Design guidelines for a virtual synthetic biology lab

Research paper

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Research project SEC (15 EC)

September – December 2015

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Abstract

Many currently developing scientific fields do not end up in secondary school laboratories, for, among others, equipment to perform research in these areas is expensive. Therefore, students are unable to experiment with new fields. One such fields is synthetic biology, in which scientist use elements of genetic information to develop whole new systems. The European Union funded SYNENERGENE project is currently developing a virtual lab to enable upper secondary students to experiment with synthetic biology. However, it is unknown what such virtual labs should look like. This study aims to find design guidelines for a virtual lab promoting conceptual and procedural knowledge on synthetic biology for upper secondary students. To do so, literature on the topic is reviewed, and two biology teacher trainers are interviewed. It becomes clear that among the most important guidelines is authenticity. The lab should focus on real scientific processes, and students should use real world equipment. Additionally, learning aims should be defined clearly, and the abstract and complex nature of synthetic biology should be dealt with using visualisations. When incorporating wishes of teachers, like low energy investment and coverage of curricular aims, the virtual synthetic biology lab has the potential to reconnect the secondary school curriculum with current scientific practice.

One of the biggest challenges in science education is the high turnover rate of new topics, and the often state-of-the-art equipment needed to perform research in these new areas (Waarlo, 2014; Zumbach, Schmitt, Reimann, & Starkloff, 2006). For this reason, new scientific topics like nanotechnology, organic electronics, and exo-meteorology are not readily taught in secondary schools. Lab exercises for these new topics are expensive, for they usually require expansive machinery and involve complicated techniques. As a side effect, experiments carried out in school laboratories are often outdated, with most school laboratory tasks being estimated to be out of date by approximately two decades (National Research Council, 2003). Moreover, these tasks do not promote a representative understanding of current scientific inquiry (Abrahams & Millar, 2008).

An example of a new scientific area of expertise is synthetic biology. Although no consensus has been reached on a definition of synthetic biology, the European Union defined it as: ‘’…the application of science, technology and engineering to facilitate and accelerate the design, manufacture and/or modification of genetic materials in living organisms’’ (SCENIHR, SCCS, & SCHER, 2014). With this, they mean ‘’… the engineering of biology: the synthesis of complex, biologically based (or inspired) systems which display functions that do not exist in nature” (EU High-Level Experts Group). So, synthetic biology is an emerging field that focusses on creating novel biological systems with applications in the areas of health, sustainability, scarcity of resources, and energy security.

In 2013, the 7th Framework Programme of the European Union funded the SYNENERGENE project. The SYNENERGENE project aims to take part in responsible research and innovation, by promoting mutual learning between stakeholders from many fields, including science, industry, civil society, education, and art. This mutual learning is achieved by creating opportunities for open dialogue on the potential benefits and risks associated with synthetic biology and its applications. Given the fact that several of synthetic biology’s applications are considered socio-scientific issues, public participation and empowerment is desired. Next to this open dialogue, the project also develops lesson modules on synthetic biology. The Utrecht University *Freudenthal Institute for Science and Mathematics Education* (FIsme), taking part in the SYNENERGENE project, is currently developing synthetic biology lesson modules intended for secondary school students.

Designing lesson modules about synthetic biology involves several challenges. Since the topic is closely related to molecular genetics, it is considered notoriously difficult for upper secondary students (Tibell & Rundgren, 2010). It involves abstract concepts, invisible phenomena, and reasoning across different organisational levels, all of which increase learning difficulty (Duncan & Reiser, 2007; Marbach-Ad, Rotbain, & Stavy, 2008). With these educational challenges, offering visualisations to students is an important means of promoting learning (Duncan & Reiser, 2007).

One way to visualise scientific concepts is by means of lab exercise. However, due to a lack of readily available and cheap hands-on laboratory kits on synthetic biology, upper secondary school students are unable to experiment with synthetic biology in the school laboratory. It is desirable to find low cost educational activities that offer hands-on and active experiences with the topic (Dymond et al., 2009). In this case, using virtual laboratories in a classroom context might offer a solution. These virtual labs should be used to offer visualisations for upper secondary school students aimed at increasing meaningful learning and conceptual and procedural understanding.

Virtual laboratories are relatively cheap, and when designed congruently, are able to promote student understanding (Rutten, van Joolingen, & van der Veen, 2012; Scalise et al., 2011). However, most research on virtual labs was carried out in a university context, and, therefore, a lack of knowledge exists on design guidelines for virtual labs intended for upper secondary students (Adams et al., 2008; Scalise et al., 2011). When designing a new virtual lab, it would be helpful to learn from prior experiences and gather information on how these virtual labs should look like, as well as what their most common pitfalls are.

The aim of this study is to find design guidelines for a virtual lab offering visualisations for upper secondary students on the subject of synthetic biology, hereby increasing their conceptual and procedural knowledge of the subject. A literature review will be carried out, searching for do's and don'ts when designing virtual labs. This literature review will mainly focus on educational challenges inherent to synthetic biology and on research on effective virtual labs. Subsequently, teacher trainers will be interviewed on the basis of a preliminary design for a virtual synthetic biology lab, aimed at gaining deepened understanding of teacher and student perspective on the virtual synthetic biology lab.

2. Theoretical background

2.1 Synthetic biology

According to the SYNENERGENE website[1], synthetic biology ''… represents the latest phase in the development of biotechnology, in which scientists are gaining unprecedented control in programming new biological functions by rewriting the genetic code. This allows them to 'design' and 'create' micro-organisms that may perform a variety of useful tasks'' (Rerimassie & König, 2013). These micro-organisms are used to produce myriad of useful products like vaccines and bio-plastics. Biotechnology and synthetic biology are two distinct fields, for in biotechnology, researchers usually use only a few traits, where a synthetic biologist is able to use multiple elements and is even able to create elements that have no blueprint in nature (Rerimassie & König, 2013). When designing new

[1] http://www.synenergene.eu/

micro-organisms, many synthetic biologists make use of BioBricks, which are synthetically produced parts of genes available for mail order.

The aforementioned SYNENERGENE project is developing a series of lessons on synthetic biology and the socio-scientific aspects related to its applications, aimed at upper secondary education. The socio-scientific issues associated with these applications lie beyond the scope of this research project, which will mainly focus on promoting conceptual and procedural knowledge by means of virtual labs as effectively as possible.

When dealing with a topic like synthetic biology, both conceptual and procedural knowledge are important. These terms are widely used in cognitive psychology (McCormick, 1997). Conceptual knowledge is *learning science*, including understanding of scientific concepts, whereas procedural knowledge is *learning to do science*, focussed more on learning to design experiments and carry out scientific techniques (Hodson, 1998; Schalk, 2006). Evidently, the method of synthetic biology is what lends this field its identity. To solely focus on one of the two types of knowledge would therefore be inaccurate. Hence, the virtual lab will focus on promoting both conceptual and procedural knowledge of students on the subject of synthetic biology. Using a virtual lab is a suitable method to promote student procedural understanding, which has been found to be more effective than traditional face-to-face labs in promoting practical skills in students (Brinson, 2015; Chien, Tsai, Chen, Chang, & Chen, 2015).

2.2 Educational characteristics of synthetic biology

Teaching synthetic biology, being a relatively new scientific field, poses several educational challenges. It is considered unwise to mix synthetic biology too much with existing practices (Kuldell, 2007). It should be made explicitly clear that common tools like PCR and bacterial transformation are not restricted to synthetic biology, bur are well established and widely used in many biological fields. However, synthetic biology education can be very effective in letting students articulate their own views, making them feel like they are members of the synthetic biology community, and raising the socio-scientific issues associated with the applications of synthetic biology (Kuldell, 2007). One example of a current educational programme on synthetic biology is the iGEM-challenge[2]. The iGEM-challenge is a competition in which students design synthetic biology applications to solve real world problems.

[2] See http://igem.org/Main_Page

Teaching topics that act on cellular and molecular levels always poses challenges for educators (Duncan & Reiser, 2007). With synthetic biology this is no different. Teaching such invisible phenomena using visualisations and hands-on activities is easier than explaining them verbally or describing them in text (Adams et al., 2008). Therefore, using virtual labs as means of visualisation might increase student understanding of the topic.

Given its basis in molecular genetics, synthetic biology acts across many organisational levels. These include the molecular-, the subcellular-, and the cellular level. Many studies have shown that upper secondary students have difficulty understanding the effect of these different organisational levels on each other (e.g: Duncan & Reiser, 2007; Knippels, 2002; Van Mil, Boerwinkel, & Waarlo, 2013; Verhoeff, 2003). Genetic processes inherently work across borders of organisational levels. This *hybrid hierarchical* nature of genetic processes is one of the biggest obstacles for students in understanding the effect of processes of the molecular level on higher organisational levels (Duncan & Reiser, 2007). When teaching about synthetic biology, in which genes and whole genomes are synthesised, these same obstacles are present.

Because it acts across different organisational levels, synthetic biology is a highly abstract field. This further complicates teaching synthetic biology at a supper secondary school level, for students have difficulty understanding abstract concepts (Marbach-Ad, Rotbain, & Stavy, 2008). In the face of these abstract concepts, interactive an hands-on digital visualisations like virtual labs are effective methods to stimulate learning (Smetana & Bell, 2012). These visualisations are especially effective didactic tools for teaching about the molecular structure of genetic elements and displaying individual steps of complex processes (Marbach-Ad, Rotbain, & Stavy, 2008). Virtual labs have great potential to offer such visualisations, and are therefore a valuable tool for educators (Edelson, Gordin, & Pea, 1999).

2.3 Virtual labs

In this paper, the following definition of a virtual lab is used.

> ‘’Virtual laboratories simulate on-screen the experiments that are traditionally performed in real school laboratories as part of biology, chemistry, and other science subjects. They provide opportunities to use virtual materials, equipment, and tools that are designed to replicate those in an actual laboratory.’’ (Scalise et al., 2011).

Next to this simulation of a real world lab, virtual labs also incorporate simulations of real world processes to facilitate learning (Scalise et al., 2011). The ‘’virtual materials’’ that Scalise and colleagues refer to can include simulations and animations. When designing a virtual lab aimed at visualising scientific concepts, using these media might be an effective tool, making visualisations an integral part of the virtual lab.

Using virtual labs as a secondary school teaching tool offers several advantages. They can be used to investigate and visualise emerging technologies in a relatively low cost and low labour fashion (Ahmed & Hasegawa, 2014). Next to this, using virtual labs offers an environmentally friendly alternative to regular experiments because for instance the need for chemicals and laboratory animals is highly reduced (Blake & Scanlon, 2007). Finally, experiments carried out with virtual labs usually take a much shorter time than normal laboratory work (Scalise et al., 2011).

2.4 Learning aims and research question

Regarding these theoretical notions, several learning aims become apparent for the virtual lab. These learning aims are formulated from the point of view of the upper secondary students (age 15 and higher) for whom the lab is intended. After using the virtual synthetic biology lab, students should be able to:

- Explain how DNA or RNA constructs are designed and synthesised during the first steps of the synthetic biology process;
- Explain how these constructs are implemented in organisms;
- Explain how these organisms subsequently start producing the desired product(s);
- Design and carry out a synthetic biology experiment;
- Explain that synthetic biology might also lead to creating entirely new species or molecules without precursors in the natural world.

These learning aims reveal that both conceptual knowledge (learning science) and procedural knowledge (learning to do science) are goals for the virtual lab. Furthermore, it can be inferred that interactive and hands on elements on the synthesis step, the implementation step, and the production step of synthetic biology should be present in the lab.

The research question for this study is: What are design guidelines for a virtual lab promoting conceptual and procedural knowledge on synthetic biology for upper secondary students?

3. Methods

3.1 Approach

With this study, design guidelines for virtual labs supporting conceptual and procedural knowledge in upper secondary students were sought from two sources. To gain insight in possible guidelines, science education literature was analysed. Both design guidelines for virtual labs, and advice on teaching about synthetic biology was sought. Based on this analysis, design guidelines for the synthetic biology virtual lab were listed. Moreover, semi-structured interviews were conducted with two biology teacher trainers. The focus of the interviews was on the teacher and student perspective, and on educational principles related to virtual labs and synthetic biology. In order to guide the expert interviews, a preliminary design of the synthetic biology virtual lab was developed. With data from these interviews, the list of design guidelines extracted from the literature was verified and enriched.

3.2 Literature study

Literature was sought using the Google Scholar database. Search entries contained terms like virtual lab, digital lab, design principle, design guidelines, pitfall, simulation, visualisation, learning effectiveness, and virtual learning environment. Literature from biology as well as other scientific disciplines, like physics and chemistry education, was gathered. Literature on synthetic biology education was sought using keywords like synthetic biology education, synthetic biology school, synthetic biology lab exercises, synthetic biology lessons, synthetic biology course, and synthetic biology high school.

For literature on virtual labs, no specific timeframe was selected. Because this research field is relatively new, all available literature dates from less than twenty years ago. When selecting literature, the titles were read first. Subsequently, the abstract of the selected titles was analysed. With this step, studies were excluded which used virtual labs as *tools* to test non-related subjects. This process led to a selection of studies with virtual labs being the focal point. Subsequently, the references from these studies were checked to look for more articles.

3.3 Interviews

To guide the interviews, a preliminary design of a possible problem situation for the virtual lab was developed (appendix 1, translated from Dutch). It revolves around using bacteriophages to remove antibiotic resistant bacteria, and using modified bacteria to treat infected burns. This design was informed by guidelines found in science education literature.

During the first phases of the design process of virtual learning tools, the opinion of experts with experience in education, science, and technology is desired (Huang, 2005). Therefore, the preliminary design was discussed with a biology education expert involved in the SYNENERGENE project. Next to this, an educational simulation expert gave his input on the theoretical background of the preliminary design. Input from both discussions provided feedback during the development of the preliminary design. During the discussion with the synthetic biology expert, ideas for possible problem situations for the synthetic biology lab were discussed, and a second, more difficult problem situation was added to the preliminary design, as an application of the initial exemplary situation. The educational simulations expert provided an overview of virtual lab – and simulation literature, to ensure the quality of the theoretical background.

To get more in-depth data on the design guidelines for virtual labs, the adjusted preliminary design was discussed with experts in teacher education. Individual face to face interviews were conducted with two biology teacher trainers, one from Utrecht University, and one from the University of Amsterdam. Both were male, one has over 20 years of teaching experience, while the other has taught for 9 years. Interviews lasted around 40 minutes, and were audio taped for data analysis. Topics that needed to be covered during the interview were listed beforehand. These topics were chosen with the guidelines found in literature, and the student and teacher perspectives in mind. The order of the topics was flexible, leaving room for the interviewee to elaborate on points of interest, thus making full use of the advantages of semi-structured interviews (Denscombe, 2003). The interview protocol, translated from Dutch, can be found in appendix 2. It was developed with input from several peers and researchers, and was peer-tested before actual interviews took place.

3.4 Data analysis

All interviews were audiotaped and transcribed verbatim, omitting vocalised pauses and non-lexical sounds like *um, mm-hm,* and *eeh*. The constant comparative method was used to find a thorough list of guidelines for the virtual lab. With this method, several cycles of reading and re-reading the data provide possible guidelines, which are compared with the data during subsequent reading sessions, to verify whether the list covers all the data (Kolb, 2012). After three of these cycles, the resulting guidelines were categorised. This method ultimately led to a sound list of guidelines for virtual labs.

4. Results

4.1 Literature study

When searching the literature databases, 13 articles, ranging from 1999 to 2015, were found that primarily revolved around virtual labs. These articles are summarised in appendix 3, showing scientific discipline, participants, data collection, and corresponding guidelines for virtual labs found in the specific article. Additionally, several guidelines come from articles on biology education and synthetic biology education in particular (Duncan & Reiser, 2007; Kuldell, 2007). The following guidelines could be extracted from the literature.

- Keep in mind the **prior knowledge** of the user
- Use as many **real world objects** as possible
- Focus on **authenticity** (let the lab react realistically to extreme values and make the user feel like belonging to the synthetic biology community)
- Specify the **learning aims** as much as possible
- Offer **scaffolding** and supporting animations or simulations on every occasion
- Do not **overload** the users **working memory** (keep the cognitive load as low as possible)
- Let the lab or embedded simulations create **cognitive dissonance**
- Offer possibilities for **collaboration** with peers
- Focus on both **conceptual and procedural knowledge**
- Apply assessment and **self-evaluation**
- Do not **gloss over its novelty**, many tools used during synthetic biology did exist already.
- Students at upper secondary level have difficulty with switching between different **organisational levels**
- Synthetic biology is **highly abstract**, which is challenging for upper secondary students
- **Invisible phenomena** like synthetic biology are difficult for students to visualise

4.2 Interviews

Data gathered from both teacher trainer interviews were categorised using the constant comparative method. Teacher trainers were anonymised using the codes 2710 and 0511. During the interviews, both teacher trainers most extensively discussed the topics ‘’authenticity’’ and ‘’concepts and curriculum’’, spending the biggest part of the interview time on these categories.

4.2.1 Authenticity

Both teacher trainers stressed the importance of the lab being as authentic as possible. The lab should display how the underlying processes really work. This includes both biological concepts like proteins being unfinished before folding, and laboratory techniques like PCR. In explaining these elements, aspects like duration of processes in real life should be made clear. The lab should also incorporate or display a myriad different lab equipment, ranging from the workbench, pipettes, and petri dishes, to advanced machinery like vortexes and incubators. With all these authentic elements, teachers want students to develop a rich and realistic image of the role of biology in society, both in the present and in the future.

Another main point mentioned by both teacher trainers was the possibility of making mistakes. For the lab exercise, this means including alternative routes, having possibilities of contamination of experiments, and even ending up with different end products. Different combinations of BioBricks should lead to different cellular responses. These different paths students are able to follow might result in a discussion of socio-scientific issues (SSIs) related to the lab: ''In an ideal case, [the superfluous BioBricks] must code for an organism that does something completely different from what is desired. That way, you directly have an SSI.'' – 2710. Both teacher trainers thought SSIs should be present in the lab.

The exercises should not follow step-by-step recipes. One teacher trainer suggested using a protocol which is malformed, for instance due to a laboratory colleague spilling some hydrogen peroxide on the protocol, rendering several parts unreadable. This way, students make use of a lab protocol, which is an authentic practice for lab personnel, but still need to think for themselves. The virtual lab could also include some trial and error experiments, for these also occur in real labs.

4.2.2 Concepts and curriculum

According to both teacher trainers, synthetic biology is a complex topic for secondary school students. It involves many difficult concepts, demanding high levels of prior knowledge. For this reason, both teacher trainers thought the lab should be aimed at 5 or 6 vwo (Dutch pre-university education, age 16-18). A possible source for topics that need to be covered before students are able to understand synthetic biology is a cahier written by *Stichting biowetenschappen en maatschappij*[3] (in Dutch, Foundation for life sciences and society).

[3] See http://www.biomaatschappij.nl/product/synthetische-biologie/

When dealing with such complex topics, the interviewees stressed the importance of using student language instead of jargon as much as possible. Next to this, the amount of complex figures is to be kept at a minimum. To ensure students do understand the language and figures used in the lab, a pilot study with several students was recommended by one of the teacher trainers.

The teacher trainers suggest that, for teachers, it is essential that the learning aims of the lab cover a sufficient amount of the curriculum requirements. They advise to link concepts from the lab to curricular aims as much as possible, hereby increasing the time efficiency of the lab exercise.

> ‘’How many lessons does the lab exercise take? Is that congruent with the coverage of the curriculum requirements? You can easily make this into a half-year task, but is that balanced? The time investment of the lab should be realistic, that is important.’’ – 2710.

They also suggest that when extracurricular elements are introduced, they should never be the main point of interest, and they could be supplied as background information. ‘’And if it is not a required curriculum element, do you want to include it as a learning aim? Because then it will be redundant for a student.’’ – 0511.

When providing students with background information, offer it internally, within the lab-environment, rather than externally, somewhere outside the lab-programme, for one teacher trainer thinks that teachers want the students to be kept in the lab-environment as much as possible. The teacher trainers also desire the lab to switch between micro- and macro scale, to explain difficult concepts using animations and visualisations. However, they suggest not delving unnecessarily deep into the content, and refrain from bringing in too many elements from chemistry and physics.

4.2.3 Learning aims and educational principles

One teacher trainer kept stressing that the learning aims of the lab dictate its structure. Together with these learning aims, the educational principles chosen by the designer are guiding the design. Do the students take part in discovery learning? Do they use the lab as application of previously studied topics? Using the lab as an intro to a series of lessons on synthetic biology asks for a different structure then when the lab is used as after several synthetic biology lessons. Defining what the lab’s learning aims are is as important as choosing what concepts to exclude from the lab.

4.2.4 Problem situation

Using a modified version of the iGEM challenge was found applicable by the teacher trainer who knew what the iGEM entails. He thought designing a genome to solve a particularly tough problem is a suitable situation in which students can use synthetic biology. Furthermore, he recommended a problem situation based on the meticillin resistant *Staphylococcus aureus* (MRSA) bacterium. This bacterium mainly infects hospitalised patients across the world, and is difficult to treat due to it resisting antibiotics of the penicillin family.

The teacher trainer suggested a game during which students need to gather small pieces of information, using synthetic biology to restore the susceptibility of MRSA strains to antibiotics. Teams of students might come up with different solutions, increasing authenticity and fortifying the game-element of the lab. According to the teacher trainer, students should be role playing as real synthetic biologists. When using this problem situation, it might be important to remember that students do not understand names of specific genes and are to be helped realise what meaning should be attributed to several representations used in the lab.

4.2.5 Student behaviour and motivation

According to one teacher trainer, students should be kept in the lab-programme as much as possible. As mentioned before, this includes offering background information internally. Furthermore, students should be working independently, in teams, asking questions to the teacher. The teacher trainers think teachers want students who think positively about biology, who enjoy performing the tasks at hand, and would like to choose a biology associated career. The lab must be designed so it motivates students. To manage this, gamification can be used. One such method is incorporating a reward system in the lab.

4.2.6 Teacher support

Both teacher trainers stated that teachers need a training before they will use the lab in their lessons. They want the lab to be as instrumental as possible, meaning they want to be able to use it the moment they receive it. This can be achieved by providing them with a hand-out, an efficient teacher manual, and the aforementioned work shop on how the lab works.

4.2.7 Technical details

Both teacher trainers thought teachers needed the lab to cost as little extra energy and effort as possible. One of the teacher trainers has experience with IT. He suggested that the lab should be technologically independent. According to him, this includes the lab being programmed in html5 script, thus taking place in an in-browser environment. He majorly stressed not using flash coding, for this invokes many well-known problems for teachers, including expired software versions, and not having the license to install necessary plug-ins. He also mentioned that students should be able to save their progress, hereby enabling the lab exercise to take place during separate lessons. It is also desirable that the lab automatically generates a log-file showing the teacher what the students did during the lesson.

4.3 Synthesis

Ultimately, combining results from the literature review and the expert interviews, a list of general and specific design guidelines for the virtual synthetic biology lab can be made (table 1).

Table 1 | Design guidelines for the virtual synthetic biology lab, gathered from literature review and expert interviews.

Literature guidelines	**Interview guidelines**
Keep in mind the **prior knowledge** of the user	Demand of prior knowledge for the lab is high, aim at 5 or 6vwo (Dutch pre-university education, age 16-18)
Use as many **real world objects** as possible	Many real molecular biology techniques should be used during the lab exercises, using a big spread of lab equipment
Focus on **authenticity** (let the lab react realistically to extreme values and make the user feel like belonging to the synthetic biology community)	Authentic practices, and authentic situations should be used as often as possible, students should act as members of the synthetic biology community, display how processes really work, let students develop a realistic image of biology, possibility of making mistakes and choosing alternative routes are important
Specify the **learning aims** as much as possible	Learning aims and educational principles should be defined clearly before designing the lab. Learning aims should cover extensive parts of the curriculum, keep the amount of extra-curricular elements at a bare minimum
Offer **scaffolding** and supporting animations or simulations on every occasion	Offering background information is desired, making use of simulations or animations
Do not **overload** the users **working memory** (keep the cognitive load as low as possible)	Use student language and refrain from using jargon, do not rely heavily on difficult figures, but following a recipe as exercise is considered ineffective
Let the lab or embedded simulations create **cognitive dissonance**	N/a
Offer possibilities for **collaboration** with peers	The programme itself does not have to include a platform for communication, however, the iGEM-challenge, in which students work in teams, was considered effective and applicable

Focus on both **conceptual and procedural knowledge**	Cover many concepts from the curriculum and explain lab techniques accordingly
Apply assessment and **self-evaluation**	Trial and error is an authentic and suitable method of learning for experiments
Do not **gloss over synthetic biology's novelty**, many tools used during synthetic biology did exist already.	N/a
Students at upper secondary level have difficulty with switching between different **organisational levels**	Visualise switching between different organisational levels, use animations and simulations if necessary
Synthetic biology is **highly abstract**, which is challenging for upper secondary students	Visualisations should be clear and simple, keep in mind how concepts are represented visually in the lab, and what these representations might mean to students
Invisible phenomena like synthetic biology are difficult for students to visualise	Using animations is important, always visualising invisible elements and showing students what is really happening

Guidelines covered by literature do not include what teachers want from virtual labs. According to the teacher trainers, this includes curriculum coverage, effective time and energy investments, technical details like user friendliness, and making use of universal coding so the lab becomes platform-independent.

5. Conclusion and discussion

5.1 Findings

The aim of this study was finding design guidelines for a virtual lab promoting conceptual and procedural knowledge on synthetic biology for upper secondary students. Table 1 lists the guidelines found in literature, and the added refinements from two teacher trainer interviews. One of the main findings of this study was that both literature and teacher trainers stress the importance of virtual labs being as authentic as possible. This includes letting students feel they are real synthetic biologists, using many real world objects and lab equipment, and incorporating alternative routes in the lab.

Educational challenges associated with teaching synthetic biology are caused by the abstract nature of the topic. This can be assigned to synthetic biology processes operating in many different organisational levels, like the cellular and the molecular levels. When teaching such abstract topics, visualisations seem to be important. Teacher trainers suggest switching between these different levels using animations, constantly informing students what they are actually looking at.

The lab should connect with curricular aims as much as possible. However, with synthetic biology being a relatively new scientific field, some of its main concepts, including sticky ends, are not covered by the current curriculum. When considering which elements to include in the lab, it might be important to add several extracurricular concepts. In doing so, the virtual lab has the potential to expand the current curriculum, which most likely is outdated by several years (National Research Council, 2003). Hereby, the lab can act as an important mediator between current scientific practice and the curriculum, which is greatly desired (Van Mil, 2007).

According to both literature and teacher trainers, defining learning aims and positioning of the lab in the surrounding programme is important. With this comes the choice of what learning principles are to be used in the lab. A discovery learning lab looks different from a lab which is mainly aiming for repeating important concepts from prior lessons. Defining the aim of the lab and its underlying principles is important during the following steps of the design process.

This study made clear that a focus on both conceptual and procedural knowledge transfer is desired by both teacher trainers. Students should be learning concepts related to the curriculum, but they should also develop their laboratory skills and become active participants with standard biology techniques used in real scientific environments. This availability of state-of-the-art techniques is one of the biggest advantages of virtual labs over more traditional school laboratories, which should therefore be used to the fullest.

5.2 Implications and further research

When teaching with hands-on methods, like using virtual labs, it is important to consider whether students are still actively learning. In other words, how to make sure that hands-on does not mean minds-off (Roychoudhury, 1994)? For virtual labs, it should be made clear that activities promote student understanding of the topic, and learning aims of the lab are realised. Both teacher trainers as well as literature stress the importance of activities being meaningful instead of relying on step-by-step recipes. The learning effect of lab exercises should be one of the main points of interest in the aforementioned pilot study.

This concern relates closely to Hodson’s (2003) division of *learning science, learning to do science* and *learning about science* . The third element of this ideology, *learning about science,* is not included as main aim of this study. When considering teaching with virtual labs, it is important to assess the effect virtual labs have on *learning about science*. There is evidence that just taking part in scientific practice is not enough to increase student understanding of the scientific process (Bell, Blair, Crawford, & Lederman, 2003). This must be kept in mind during following developmental phases of the virtual lab.

Both teacher trainers stress synthetic biology is too complex for 4vwo (Dutch pre-university education, age 15). They suggest designing the lab for students in 5 or even 6vwo. However, most schools teach the topic DNA and cells most extensively in 4vwo. This might result in students at 4vwo level having a better understanding of genetics than their older peers, because the topic has more recently been discussed. Further research is needed to confirm which years this synthetic biology lab needs to be aimed at.

5.3 Reflection on method and final remarks

Regarding this conclusion, several things need to be kept in mind. To increase the validity of this study, a bigger and more diverse set of teacher trainers should be interviewed. Only two Dutch, male teacher trainers were interviewed. Adding non-Dutch and female teacher trainers' opinions on the virtual lab might increase its usability and effectiveness by giving a more complete picture. Reliability issues can be taken care of by letting other researchers perform data-analysis, seeing whether they end up with the same guidelines.

Subsequently, teachers and students themselves might also introduce new elements and guidelines which need to be incorporated in the lab. Following steps in the design process should definitely include pilot-testing the lab with a group of students. This was made clear by one of the teacher trainers as well as literature. This pilot study should focus on clearness of the lab exercise, language use, structuring of the lab, and applicability of the problem situation, among others. Additionally, the following stages of developing the lab should be carried out in collaboration with IT experts (Huang, 2005).

This study was performed on a relatively small scale. However, its results will influence the design process of the SYNENERGENE virtual synthetic biology lab. Moreover, other projects might also be able to use several general guidelines from this study. Given the fact that a big part of the studied literature comes from different scientific disciplines, results of this study might be applicable in fields outside biology education.

When designing virtual labs, many different elements should be taken into account. However, the medium offers a big range of possibilities and advantages, which other educational means do not cover. With the guidelines found during this study, designing virtual labs will potentially be more effective, resulting in valuable tools for educators across many different disciplines. Hereby, students will be able to experiment with state-of-the-art science topics like synthetic biology, hopefully leading to increased understanding and renewed interest in these specific fields.

Acknowledgements

First of all, Christine Knippels is thanked for the amount of energy she was always willing to invest in the project. Even though she was constantly busy, she was very involved with the project, which was really supportive. Next, both interviewees, and experts Dirk Jan Boerwinkel and Nico Rutten are thanked for their participation in this study. Arthur Bakker is also thanked for his input and his dedication to the project. Manon ten Asbroek is thanked for being a constant factor of support and a reliable discussion partner. The students at the research project sessions are thanked for their constructive feedback, and Linda Mulder is thanked for volunteering for the pilot interview. Lastly, Liesbeth de Bakker is thanked for opting to be second corrector.

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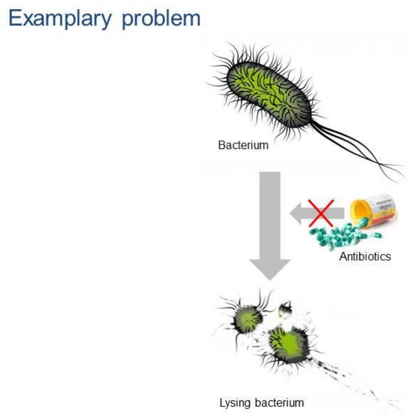
Appendix 1 Problem situation discussed during interviews (translated from Dutch)

1



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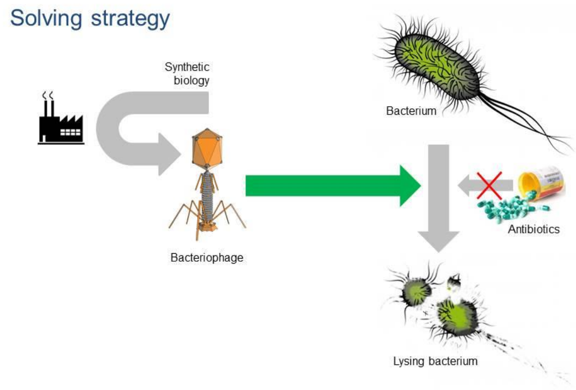

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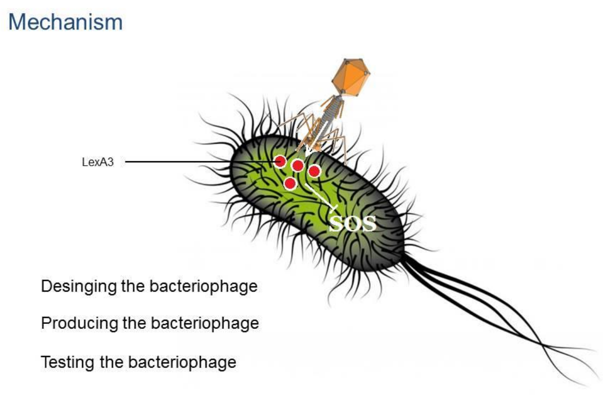

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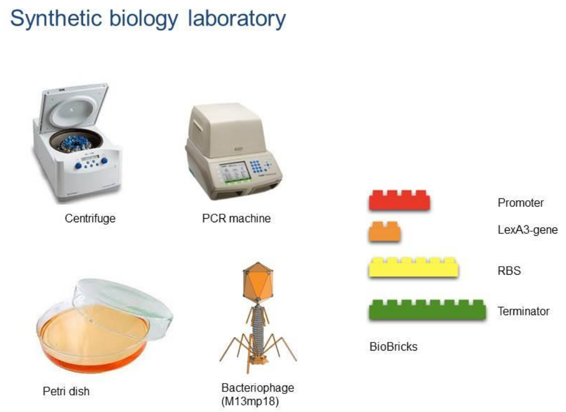

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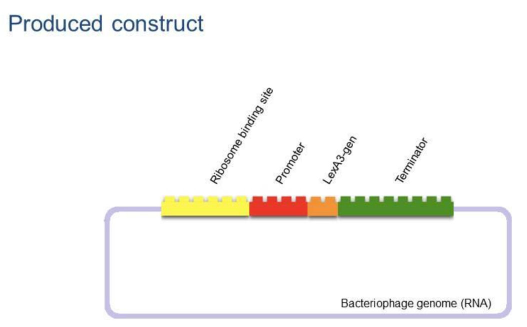
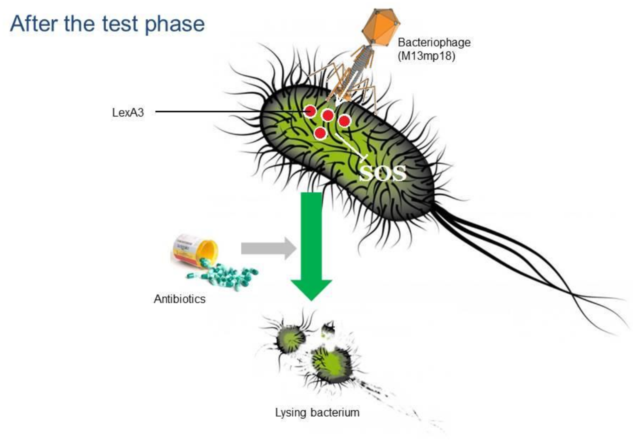
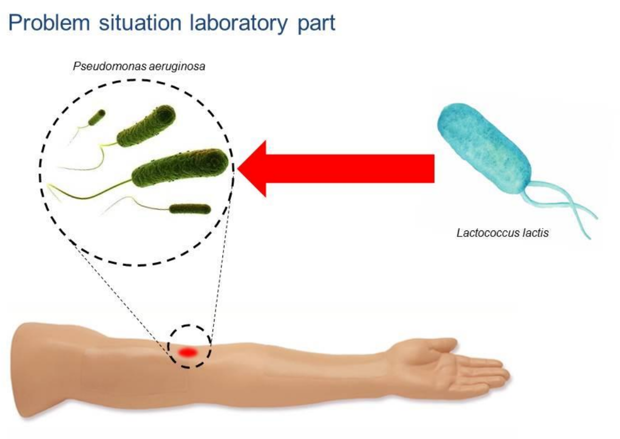

Produced construct
Ribosome binding site
Promoter
LexA3-gen
Terminator
Bacteriophage genome (RNA)

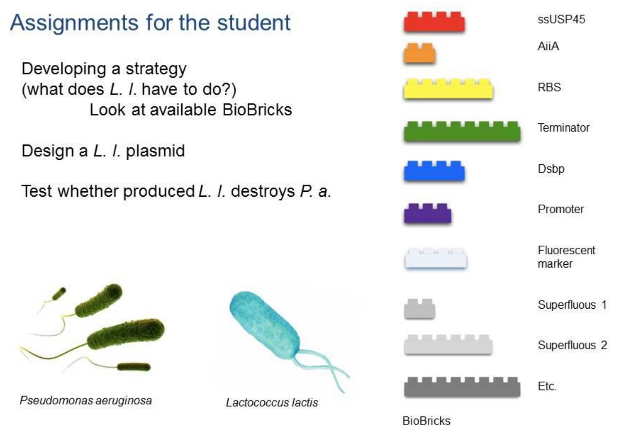
6


After the test phase
Bacteriophage
(M13mp18)
LexA3
SOS
Antibiotics
Lysing bacterium

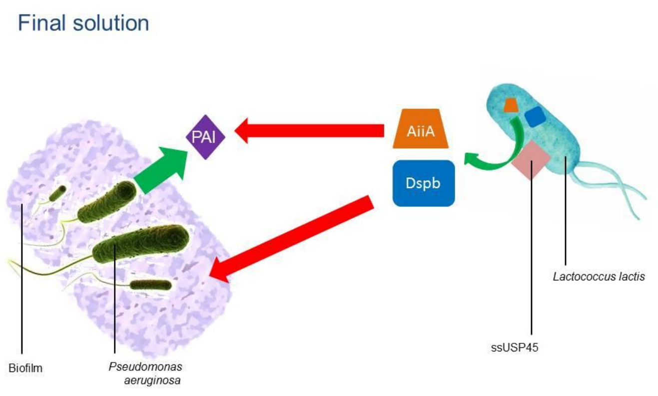
7


Problem situation laboratory part
Pseudomonas aeruginosa
Lactococcus lactis

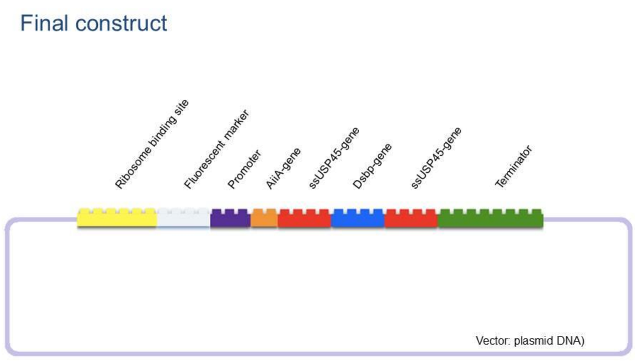
8


Assignments for the student
Developing a strategy
(what does L. l. have to do?)
Look at available BioBricks
Design a L. l. plasmid
Test whether produced L. l. destroys P. a.
Pseudomonas aeruginosa
Lactococcus lactis
ssUSP45
AiiA
RBS
Terminator
Dsbp
Promoter
Fluorescent marker
Superfluous 1
Superfluous 2
Etc.
BioBricks

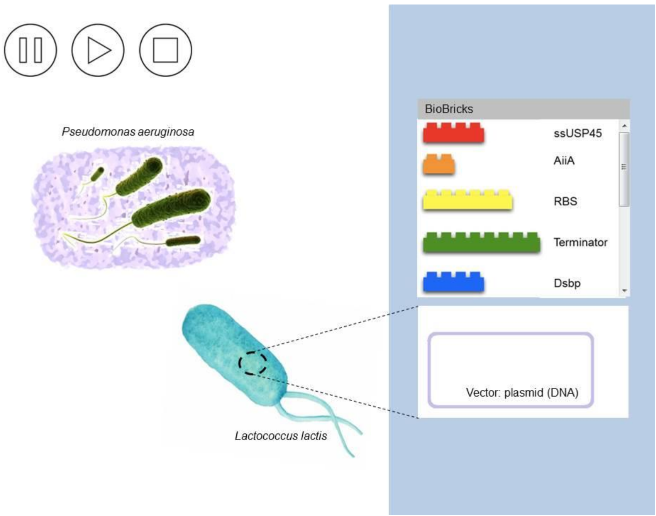
9


Final solution
PAI
AiiA
Dspb
Lactococcus lactis
ssUSP45
Biofilm
Pseudomonas aeruginosa

10


Final construct
Ribosome binding site
Fluorescent marker
Promoter
AiiA-gene
ssUSP45-gene
Dsbp-gene
ssUSP45-gene
Terminator
Vector: plasmid DNA)

11



12

Explanation to LactoAid iGEM project (Groningen)

Problem
Burn marks are often infected with Pseudomonas aeruginosa (P. a.) and Staphylococcus aureus. In this explanation we focus on Pseudomonas. Treatment is difficult and often includes using antibiotics, which can trigger resistance.

Aimed solution
Introduce benign bacteria into the compress which are able to recognise and inhibit P. a. so the immune system can cope with the infection more easily.

Information on Pseudomonas
P. a. produces signal compounds (auto-inducers, PAI, in P. a. also called AHL) which the bacterium uses to communicate with other individuals, so it can react to the bacterium density (quorum sensing). When disabling this system, P. a. growth can be stopped. Additionally, P. a.-like bacteria form biofilms, structures that hinder our immune system in dealing with the bacteria. By inhibiting biofilm production, P. a. growth can be stopped via a second way.

Bacterium choice for solution
Lactococcus lactis has been proven to be harmless, it creates lactic acid, which inhibits infections itself, can be freeze dried which simplifies production and integration with the compress, and it does not form spores. This bacterium can be used as a 'chassis' to incorporate new constructs via plasmids.

Systems to be built in Lactococcus
Gene that inhibits biofilm production and hereby inhibits P. a. growth
Gene for enzyme (AiiA) which destroys signal molecule P. a. (AHL) and hereby inhibits P. a. growth
Additionally needed: gene for helping molecules which transports these molecules across the Lactobacillus membrane, to be coupled to preceding genes, because normally both these products are not excreted.
Promoter which reacts to availability of P. a. so the compounds are produced only when the pathogen is present. For this, it is needed that P. a.-specific compound (PAI) is recognised and bound (by receptor LasR), and that the product induces the promoter.
A fluorescent marker, to be placed behind the promoter, which measures whether the promoter is active. This marker can also be used to check whether compounds are indeed transported across the membrane.
In a construct are always also a ribosome binding site (RBS) and two terminators.

Construct will be;
Promoter (pLas I) inducible by compound from P. a. + ribosome binding site (RBS) + gene for fluorescent marker + gene for supporting compound (ssUSP45) coupled to gene for anti-biofilm molecule (Dspb) + gene for supporting compound (ssUSP45 again) coupled to gene for enzyme which destroys signal molecule P. a. (AiiA) + double terminator.

(Boerwinkel, 2015)

Appendix 2 Interview protocol (translated from Dutch)

Main question: What are design guidelines for a virtual lab promoting learning of conceptual and procedural knowledge on synthetic biology for upper secondary students?

Aim of interview: With this interview, I hope to gather your opinion on how virtual labs should look like when they are aimed to promote conceptual and procedural knowledge building in upper secondary school students.

Associated institution: The *Freudenthal-Institute for science and mathematics education*, taking part in the EU *Synenergene*-project.

Type of questions: First, four closed questions on your teaching experiences, subsequently we discuss a virtual lab context and you may comment freely.

Audio recording: The audio file will stay within the Freudenthal Institute, the data will be handled anonymously.

Length of the interview: The interview will take approximately one hour.

Regulations: Do you agree with me using the data from this interview for my research project?

Interview questions

Part 1	Background information

1. How long have you been a teacher?
2. Which levels did you teach most?
3. Where does your biological expertise lie?
4. On which themes did you give a lot of practical assessments, or did you develop practical assessments?

Part 2	The context	free association, please feel free to comment at will!

Synthetic biology

During my research project, synthetic biology will be defined as the design of new biological systems, without precursor in nature.

Digital lab

Digital labs are virtual environments in which students are able to experiment with certain subjects. It provides space for interaction, but also utilises animations, simulations, etc.

Key subjects

- Available prior knowledge
- Placement of background information / animations / simulations
- Where are visualisations needed?
- How thorough do biological concepts need to be explained? (repeating/new; final requirements (Dutch *''eindtermen''*); sticky ends, synthesis step, etc.)
- What part of the subject matter must be provided, how much does the student have to think of himself?
- Is this context interesting for upper secondary school students? Why? Which other contexts are possible?
- Does the order of the lab make sense / is it suitable / is it effective?
- What do teachers want from a virtual lab?
- Where does the lab connect with the curriculum?
- Where do students need support in switching between organisational levels?
- What are pitfalls for this virtual lab?

Part 3	Final remarks

5. Do you have any final remarks on the interview?
6. Do you wish to say anything on the research project?

Appendix 3 Table s1

Table s1 | Articles studied for the literature study on guidelines for virtual labs, displaying author(s), year, scientific discipline, participants and data collection details, and reported guidelines for virtual labs.

Author(s) and year	**Discipline**	**Participants and data collection**	**Guidelines for virtual lab**
Adams et al., 2008	Physics, chemistry, physical science	200+ student interviews	Real world objects and contexts stimulate learning, real world objects reduce cognitive load, place focus on learning aims, animations or simulations are effective scaffolding tools, virtual labs are effective in creating cognitive dissonance
Blake & Scanlon, 2007	Physics, biology	Studies of three simulations, 160 students in total	Keep virtual lab simple
Brinson, 2015	All scientific disciplines	Review of 56 articles on traditional versus non-traditional lab exercises	Virtual labs are effective in showing techniques and research process
Chien, Tsai, Chen, Chang, & Chen, 2015	Chemistry	1 lab, 50 secondary school students	Virtual labs are effective in showing techniques and research process
Edelson, Gordin, & Pea, 1999	Geoscience	Four generations of simulation software	Use a context that connects with prior knowledge
Finkelstein et al., 2005	Physics	1 lab, 363 university students	Virtual labs cause less distraction than traditional face-to-face labs
Huang, 2005	Medicine	Experience gained from the ‘’Virtual Labs project’’	Real world contexts give incentive for learning, display learning aims, use ICT scaffolding tools

Marbach-Ad, Rothbain, & Stavy, 2008	Biology	1 computer animation (interactive), 248 secondary school students	Simulations are effective in explaining processes with multiple steps
Mickell & Danner, 2007	Biology	38 university students, traditional versus non-traditional lab exercises	Students prefer virtual labs in which they are able to communicate
Scalise et al., 2011	All scientific disciplines	Review of 79 studies, effectiveness of virtual labs in secondary school education	Real world contexts give incentive for learning, refrain from showing unnecessary elements, animations or simulations are effective scaffolding tools, explain abstract concepts, a discussion and exchange environment should be present in the lab
Smetana & Bell, 2012	All scientific disciplines	Review of 61 studies, effectiveness of simulations in elementary education, secondary school and college	Provide scaffolding for students; in using cognitive dissonance with labs, the role of the teacher is important
Yueh, Chen, Lin, & Sheen, 2014	Nano-technology, biology	1 e-learning project, design based research, instructional designers and context experts	Make learning aims explicit, provide feedback and let students reflect on their actions
Zumbach, Schmitt, Reimann, & Starkloff, 2006	Biology	1 virtual lab, 43 secondary school students	Connect with prior knowledge, virtual labs are able to promote conceptual and procedural knowledge, virtual labs offer possibilities for communication