



# Experience Day Regenerative Medicine and Technology



**Maastricht University**





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## Programme

### Preparation

During your first Problem-Based Learning session, you will work on a case.

To be able to discuss this case during the Experience Day, we recommend you to read the case in this information booklet and review the links to the literature sources. Studying these literature sources is called self-study. This is necessary to answer the learning objectives from the pre-discussion of the case.

### Programme groups

Time	Activity
Present at 13:00	Welcome at our Randwijck Campus
13:00-13:10	Informal Get to Know each other
13:10-13:45	Lecture – <i>Can we rebuild a cell's home?</i>
13:45-14:45	Laboratory workshop: Synthesis of Alginate Hydrogel Beads and Analysis of Dye Loading and Release
14:45-14:55	Library Tour
14:55-15:25	Campus Tour Randwijck
15:25-15:40	Demo Problem-Based Learning: preliminary discussion of the case
15:40-16:30	Problem-Based Learning: experience yourself (tutorial group)
16:30-17:00	Q&A with our student ambassadors

### Lecture

In this lecture you will learn about the environment outside of the cell – the extracellular matrix. An extremely important component of cellular behavior. We will take inspiration from the natural environment and try to recreate synthetic versions for tissue engineering.

### Laboratory workshop

During this practical session you will learn how to synthesize an alginate-based hydrogel beads, incl. which properties can be customized to reach a desired hydrogel outcome. The designed experiment combines the hands-on experience of regulating alginate gel fabrication with the use of basic instrumentation techniques to learn about structure-property relationships and associated hydrogel applications.

### Follow-up

A few days after the event, you will receive an email with information about application and student experiences.

## Problem-Based Learning (PBL)

Problem-Based Learning (PBL) offers you a different way of learning from traditional university education. You work in small tutorial groups, engage in hands-on training and attend (far) fewer lectures. Under the supervision of a tutor, you team up with ten to fifteen students to tackle real-life challenges. PBL is an active way of learning that gives you better retention of knowledge, enhances your motivation and encourages you to develop skills that are essential for the labour market in the 21st century.

In PBL you are personally responsible (under supervision, of course) for what you learn. This requires you to play an active role in the learning process.

In short: PBL is all about you, your tutors are very approachable and you learn together in a dynamic way, helping form you into an assertive professional.

### Some advantages

#### *You learn together, in a dynamic way*

Because you work actively on real-life issues, the theory sticks better in your mind and you learn to apply your knowledge to all sorts of questions. The very different backgrounds of your fellow group members not only make for lively discussions, but also mean you gain experience cooperating in culturally diverse teams.

#### *You acquire skills for life*

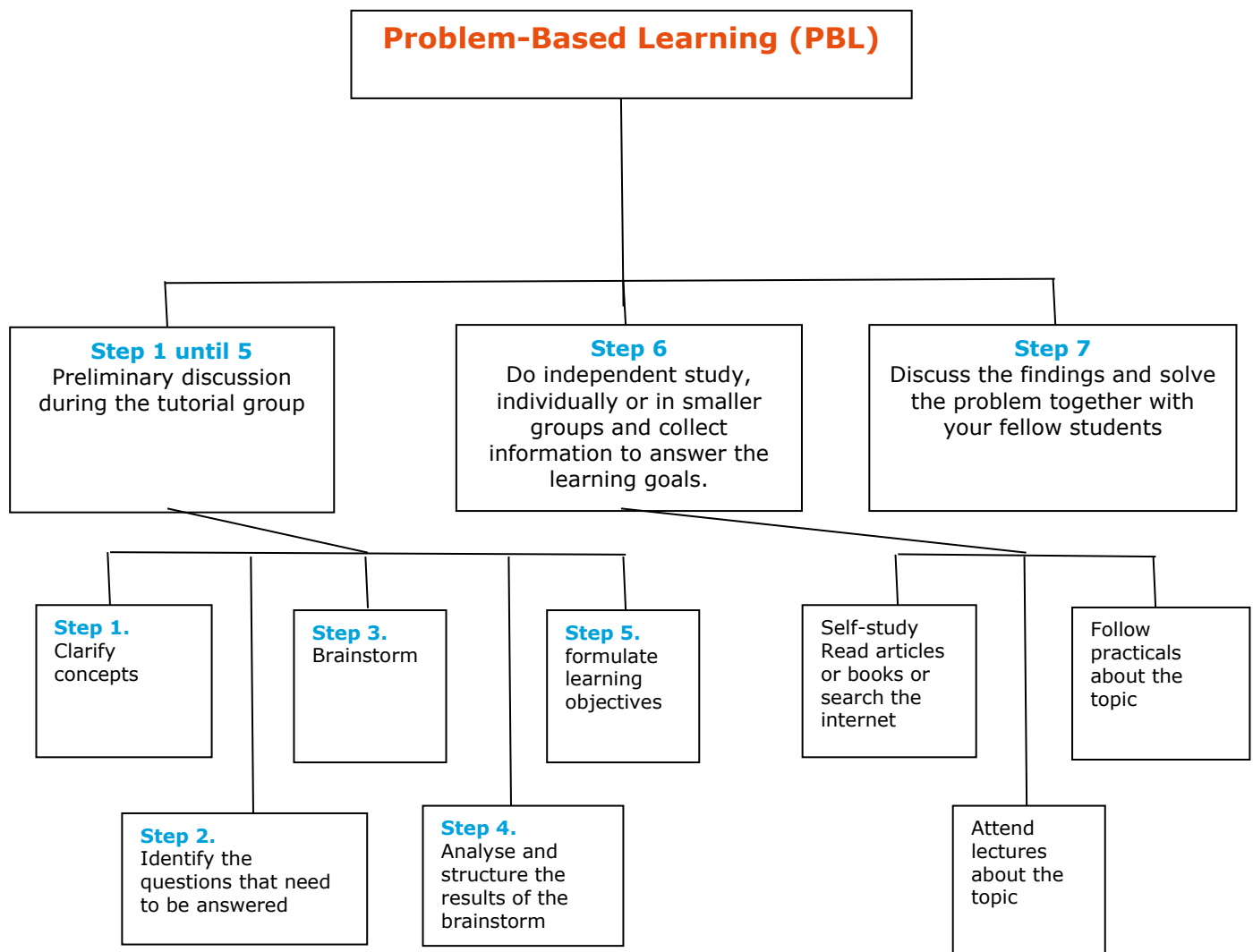
Our graduates serve as the evidence that Problem-Based Learning is effective. They are assertive, independent and professional. They are especially skilled in analysing complex issues, gathering and structuring information, working in international teams, leading discussions, and forming and presenting ideas.



**Source:** YouTube: *Problem-Based Learning at Maastricht University*

## The seven steps of PBL

In its essence, PBL involves seven steps that you follow with your fellow students in a tutorial group. Together with your group, you analyse a case. Often, the problems you analyse are also the subject of important academic research being conducted at Maastricht University. During the preliminary discussion, you formulate learning objectives that you all have to study at your own for the next meeting. You can find more information about the seven steps of PBL at the next pages.





## **Preliminary discussion (step 1 until 5):**

### *1st meeting with tutorial group*

During the preliminary discussion, the group established which knowledge is already present with respect to the task set. In this way, the existing knowledge is activated, providing a starting point for the search for additional knowledge.

### **Step 1. Clarify concepts**

To avoid confusion or misunderstanding, the concepts used in the task set are first clarified. This enables all participants to start from a common starting point.

### **Step 2. Define the problem**

The essence of the task is determined in order to establish the boundaries of the topic.

### **Step 3. Brainstorm**

Refreshing and establishing the knowledge present within the group (activating previous knowledge), followed by a process of providing as many explanations, alternatives and/or hypotheses as possible for the underlying problem.

### **Step 4. Analyse and structure**

Classifying explanations provided in the brainstorming session, indicating their interrelationships.

### **Step 5. Formulate learning objectives**

Determining on the basis of the explanations given what knowledge is still lacking and what has remained unclear. On the basis of this, learning objectives are formulated.



## Self-Study (step 6):

*In your own time*

### Step 6. Self-study

On the basis of specific questions (learning objectives), acquiring knowledge that is understood and can be applied.

- Scheduling: finding regularity and a proper balance between study time and time off, making efficient and effective use of the available time.
- Selecting sources of information: looking for relevant sources of information and selecting the appropriate ones, in terms of quality and quantity, with sufficient depth, for effective studying.
- Studying sources: acquiring new information that one understands and is able to apply in such a way that an answer can be given that is in line with the learning objectives, and the information can be applied, for example to solve the problem set in the task.
- Preparing report: looking back critically at existing knowledge, making links with the preliminary discussion and learning objectives. On the basis of the latter, preparing what must be dealt with in the tutorial group in order to participate efficiently and effectively.

## Discussion and solution (step 7):

### Step 7. Discuss the findings

In a discussion with fellow-students, answer and learning objectives are presented, questions are asked, and unclarities are discussed. After the discussion, each student knows whether the new knowledge has been understood, the subject matters had been studied with sufficient depth, and the subject matter can be explained to others.

## Case: Hydrogel Implant for Myocardium Regeneration

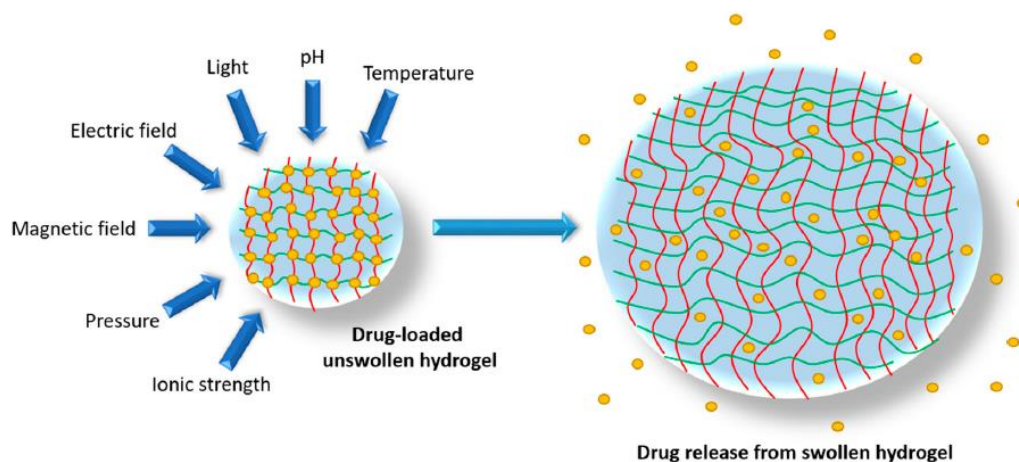
Hydrogels are water-rich materials that are capable of interacting with its surrounding microenvironment and with the possibility to deliver small molecules, growth factors, cells or combination of these into affected tissues or organs.

Myocardium infarction (MI) is a major heart disease which generally affects a portion of tissue leading to the tissue death (termed necrosis), ventricle dilation, and cardiac dysfunction, which can ultimately result in heart failure.

Hydrogel-based therapies have already been introduced for many applications. Some examples include contact lenses, hygiene products and wound dressings. More specifically scientists are now seeking to study how hydrogels can be applied in the context of MI treatments. Could hydrogels also be injectable? Naturally, such innovative ideas also carry many challenges that impede the product from entering the clinic.

Additionally, hydrogel-based therapies must meet specific requirements to be considered an effective treatment. Think about the properties a hydrogel must exhibit (e.g., injectable/solid/mechanical strength/ability to interact with microenvironment/cell viability/swellability etc.), factors that can help mimic the native extracellular matrix (ECM) and boost tissue regeneration of affected organs.

Moreover, the form of administration and stability of such a treatment is also important to determine the positive patient outcome. What other potential future tissue engineering and manufacturing techniques are there and how can we ensure optimal functioning of the device prior to implantation? All of these are essential points a regenerative medicine scientist must consider in designing new therapies.



**Figure 1.** Swelling of a drug delivery hydrogel in response to various chemical and physical stimuli. Red and yellow lines indicate the interwoven matrix structure of a hydrogel, with the yellow dots representing drug molecules. Source: *Pharmaceutics* **2018**, 10, 71.





## Literature sources

<https://www.snexplores.org/article/explainer-what-is-a-hydrogel> (hydrogel simplified explanation)

<https://www.intechopen.com/chapters/51535> (Hydrogel properties, types and applications)

<https://encyclopedia.pub/entry/7864#:~:text=An%20injectable%20hydrogel%20is%20generally,injected%20into%20the%20human%20body.> (injectable hydrogels)

<https://www.mdpi.com/2306-5354/10/2/165/pdf> (hydrogels applications in myocardium infarction)



## Seven Step Approach:

1. Clarify concepts
2. Define the problem(s)
3. Brainstorm
4. Analyse and structure
5. Formulate learning objectives
6. Self-study
7. Discuss the findings

## Laboratory workshop "Synthesis of Alginate Hydrogel Beads and Analysis of Dye Loading and Release"

Polymer chemistry is a vital part of regenerative medicine, where the production of hydrogels is a frequently used approach to mimic the environment of the cells, or to provide tools for grafting, drug delivery, etc. These hydrogels are highly customizable in terms of biodegradability, biocompatibility, and affordability. A classic example of a hydrogel is an alginate-based hydrogel, with alginate being derived from brown algae. Because of its biocompatibility, it has already been used for wound dressing and bioprinting.

Students will learn how to regulate the size of alginate beads by varying dropper diameter. Students produce alginate beads by extrusion dripping of alginate solution (0.5 wt %) into a curing solution of  $\text{CaCl}_2$  (1 wt %) using a plastic pipet and syringes with 16- and 27-gauge needles (Figure 1). Erythrosine B, a red coloring dye, was added to the polymer solution at a concentration of 1 mg/mL for improved visualization and precise determination of the size of alginate beads. When the polymer drop enters the  $\text{CaCl}_2$  solution, positively charged  $\text{Ca}^{2+}$  ions interact with the negatively charged carboxylic groups ( $\text{COO}^-$ ) of alginic acid, resulting in ionic cross-linking of the alginate polymer. Once cross-linked, calcium-cross-linked hydrogels have been proven to have no or minimal deleterious effect on cell viability and proliferation. Students retrieve the alginate beads from the solution via filtration and take a picture of the beads adjacent to a ruler.

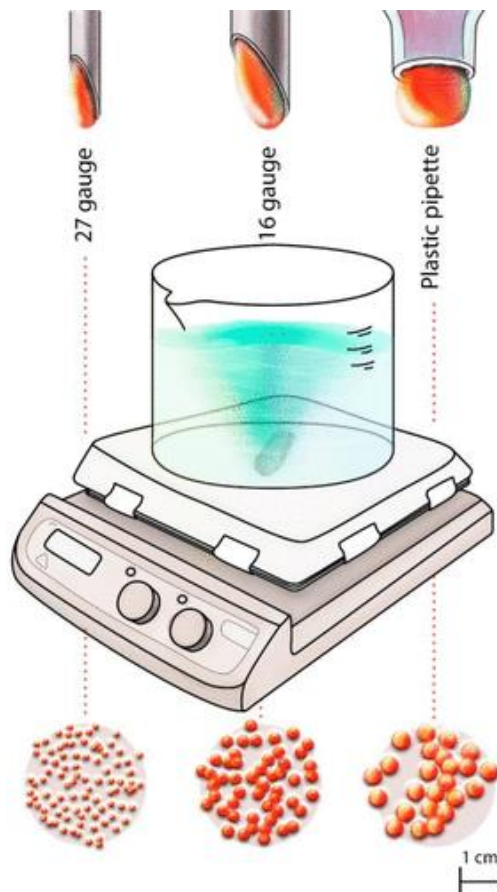


Figure 1. Schematic representation of the alginate bead synthesis using droppers various opening sizes (27- and 16 gauge syringe needles and a pipet tip).

## **Materials**

### **Chemicals**

- Alginic acid sodium salt (Alginate)
- Calcium chloride ( $\text{CaCl}_2$ )
- De-ionized (DI) water
- Erythrosine B

### **Pre-weighed**

- $\text{CaCl}_2$
- Alginate+Erythrosine B
- dH<sub>2</sub>O water for alginate/erythrosine B and  $\text{CaCl}_2$

### **Supplies**

- |                            |                                |
|----------------------------|--------------------------------|
| • Plastic pasteur pipettes | • Rulers                       |
| • Bench pad                | • Beakers                      |
| • Stir bars                | • Spatulas                     |
| • 15 mL falcon tubes       | • Stir plates                  |
|                            | • Petri dishes (glass/plastic) |

### **Per group of students (2 students)**

- 1 stirrer with beaker (250 ml)  $\text{CaCl}_2$
- 1x 15 mL tube alginate solution
- 1-2 pasteur pipette
- Spatulas (for fishing out beads)
- Rulers for measuring the beads

### **Protocol**

1. Pre-made: alginate solution (0.5 wt%) + 0.5 mg/mL Erythrosine B by dissolving 125 mg alginate and 12.5 mg erythrosine B in 25 mL dH<sub>2</sub>O (15 mL tube).
2. Vortex the alginate solution
3. Prepare the  $\text{CaCl}_2$  solution (1 g/100 mL); each group makes 150 mL. After dissolved, keep stirring at low speed
4. Use Pasteur pipette to carefully make drops into the  $\text{CaCl}_2$  solution. For the first experiment, keep the pasteur pipette about 2-3 cm above the  $\text{CaCl}_2$  solution, and create 10-15 beads
5. Wait for 5 minutes to polymerize
6. Take out the spheres with spatula (put in petri dish)
7. Measure bead sizes using a ruler and look at the shape; write down your results
8. Now repeat step 4, but keep the pasteur pipette about 10-15 cm above the  $\text{CaCl}_2$  solution. Create at least 10-15 beads.
9. Wait for 5 minutes to polymerize
10. Take out the spheres with spatula (put in petri dish)
11. Measure bead sizes using a ruler and look at the shape; write down your results
12. Compare results with other groups.