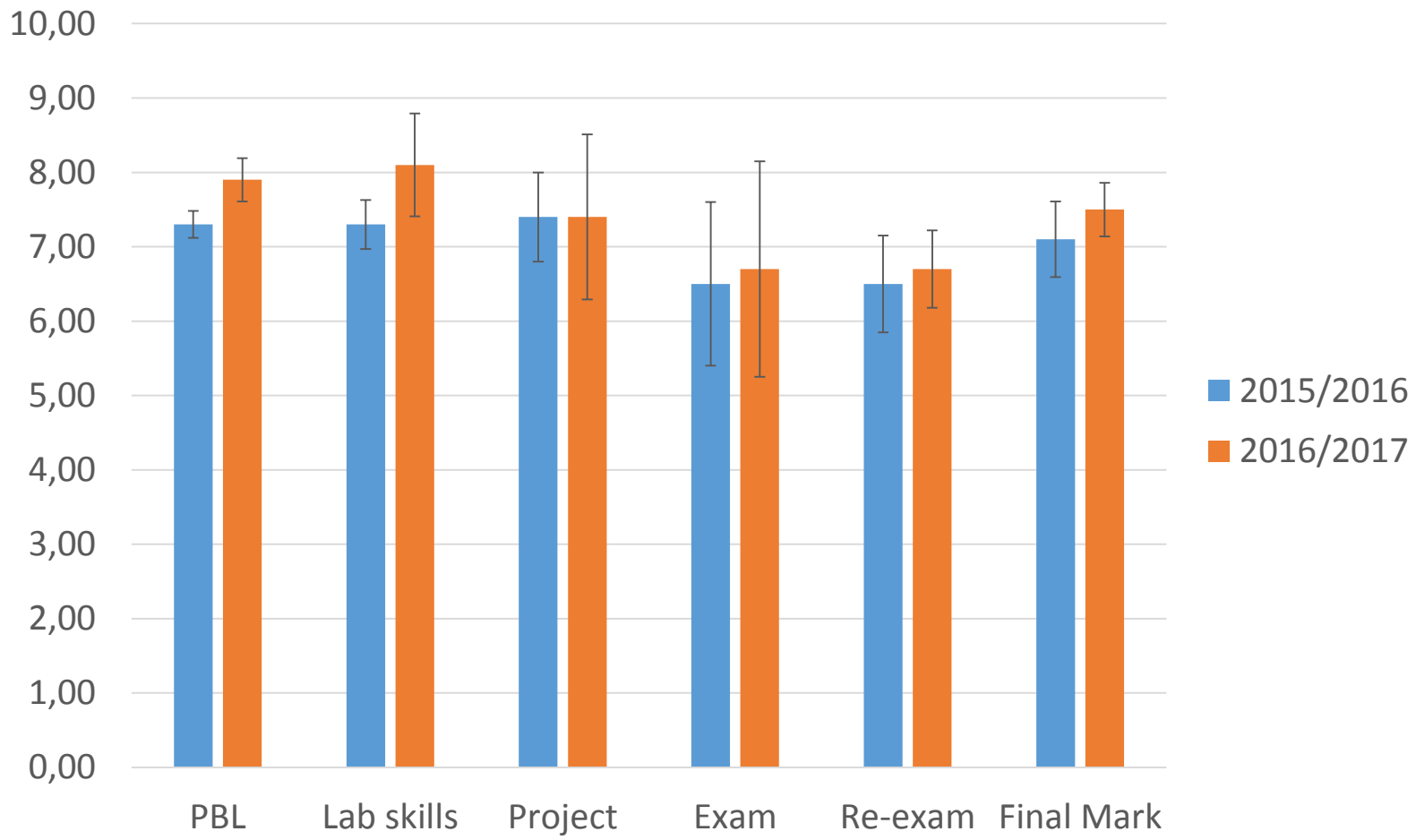
Project | 50%

- Project plan
  - Individual presentation (5%) and document (10%)
- Design (5%)
- Report (20%)
- Group presentation (10%)

Marks

	Educational format	n	average	Standard deviation	# < 5.5	max	min	# elements
2015/2016	PBL	28	7.3	0.18	0	7.7	7.0	11
	Lab skills	28	7.3	0.33	0	7.9	6.8	4
	Project	28	7.4	0.60	0	8.3	6.6	5
	Exam	28	6.5	1.1	5	8.5	4.1	1
	Re-exam	5	6.5	0.65	0	7.2	5.8	1
	Final Mark	28	7.1	0.51	0	8.1	6.2	-
2016/2017	PBL	26	7.9	0.29	0	8.2	7.2	11
	Lab skills	26	8.1	0.69	0	9.0	5.8	4
	Project	26	7.4	1.11	1	8.0	2.1	5
	Exam	25	6.7	1.45	5	8.7	4.0	1
	Re-exam	7	6.7	0.52	0	7.6	6.2	1
	Final Mark	26	7.5	0.36	1	8.1	1.7	-

Marks


10,00
9,00
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0,00
PBL
Lab skills
Project
Exam
Re-exam
Final Mark
2015/2016
2016/2017

Evaluations

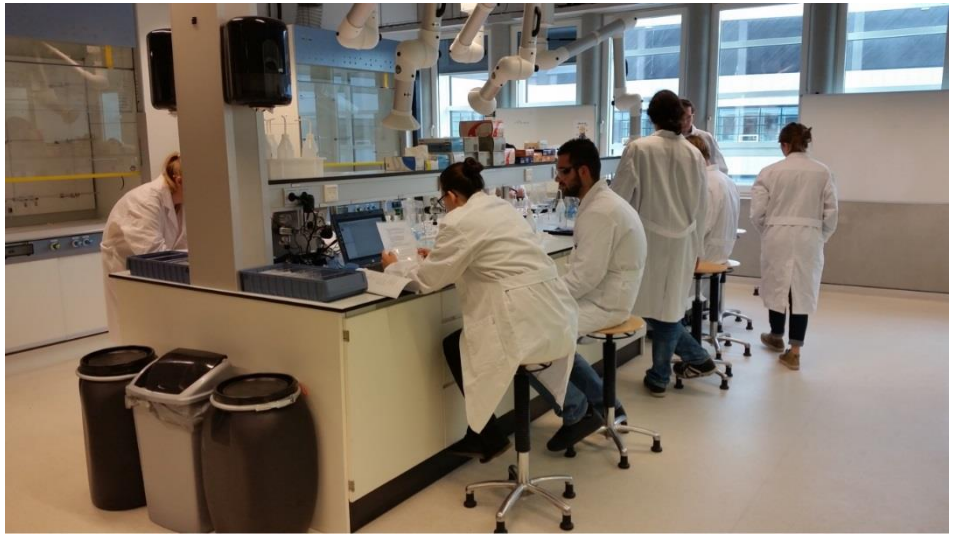
Evaluation

- Feedback during module
  - Students
  - Teaching team
- Feedback after module
  - Students SEQ evaluation
  - Teaching team

Feedback students

- Contact hours
- Get to know the students
- Open for questions/suggestions
- Adjust if possible

- Example is that students were confused in which group they are placed.
  - Solution: table send via blackboard



Feedback teaching team

- Once a week sit together
- Discuss how it is going
  - PBL
  - Skills practical
  - Project
- Adjust if possible

Examples

Example of the minutes from 24-11-2016

- **Lab skills:**
- -(Martijn) Last week's lab skills went quite well, but most of the groups were unprepared which cost them some time in reading the manual on the spot, which results on not finishing on time. Grading of the lab journals will be done the coming week.

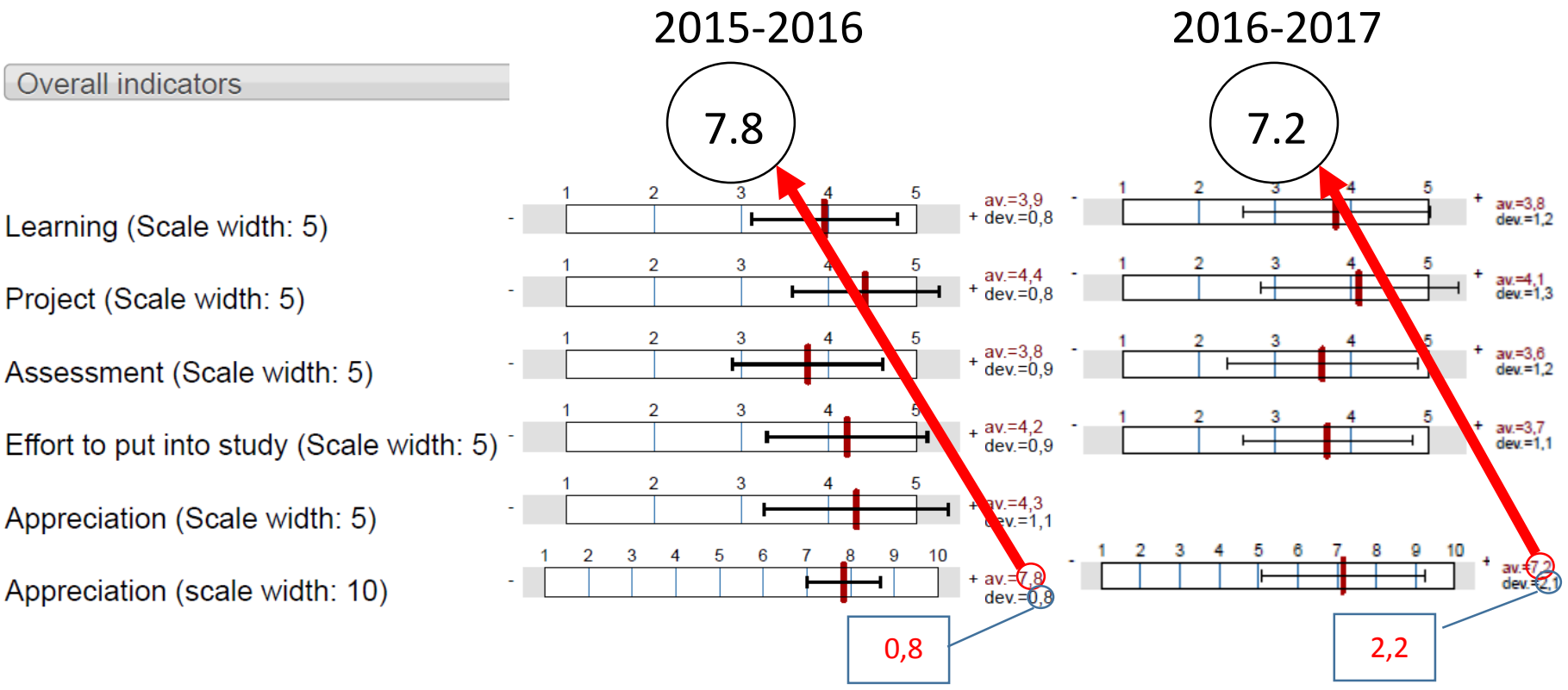
- Action points for next week:
  (**Tutors**) Lab skills tutors can find the schedule on the draaiboek and info about their job on the Lab skills manual (both can be found on BB). For further questions ask Paul.

- **Project:**
- -For all groups the project is in very early stage but everything seems on track.
-
- Action Points:
- (**Jan**) The students should be informed about a peer-review grading of the project.

Examples

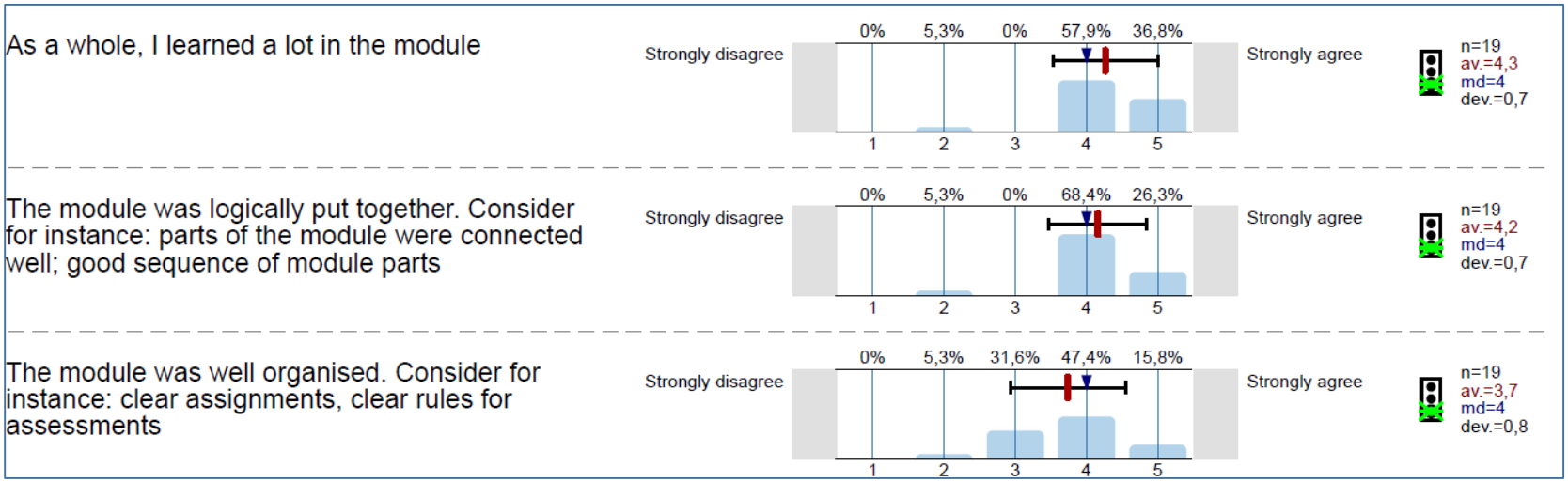
- **PBL:**
- -PBLs are improved compared to last year
- -The students were slightly confused about the general goal of PBL 3- Measurement methods. This may have come from the different nature of the reading material (i.e. absence of a chapter in the tutorial about this PBL).
-
- Action points:
- (**all**) A tutorial document for the whole course should be made.
- (**all**) Unexperienced tutors should not be in the same PBL (for next year).
- (**all**) The training course for PBL should be followed for new tutors (for next year).
- (**all**) The grading criteria for the PBLs should be known to all, and all the filled assessment forms should be placed in the "box" mentioned by Mathieu.
- (**all**) In case that a learning aim is not met by any team, a small "lecture" should be given after the presentations to clear up any misconceptions.
- (**all**) The student names of each team should be written in the assessment forms because students have changed PBL teams and we need to keep track of these changes. The groups on blackboard should be updated with these changes.
- (**Paul**) Paul should be aware of the student changes mentioned above so he gives the correct grade to the students in the excel file.

SEQ Evaluation

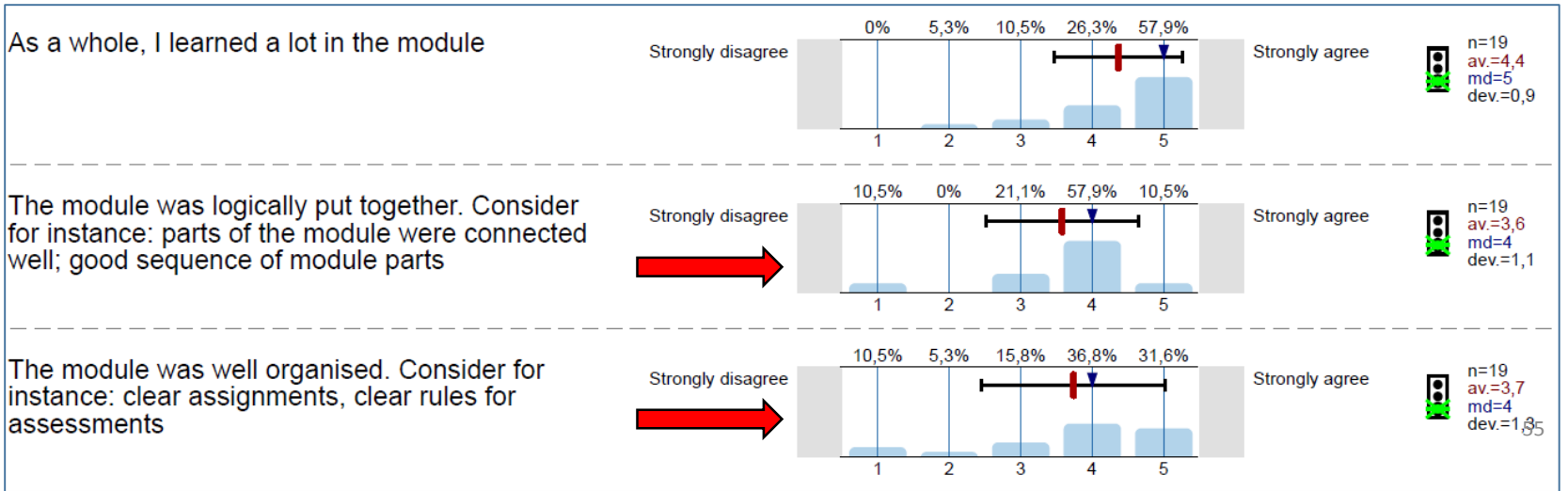


SEQ Evaluation

SEQ results 2015-2016



SEQ results 2016-2017



Improvements 2015-2016

PBL

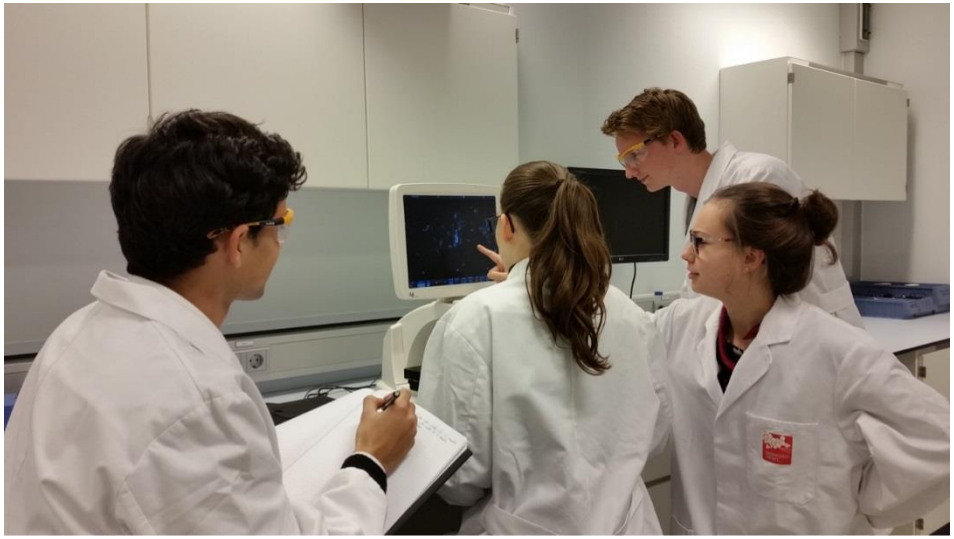
- Adjust 1st four PBLs
  - Especially length and information sources
- Change the order of given PBLs
  - Put “boring” PBLs together with “cool” PBLs
- Everyone should check their learning objectives
  - Adjust them and make them S.M.A.R.T
  - Add objectives to all PBLs
- Learning objectives should match with exam-questions

Improvements 2015-2016

Skills

- Adding assessment criteria
- Implementing spectrophotometry in skills practical
- Let students prepare practical in advance
  - Saves time

- More time for example cells practical
  - Students are slow, since they are new into the topic



Improvements 2015-2016

Project

- Add a weekly meeting with supervisor

- Arrange the SA ‘s on time and instruct them
  - Communication,
  - Reservation of setup
  - Ordering materials

Module 10 LOC 2017-2018

PBL

- Adjust 1st four PBLs
  - Especially length and information sources
- Change the order of given PBLs
  - Put “boring” PBLs together with “cool” PBLs
- Everyone should check their learning objectives
  - Adjust them and make them S.M.A.R.T
  - Add objectives to all PBLs
- Learning objectives should match with exam-questions

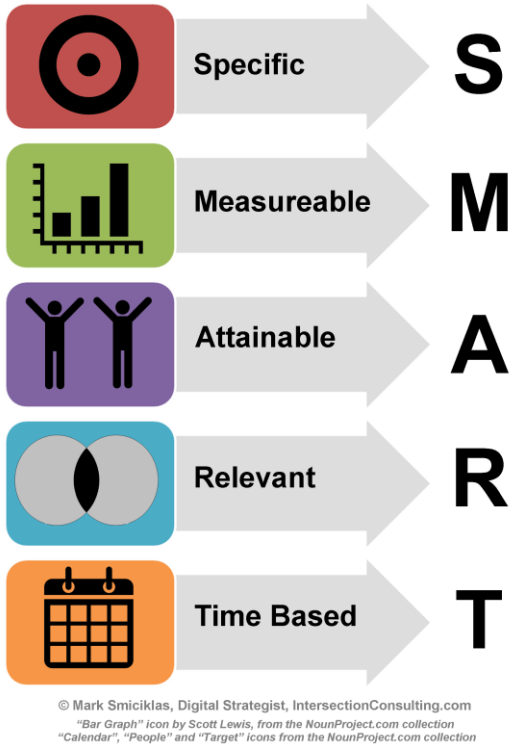
Still too long

Reader made!

Students “stayed”

Students know what to learn

Better fit



Module 10 LOC 2017-2018

Skills

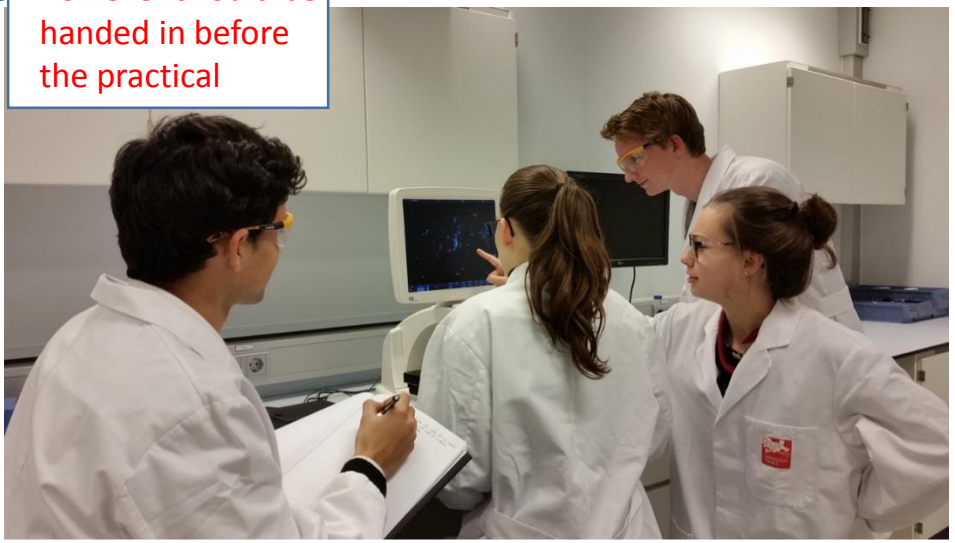
- Adding assessment criteria
- Implementing spectrophotometry in skills practical
- Let students prepare practical in advance
  - Saves time
- More time for example cells practical
  - Students are slow, since they are new into the topic

Writing a labjournal is a criteria

Is done and will replace a part of the general skills

Saved time, however should be handed in before the practical

Students are finished on time



Module 10 LOC 2017-2018

Project

- Add a weekly meeting with supervisor

Students are kept on track.
Supervisors are more involved

- Arrange the SA ‘s on time and instruct them
  - Communication,
  - Reservation of setup
  - Ordering materials

Less chaos
for the SA’s

Went a little better
however still room
for improvement

Questions…?

Questions?