Conceptualisation of synthetic biology using a virtual synthetic biology laboratory:

An explorative design based research.

Research paper

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Abstract

Students are often unable to experiment with new fields in biology because most developments in the scientific world are not practiced in secondary school laboratories. Likewise synthetic biology is not yet integrated in the curriculum. Synthetic biology is an innovative science in which scientists use elements of genetic information to design and develop whole new biological systems. In this study a virtual lab was developed, for the SYNERGENE project, enable to support upper secondary students' conceptualisation of synthetic biology. Using a real world context in a problem based setting students get to experiment with this new field of biology. This study aims to get insights what learning activities foster this conceptualisation and to find guidelines on the usability and feasibility of this designed virtual lab. To do so the virtual lab was designed based on guidelines gathered from literature. Furthermore, it was tested in four different classes with secondary school students. Data was collected from student answers of the virtual laboratory questions, surveys and interviews with students. It becomes clear that the learning activities do foster students' conceptualisation. Furthermore the information and visualisations of this virtual lab is valued positively and clear. Additionally guidelines for usability and feasibility are found. Moreover, the visualisations and text of virtual lab should be quicker and feedback should be more specific. This study was one of the first steps in a design based project, therefore more design cycles have to be done to develop this virtual synthetic biology laboratory.

Introduction

Synthetic biology is a new area of research, which is developing rapidly and integrates biology, technology and biological engineering. This innovative field of research focuses on designing and constructing new organic structures by using small biological building blocks are called 'BioBricks' and are used to synthesize whole biological systems. A future perspective is that we can engineer organisms with innovative characteristics. For example, micro-organisms can be designed and constructed who can break down toxic waste, destroy cancer cells or produce specific drugs. Because this field of biology is new it has not yet been integrated in the curriculum of secondary biology education.

Moreover synthetic biology is a complex subject, which combines topics like molecular biology and genetics, different lab techniques and biological engineering. For students of secondary education it as found that these topics are difficult to learn and teach (Duncan & Reiser, 2006; Knippels, Waarlo & Boersma 2010). Not only is this topic innovative, it can be controversial and that is why it is necessary to teach children what synthetic biology means and to make proper education trajectories and products. Moreover social and ethical questions can be raised around this new form of biology. Consequently, it is important for students, being possible future scientists as well as future citizens, to have the appropriate knowledge and objective view on this topic to form a critical opinion about synthetic biology and its applications. Besides, so far there are only a few lesson modules about the application and ethical part of synthetic biology available, which students can use to understand the principles of synthetic biology and discuss it. Nevertheless the conceptual and procedural aspects of synthetic biology are not addressed in these modules, therefore new teaching and learning material is needed.

To support the conceptualisation of synthetic biology visualisation is used. The abstract topics of molecular biology and genetics are successfully taught by using visualisations (Marbach-Ad, Rotbain & Stavy, 2008; Gilbert, 2005). Since synthetic biology combines these subjects visualisation can be used to teach synthetic biology. One way to teach and visualise molecular genetics is using virtual labs (Marbach-ad, Rotbain, & Stavy, 2008). Virtual labs are proven to be effective tools for improving students' comprehension about research and techniques (Chien et al, 2015) and promotes visualisations of the different abstract concepts of molecular biology and genetics (Marbach-ad, Rotbain, & Stavy, 2008). Therefore, such a computer tool can engage students in active learning about synthetic biology. More importantly it could help the students to visualise different concepts of this topic and foster understanding synthetic biology. For this study a virtual laboratory to foster students' conceptualisation on synthetic biology is designed and tested. In this virtual lab students can design new DNA structures to solve a realistic problem using synthetic biology.

It is known that the use of virtual labs and computer-based programs can facilitate learning and teaching scientific subjects (Scalise et al. 2011). For synthetic biology such a computer-based program has not yet been developed or tested. However a first step is made by van Harskamp (2015). For this virtual lab guidelines and learning aims are formulated, both based on literature research and interviews with teacher trainers.

This design-based research contributes to the SYNERGENE project. It is a mobilisation and mutual learning action plan (MMLAP). This research is a subproject linked to the bigger SYNERGENE project that "aims to contribute to Responsible Research and Innovation in synthetic biology" (SYNERGENE, 2016). This virtual lab is tested as an extension of two different lesson series designed for the European funded SYNERGENE project.

Taken together the aim of this research is to foster students' conceptualisation of synthetic biology using visualisation within a virtual lab and gain insight on the learning activities and guidelines for this lab that could help students of pre-university education to get a better understanding of synthetic biology.

Theoretical background

Synthetic biology

Synthetic biology is "the application of science, technology, and engineering to facilitate and accelerate the design, manufacture, and/or modification of genetic materials in living organisms to alter living or non-living materials" according to the SCHER (Scientific Committee on Health and Environmental Risks), SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks) and SCCS (Scientific Committee on Consumer Safety) (SCHER, SCHENIHR and SCCS, 2014).

SYNERGENE project defines synthetic biology as: rewriting the genetic code on DNA to program new biological functions. Therefore, micro-organisms can be designed and engineered, that perform diverse useful tasks. Synthetic biology is different from the "traditional" biotechnology because it uses newly constructed biological parts to create new characteristics, instead of modifying the existing DNA or replacing small parts of DNA. These biological building blocks are called ‘BioBricks’ and can be put together to create a novel biological structure with completely new traits (SYNERGENE, 2016).

This new development of biotechnology gives biologists a more design-based perspective on biology (Rerimassie & König, 2013). All over the world scientists embrace this new discipline. This is because future perspectives cause high expectations of this new area of research such as redesigned bacteria that produce new medicines or heavily genetically altered algae that produce energy. Nevertheless, it also raises moral questions and concerns about the role of mankind to modify and create new traits for living organisms (Rerimassie & König, 2013). Therefore, it is important to stress that students need to know what synthetic biology is and how it works, in order to empower the dialogue on this subject with the right knowledge.

Virtual labs

To help students understand concepts of synthetic biology a virtual lab is designed by a software engineer based on the advised learning activities and guidelines (Harskamp, 2015). This virtual lab is able to follow up one or a series of lessons on synthetic biology and could help to visualise this complex topic. According to Scalise and colleagues (2011) a virtual lab is an on-screen simulation of experiments traditionally performed in real school laboratories as part of biology, chemistry and other science subjects. In addition the use of virtual materials and tools, to replicate those in actual school laboratories, virtual labs can also simulate real world processes to promote learning and concept building of students from grade 6-12 (Scalise et al., 2011). Most studies found that virtual labs are equally effective in terms of learning concepts for students of senior high school (Chien et al., 2015). Students in the second or third year of their study, who used the computer to replace the traditional tools, outperformed the students who used the traditional equipment (Finkelstein et al., 2005). They did better on both conceptual knowledge and in understanding using real equipment. Henceforth, a virtual lab can be used as a practical and feasible replacement for a traditional lab.

Practically speaking a virtual lab is more efficient than a real lab. There is less distraction from all the tools and there can be focus on concepts and techniques. It is more feasible due to reduction of costs, time and practical reasons (Chien, Tsai, Chen, Chang & Chen, 2015). A virtual laboratory is used on computers and can be done anywhere and anytime. The students cannot get distracted by materials, new surroundings and the focus can really be on the problem and subject.

Design guidelines for teaching synthetic biology in a virtual environment

Teaching SynBio is including and connecting knowledge on living systems, inheritance, genetics and molecular biology. To integrate a new field such as synthetic biology into educational programs and curriculums on high schools is not easily done. There are several educational challenges to cope with, like reasoning across different organisation levels, which can be very abstract for students (Knippels, 2002). The different organisation levels include the molecular level, the subcellular level and the cellular level. Besides, the genetic processes work even further across these organisation levels. Duncan and Reiser found (2007) that students find it very difficult to understand the effect of molecular processes on different organisational levels. In addition, many studies found that this obstacle of reasoning across organisational levels can be dealt with by modelling the biological mechanisms (Duncan & Reiser, 2007; Knippels, 2002, Van Mil, Boerwinkel, & Waarlo, 2013).

As mentioned before the use of virtual labs promotes learning due to visualisations of different abstract concepts of synthetic biology (Marbach-ad, Rotbain, & Stavy, 2008; Chien et al, 2015). The dynamic nature of molecules and molecular interaction is difficult to understand from text-based presentation. Therefore, graphic visualisation is found to be effective in teaching molecular biology (NSF, 2001). The study of Gilbert (2005) shows the positive effect of computer animation and illustration activities on high school student achievement in molecular genetics. Moreover in comparison to traditional instruction computer animation improves the achievement when teaching dynamic processes and DNA structures (Marbach-ad et al., 2008). Since a virtual lab could model the mechanisms of synthetic biology and visualises the complex concepts a virtual environment could support conceptualisation of high school students.

Besides modelling the mechanism of synthetic biology, a virtual lab can encounter the conceptual knowledge, so the ‘know why’ part. However, this goes hand in hand with the ‘know how’ part of synthetic biology, also known as procedural knowledge (McCormick, 1997). The conceptual part focuses on the relationship among concepts. When students can make links between different concepts within synthetic biology it is called ‘conceptual understanding’. Procedural knowledge, on the other hand, concerns the processes, problem thinking and strategic thinking (McCormick, 1997). The learning activities and feedback loops of the lab could support the students’ conceptualisation of synthetic biology. Visualisation of the process and understanding the ‘know how’ can help students gain conceptual knowledge. Therefore, it is important to stress that virtual labs can promote conceptual and procedural understanding of synthetic biology

An important aspect of virtual laboratories and environments is that they can be used to create contexts or real world settings. A context can be used to connect the new concepts of synthetic biology with prior knowledge of the students (Edelson, Gordin & Pea, 1999). Moreover Huang (2005) found in his study, on medicinal virtual labs projects, that real world contexts can stimulate learning. Later this was also showed in a study with student interviews of Adams et al. (2008). In this study a problem based setting is used to create a structure for the learning activities of the virtual synthetic biology laboratory. This is mainly due to relate the learning process to a real world context, which promotes learning and conceptualisation.

To support the effect of the visualisations within a virtual lab students have to interact with the computer program and get activated. Moreover students can learn from trial and error and interactive activities with a computer tool like a virtual synthetic biology lab (Brinson, 2015; Chien, Tsai, Chen, Chang & Chen, 2015; Klahr, Triona & Williams, 2007). Therefore the learning activities are designed to promote active learning, by creating hands-on tasks. To help students actively the program has to give feedback on the interactions. This way the learning activities have a constructive approach. Consequently, they enhance teaching through active engagement using visualisations (Marbach-Ad, Rothbain & Stavy, 2008).

This lab could support visualising various concepts of synthetic biology and give students hands-on learning-material to foster conceptual understanding. Therefore the research questions of this study is:

How can a virtual synthetic biology lab foster students' conceptualisation of synthetic biology?

- What teaching and learning activities are helpful in conceptualisation of synthetic biology?
- What are guidelines for the usability of a virtual synthetic biology lab?
- What are guidelines for the feasibility of a virtual synthetic biology lab?

This design-based research focused on gaining more knowledge about meaningful learning activities. Therefore, learning activities are not be step-by-step-tasks, but students have to participate actively and are cognitively challenged by the tasks to gain more insight.

Methodology

To gain more insight into possible learning activities for the virtual lab, literature on science education, teaching synthetic biology and the use of virtual labs was searched and analysed. These insights were used to design and develop the learning activities of the virtual laboratory. These learning tasks were designed in a problem based setting. The learning activities were designed using the guidelines of Van Harskamp (2015) and were evaluated subsequently. Besides, the sequence of these learning activities were also evaluated to connect the learning goals of the virtual lab.

Design based approach

A design based was approach was adopted for this research. A design based approach contains different phases. In the first phase, the exploration phase, literature is consulted to support designing the learning and teaching activities. The exploration phase is followed by the design phase and results in a product. This product is tested, analysed and redesigned (Bakker and van Eerde, 2013).

Exploration phase

In a first literature study by Van Harskamp (2015) learning and teaching difficulties about conceptualising synthetic, molecular biology and virtual labs was studied. Van Harskamp (2015) has interviewed teacher trainers to gain insight in these possible learning and teaching difficulties. The insights from the literature research and Van Harskamps' (2015) findings were used to formulate learning goals and design guidelines for the virtual learning activities. Moreover, these insights were enriched with literature on visualisation of molecular biology and virtual laboratories.

From other design studies and existing virtual biological laboratories ideas were extracted which could help designing different learning activities within this virtual synthetic biology lab. To determine students' prior knowledge and expectations on thinking and understanding, teachers and students were consulted.

Design phase

From the exploration phase most of the insights were used to develop learning activities and visual representations for the virtual laboratory. Insights in prior knowledge and expectations on thinking and understanding were used to construct the hypothetical learning trajectory (HLT), which can be found in table 1. The designed materials were discussed with the second author, pre-university biology teachers and two university students. To increase the validity the feedback of different professionals on the designed material was implemented.

Test phase

First of all the HLT was pilot-tested to gain a better view on possible errors or difficulties within the design. This pilot-lesson of 45 minutes was held with the three biology teachers, who walked through the virtual lab and answered 7 questions from a short survey (appendix 3). These teachers taught the students who were involved with the actual test cases. The designed learning activities and visual representations were redefined based on the findings of this pilot study in order to reach the students' needs to solve these problem based activities and to support conceptualisation of synthetic biology.

Subsequently the learning activities of this the virtual synthetic biology laboratory were tested with students. To see which learning activities foster conceptualisation of synthetic biology the outcomes were compared with the formulated learning expectations from the HLT. Moreover the virtual lab was also tested on its usability and feasibility. The expectations were tested in four upper secondary biology classes during a 45-minute lessons.

Table 1. An overview of the four different cases and the collected data.

	Students (N)	***VL***	***Survey***	***Interview***	***Recordings researcher***	***Recordings teacher***	***Video***
6.1	18	18	18	2	1	1	1
6.2	17	17	17	0	1	1	1
6.3	19	19	19	2	1	1	1
6.nt	21	21	21	2	1	0	1
Total	75	75	75	6	4	3	4

Participants

The different cases all took place at a Dutch high school of pre-university education in Utrecht. This high school has a Christian signature, which is mostly expressed in rules and morals. The virtual lab is tested in four classes of 12^{th} grade students, age of 17-18. One of these classes is an NT-class, which contains a selection of beta science-oriented children.

Data collection and processing

During the test phase different types of data were collected, to test the HLT and to analyse the lessons, see table 1 for an overview. First the students filled in questions during the virtual laboratory activities. These were digitally collected when the students were finished. The lab contained nineteen open-ended questions and can be found in appendix 2. The student answers from these questions were used to collect data on the conceptualisation of synthetic biology. The students had to explain their actions, describe certain concepts in their own words, interpret data and applicate their knowledge on this subject.

At the end of the lesson a survey was administered to collect data on the usability and feasibility of the virtual lab. The usability is the clearness of text information and visualisations, about the control of the virtual lab, the case/problem and the learning goal of this virtual lab. The feasibility refers to the consuming time, the speed and level of the virtual lab. Besides it is important to check if students got stuck somewhere during the learning activities and if the feedback was helpful. Moreover the virtual lab was also reviewed if it connects to the prior knowledge of the students.

From the questionnaires information was gathered on how students valued the learning activities and their learning outcomes. These questionnaires consist of eleven closed (5 point Likert-scale) and eight open items (appendix 4). Moreover from the open items the Cohen's kappa was calculated to see whether the codes used during the analysing phase were reliable.

Six students of students were interviewed to elaborate the answers on their questionnaire (appendix 5). From one class of each teacher two students were randomly chosen. Therefore, and due to practical limitations there were no students from class 6.2 interviewed (see table 1). This is to get more in-depth data and therefore more insight on the feasibility and usability of the virtual laboratory. The conducted interviews were semi-structured, consequently there was room for the students to elaborate and speak more widely. The audiotaped interviews were transcribed verbatim.

Analysing students' conceptualisation

The students' conceptualisation of synthetic biology was determined by analysing the results from students answers from the nineteen virtual lab questions, four open items from the questionnaires, interviews and field notes. The actual learning gains were analysed through comparing the outcomes of the HLT with the actual learning trajectory in retrospective. For analysing the conceptualisation the answers from the virtual laboratory, answers from the survey questions related to the conceptualisation and the interview answers were coded. As mentioned before the spoken answers were all transcribed. Firstly the answers of the virtual lab questions were valued correct or incorrect to get an overview on how the students responded compared to the HLT and learning goals. Secondly all the answers on conceptualisation of the virtual lab, the questionnaires and the interviews were segmented and open-coded per question. Therefore, codes on conceptualisation like “visual”, “text”, “educational” and “motivation” were used. Then the segments were axial-coded, for example “educational - level”, “educational – connection [to prior knowledge]” and educational – experience of learning”. A second coder checked all the codes for the different segments and the Cohen’s kappa was calculated for every item to measure the inter-rater agreement.

Analysing students’ opinions on usability and feasibility

Besides the learning outcomes, the opinions of the students on the designed virtual laboratory was also collected. In these questionnaires, by means of a 5-point Likert scale, and interviews the students were asked if it was enjoyable, if the program is feasible, if they find the exercises too difficult or too easy. More specifically in the interviews the students were asked to recall the different aspects of the virtual lab, what they had done, why and what their outcomes were. Then there was space for the students to give their opinion about the different learning activities, about the visualisations and information of the virtual lab. Likewise the answers of the students were used to improve the design of the virtual laboratory. The answers about usability and feasibility were analysed in the same way as described above. Similarly these answers were segmented and open-coded per question. Therefore, codes on feasibility and usability like “visual”, “text”, “feedback” and “use [of the program] were used. Then the segments were also axial-coded, for example “visual - speed”, “feedback - amount”, “text – speed” and “text amount”. Equally for these segments a second coder ran through the segments and to measure the inter-rater agreement the Cohen’s kappa was calculated for every question.

The designed lesson

Practical aspects

The virtual lab is built with PowerPoint, however it is possible for the students to interact with the program, to make mistakes and receive feedback. The virtual lab is designed to be finished within 45 minutes. Moreover as mentioned before, the students were introduced to the subject of synthetic biology using two different modules on the ethical part of applied synthetic biology and all the students received biology lessons on genetics. Therefore the assumption is made all the students had the same prior knowledge. For this research two lesson modules on synthetic biology that are already designed and tested are used as an introduction to this virtual laboratory (Overbeek et al., 2001; Azevedo & Knippels, 2015). This lesson module consists of three lessons in which the concept and applications of synthetic biology is taught. Therefore the focus of this virtual synthetic biology lab *is* on the understanding of the scientific part of synthetic biology. The lesson module teaches the conceptual or 'why' part and the virtual lab the procedural or 'how' part of synthetic biology (McCormick, 1997; Zumbach, Schmitt, Reinmann and Starklhoff, 2006).

Hypothetical learning trajectory

Based on the defined guidelines of van Harskamp (2015) and other findings in the literature activities for a virtual synthetic biology lab were designed, to concretise abstract concepts. A hypothetical learning trajectory (HLT), see table 1, was constructed with the different learning activities of the virtual synthetic biology laboratory. Choices regarding the learning activities, which are made designing the virtual lab, will be explained and justified in the following section "The learning activities". The order of the learning activities are due to the problem based setting. This is due to relate the learning process to a context, which promotes motivation and comprehension as described above (Graaf & Kolmos, 2003).

The learning activities

The learning activities of this laboratory start with an animation, introducing a biological problem, which the students have to solve using synthetic biology (Scalise et al., 2011). This is learning activity 1 (LA 1) in table 2. This table presents a hypothetical learning trajectory, in which the different learning activities are summarized. In appendix 1 some screenshots from the virtual laboratory can be found. For this virtual lab one of the applications from the module has been selected and developed to fit in this virtual lab. The selected application is about the LactoAid bandage. Students from the University of Groningen competed in the iGEM-competition with their design of synthetic created DNA for the useful bacteria *Lactococcus lactis* preventing burning wounds to get infected by infection causing bacteria like *Staphylococcus aureus* and *Pseudomonas aeruginosa* (Meijer et al., 2014). The problem introduced to the students is about the infections of burning wounds caused by these bacteria and the need to reduce the excessive use of antibiotics to cure these infections. The context of LactoAid is chosen because it is introduced in the lesson module. More importantly, the context connects with the prior knowledge of the students (Edelson, Gordin and Pea, 1999; Zumbach, Schmitt, Reinmann and Starklhoff, 2006). Because the LactoAid-application is a real world context, students can relate to the problem and this context can help to give incentive for learning (Huang, 2005).

Once the students know what the problem is they have to fix, they get to the designing part (LA 2). The students have to design the DNA-construct by themselves using the information on the bacteria and the selection of BioBricks. Just like real scientists the students have to look up the right BioBricks in a catalogue and choose the right pieces and put them in order. Here the students have to use their own biological knowledge about ribosome binding sites, promoters, genes and terminators and combine it with this new application of synthetic biology. The students have to make the right selection using the information on the bacteria and the information of the different BioBricks. Besides, the students have the sequence of the parts correct in order to get a useful and functioning DNA-construct.

While the students are making the construct, the virtual lab gives them feedback on the choices and order of the BioBricks (LA 3). When they are constructing the DNA, the students receive direct formative feedback on the screen. There are only a few comments available like: “the DNA-construct is not yet finished, you missed some BioBricks” or “the DNA-construct will not be translated, you missed some BioBricks or you’ve chosen the wrong BioBricks”. With this feedback the students redesign their construct until they get a working DNA-fragment. When this formative feedback stops, the students know they have got a working DNA-construct. However, the working DNA-construct can still contain wrong genes.

When the students are finished making the DNA-construct, the program let them go further if this construct works. The next step is for the student to look up information on the bacteria *P. aeruginosa* and four different host organisms by clicking on the index. Then the students have to choose the right organisms, in which eventually the construct is placed in (LA 4). Due to scaffolding the students can choose how much information they need. They can even go back within the virtual lab to watch the visualisation on the infection again if needed (Scalise et al., 2011; Smetana & Bell, 2012).

When the students are done reading the information on the different organisms and chose the right bacteria they get to virtually test their DNA within their chosen bacteria (LA 5). Students can check their DNA-construct to click on a “test” button and virtually send it to a test-laboratory. The students then get to see an animation of what biologists do in a real laboratory with the designed DNA-construct. Techniques like PCR and implementing DNA in organisms are shown in this animation.

After the animation students get output of the data collected from the virtual and illustrated laboratory. The output is given in graphs and patient information. The students have to interpret the data from the graphs and explain what they see and whether their DNA construct had the right genes (LA 6). It is important to ask students to interpret and compare results, this asks for high order reasoning (Scalise et al., 2011).

If the construct contained the right genes the students were done with the virtual experiments and got to finish the problem. This last learning activity consists of a short final "conversation" with the patient, in which the doctor explains that this new treatment with synthetic biology worked. This conversation is followed by a short animation of how the genes in the bacteria work and how this bacteria fights the infection and cures the patient (LA 7).

Table 2. The hypothetical learning trajectory of the different exercises of the designed virtual synthetic biology laboratory.

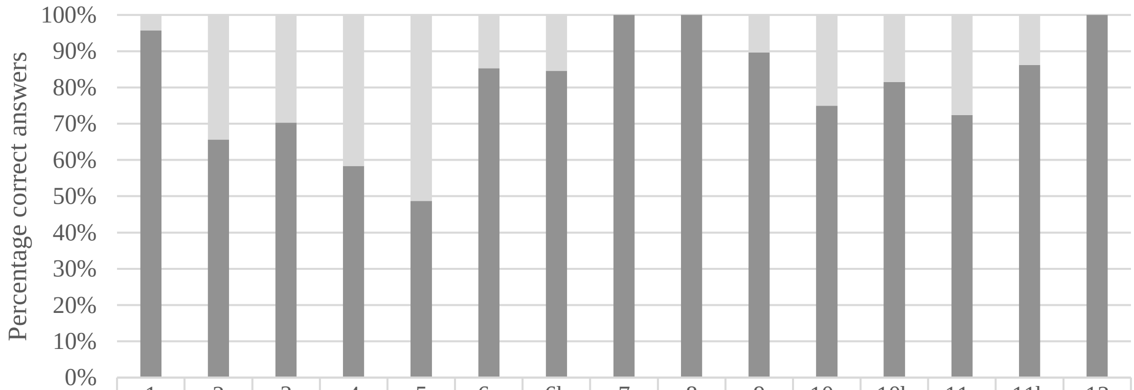
No.	Learning activity	Student activity	Conjecture of how students would respond
1.	Introduction of the problem with an animation.	Students watch the animation	Students get insight of what the problem is and what their roll is going to be solving this problem.
2.	Design a DNA construct that optimally helps the immune system to defeat the infection causing bacteria. Students have to choose the right BioBricks out of the database and place them in the right order on a plasmid. The catalogue provides the BioBricks of bits of information.	The students build DNA construct consisting of different BioBricks in the right order.	The students get to know different parts of a DNA, like a gene, ribosome binding sites, terminators and promotors.
3.	The students receive with feedback on their moves from the virtual lab.	Receive feedback and implement the feedback.	The student gains knowledge about the different parts and know which to choose and in what order to put the BioBricks.
4.	Looking up information of *P. aeruginosa* in index within the virtual lab.	Students click on index and find their information on the bacteria.	Students gain knowledge on the characteristics of the infection causing bacteria. - Bacteria create a biofilm Bacteria communicate together to improve density
5.	Test the constructed DNA. The virtual lab shows a short animation on how the DNA is printed, centrifuged, PCR-ed, western plotted and implemented in useful bacteria.	Students watch the animation	Students gain insight in what happens with their designed DNA in a real laboratory and which techniques are used.
6.	The virtual lab gives the students feedback on how they did it in terms of a graph and patient/wound feedback. If the constructed DNA is incomplete they get a neutral patient with a wound that still is infected, the graph shows the results of the effect on the infection causing bacteria. They can click on redesign. → Activity 5.	Students receive different kinds of feedback and can choose which feedback (graphs, patient dossiers etc.) they use.	The students learn to interpret different kinds of data and to reflect on their DNA-construct with this feedback in forms of graphs or patient dossiers.

	The students can repeat the cycle of 5 and 6 till they get the DNA construct correct. If their DNA is correct they receive a happy patient and a graph with the results of the effect on the infection causing bacteria and can click on create bandages. → activity 7		
7.	Animation of a happy patient. But also newspaper headlines of possible consequences. “New medicines discovered to treat all infections, never antibiotics needed”; “jobs in antibiotics industry disappearing, because of new treatments with SynBio”; “Cornfield disappeared after incident with photosynthesis gene in SynBio lab”; “bacteria with SynBio DNA evolve on their own”.	Students see different headlines with diverse reaction on synthetic biology.	Students realise that synthetic biology can be a new field in biology science and can have useful applications. However they also realise that synthetic biology is not yet the answer to every medical issue, like reducing the use of antibiotics.

Results

Conceptualisation

Student answers of the virtual lab. To see whether the virtual lab fosters the conceptualisation about synthetic biology with pre-university students the virtual lab answers were collected and analysed. Answers were compared with the hypothetical learning trajectory.



	1	2	3	4	5	6a	6b	7	8	9	10a	10b	11a	11b	12
Wrong	3	22	19	25	20	5	4	0	0	3	7	5	8	4	0
Correct	67	42	45	35	19	29	22	30	29	26	21	22	21	25	29

Figure 1. The items are presented on the x-as, while the percentage of the correct and incorrect answers is presented on the y-axis. In the table the amount of correct and incorrect answers are presented.

The first thing that stands out from figure 1 it that the amount of question answered, whether it was correct of incorrect, decreases during the simulation. In the beginning 70 students were able to answer the first question, at the end around 30 students were able to answer the last questions.

All students managed to complete a working construct. 67 of the 70 students made these constructs completely correct. This means that the construct was working, so the students chose the right BioBricks, put them in the right order and chose the right genes. More specifically the 3 students who were incorrect, did manage to make a working construct, but chose the wrong genes.

Most students, 42 out of 64, were able to answers the question for which they have to explain what the difference is between synthetic biology and current biotechnology correctly. The other students were incorrect or incomplete.

An example of a correct answer:

S 57 *“In current biotechnology, the DNA is taken from another organism, while in synthetic biology the DNA is made by a machine. So you can design it yourself too.”*

An example of an incorrect answer:

S 9: *“Synthetic biology is synthesising DNA. Current biotechnology deals with technological applications in healthcare (machines, prostheses).”*

Of the 64 answers that were given on the question "what happened if the DNA-sequence CTTAAG/GAATTC is presented twice in the plasmids, when you add the restriction enzyme EcoR1?" 45 students answered correctly. On the question "why are the transformated bacteria exposed to ampicillin?" 35 of the 60 students answered correctly. The principle of gel electrophoresis was understood by the students. To the question of which colonies succeeded in cloning 34 students gave the right answer and 22 out of the 26 students gave a correct explanation. The question of how much base pairs the built-in DNA construct consisted was difficult to answer and 19 out of 39 students gave the correct answer, so 20 students were wrong. The questions about the control test were answered well, the closed questions were answered by all the respondents, the inquiry, which prompted an explanation of what was checked, was answered by 26 of the 29 well. 21 out of 28 students answered the question which effect the DNA construct has on the formation of biofilm. In addition, 22 of the 27 students give the right gene that causes this. In addition, 21 of the 29 students give the right answer to the question what effect the DNA construct on the AHL signal molecules of *P. aeruginosa* gives to the 25 of the 29 students the right gene.

Survey. As described in the method section the survey consisted of closed items with a 5-point Likert scale and open items in which students could explain their answers or could give remarks on this virtual lab.

Table 3. Subjects and average value of closed items.

Item	Subject	Av.	N
5	Overall	4,1	75
6a	Visual	4,4	75
6b	Learning	3,9	75
6c	Feedback	3,6	75
7a	Too long	3,2	75
7b	Too short	2,1	75
7c	Control	4,0	75
7d	Case	4,3	75
8a	Prior Knowledge	3,9	75
8b	Level (hard)	2,3	75
8c	Information	4,1	75

Table 4. Subjects and Cohen's kappa of open items

Item	Subject	Cohen's κ	N (students)	N (fragments)
5	Overall	0,68	22	34
6d	Clear	0,69	10	11
7e	Usability	0,72	17	20
9	Level	0,74	26	31
10	Adjust	0,82	41	47
11	Learning	0,70	59	68
13	Remarks	0,84	9	10

In the two tables (table 3 and 4) results from both the closed and open items are represented. From the closed items the average values of the 5-point Likert scale is shown and from the open question the Cohen's kappa is presented. All the closed items, so table 3, are on usability and feasibility. Nevertheless the open items in table 4 are partly about the conceptualisation. After a few items there was room for the students to explain their answers or leave a remark. For example after the closed-items 6a, 6b and 6c (table 3), the students could elaborate at the open-item 6d. To be more precise mostly on items 5, 10, 11 and 13 students respond with answers on conceptualisation. Moreover a complete overview of the items from the questionnaire can be found in appendix 4.

As can be seen in table 4, not all students answered the open questions, because these were to explain or elaborate their answers on the closed items mostly.

So the goal of the survey was mainly to check the usability and the feasibility, however there was one item which asked the students to write down in their own words what they thought synthetic biology meant. 50 of the 75 people gave correct description. For example:

> S8: [12] “By making DNA by yourself and inserting it into a bacterium, changing the characteristics of this bacterium.”

One closed item (6b, table 3) in the survey asked implicitly about the conceptualisation, because it referred to the clarity of the program. This was about the students’ educational value of the virtual lab. Therefor some of the responds were on the conceptualisation, for example the following quotes translated from Dutch. Between the square brackets the number of the item belonging to the answer is noted.

> S8: [5] “Instructive, by doing something else, other than normal.”

> S 10: [11] “Yes, how does synthetic biology work precisely and what steps are needed (in practice).”

> S 44: [11] “Yes, by seeing the process, I got a better picture of synthetic biology.”

Interview. To get a more in-depth insight in how the learning activities foster the conceptualisation, the same subjects that were asked within the survey were also addressed in depth during semi-structured student interviews. Therefore they were first asked to describe synthetic biology in their own words. Within the surveys the students gave very short answers, however within this interview the students could elaborate. For example:

> *Quote 1:*
>
> *I: “Can you explain in your own words what synthetic biology is?”*
> *S 42: “uhm .. that uhm ... just look on the computer in a catalogue for different BioBricks or so and uhm.. synthetic biology is that you make uhm .. Yes some kind of artificial DNA and then let it print through the computer, kind of, and that in your DNA stops kind of saying you cut a piece and paste it into another piece.”*
>
> *Quote 2:*
>
> *I: “Can you describe what synthetic biology means in your own words? What you think it means?”*
>
> *S 41: “Yes. That's you have DNA, you make up yourself or you ordered an uh ... a sequence of ACTGtjes. That's done with a kind of printer by a company somewhere and then you can do that with what you want to paste it into a bacterium or that's what they usually do.”*

From quote one and two it is shown that students do not give the exact same answers, but both answers contain a correct explanation of synthetic biology.

After the students were asked to explain synthetic biology, they had to recall the problem they had to solve and how they used synthetic biology to do so. In the next example the student already explained what the problem was, now the student tries to explain how synthetic biology was used to solve this problem.

Quote 3:

S 2: "The problem was that the burns were infected with a particular bacterium and that bacterium could not be eliminated by the normal white blood cells and something else had to be devised."

This quote was an answer to the question if the student could tell what the problem was. It shows that the student was able to recall the problem and explain why the infection wouldn't heal and gets infected.

Quote 4:

I: And okay and how did you use synthetic biology to solve this?

S 42: Uhm yeah oh yes, we have added BioBricks, so yes Promoter and an uh terminator and such things, but uh the genes were the uh, I believe, DspB I do not know the full name.

I: that's correct

S 42: To break down the biofilm due to hydrolysis, such thing as AiiA and that uhm that stops the uh the functionality of the AHL receptors.

I: Yes correct. Can you recall which other BioBricks you used? You already said terminator, promotor and those two genes.

S 42: And uh the receptor bindings site, RBB?

I: Yes the RBS, that's the 'ribosome binding site'.

S 42: Yes RBS! Ow yes that ribosome thing.

This answer shows that this student could recall the different thinking steps and actions using synthetic biology for solving the problem.

One of the techniques the students came across during the virtual lab was gel electrophoresis.

Quote 5:

I: "...Do you still know what happened with the electrophoresis, what did you check?"
S 2: "Yes uhmm. The length of the base pairs. The size, the amount of the base pairs actually."
I: "Mm.
S 2: "Because DNA is negative or positively loaded, so it is pulled to the other side, so it

seemed to me as if some genes were present and some not uh ... and that there was not a mix of successful plasmid and unsuccessful plasmids."

With this answers the student shows he knows how gel-electrophoresis works by explaining the process. Moreover, the student also knows what it means and how to interpret the outcome.

Besides the different techniques the students get realistic results they have to interpret and discuss at the end of the virtual lab. These results are presented as graphs. The next quote gives an example of an interpretation of these results:

Quote 6:

I: "And uh .. And the piece, oh yeah, the very last piece where you went to see if your genes actually worked, with those charts.

S 68: "Uhm ... I also found that clear yes.

I: "What did you see?

S 68: "That less AHL and that biofilm was made.

I: "So in your situation there was a graph that did not go up anymore?

S 68: "Yes."

I: "Was it clear to you what that meant, what did that mean? What did you fill in? S 68: "That the bacteria took biofilm away that prevented the immune cells from catching the bacteria."

Within this quote it can be read that the student came up with their own interpretation of the graphs. This students shows he knows that less AHL and biofilm is made looking at the graph. He is also able to explain what this means for the bacteria and the immune cells.

Usability

Survey. Some items asked directly about subjects on usability and other items were more open. Students could either way say something about controlling the program, clarity, information, goal and visualisations. The values of the closed items about the usability are also shown in table 3. Remarkable high values are the ones for visualisations (4,4; item 6a), control (4,0; item 6), information (4,1; item 8c) and case (4,3; item 7), indicating that the students valued these facets on usability of this virtual lab positive. Some explanations from students were for example:

S 22: [5] "Interactive and informative."

S 38: [9] "Theory was complicated, but clearly explained"

S 23: [10] "It is a shame we had to press the pipette and not to drag itself."

S 42: [5] “Crazy! New ways to learn and handle the matter.”

S 66: [5] “Very professional animations.”

Interview. Besides the content of the virtual lab and the conceptualisation of synthetic biology the usability and feasibility was also questioned in depth during the interviews. For the usability the students were asked about the clarity of the program. Therefore they were questioned about the goal of this lab, the clarity of the program and the control of the program. A few examples were taken from the interviews to show what students had to say.

Quote 7:

S 60: “Uhm .. Yes, I really liked it, you were guided through it, but you had to think about all those questions, okay, I'm aware of what I'm doing, but that worked just fine. The diversity doing and answering”

Quote 8:

I: “The instruction for the assignment was clear. Did you know what to do?

S 68: “Yes.”

I: “It was clear what was expected of you?”

S 68: “Yes.”

I: “And what was the purpose of the assignment?”

S 68: “Yes.”

I: “For what was the end of the goal?”

S 68: “Uh, to make sure that the immune system could deal with the infection.”

The other interviewees gave answers in the same sense. There was no student who thought the virtual lab and its instructions were unclear or could not translate the goal of this virtual case. Besides the clarity of the program the students were asked about the visualisation and information present within the simulation.

Quote 9:

S 60: “Yes, it was just plain explained clearly step by step and it was not that you had to do one hundred things equally and it was just plain clear actually every time what had to be done. So that was fine.”

I: “And what did you think of the moving visualisations, of the molecules that went back and forth, biofilm”

S 41: “Yes, that often makes it clear, because then uhm, then I see that a biofilm is produced from that bacterium and that it's all surrounds it. And that the white blood cells really cannot reach it, so I liked the movements.”

As can be read in quote 9 the visualisation were helpful for this students. This student gives an example of a visualisation which fostered the understanding of the problem of the immune system not being able to attack the infection causing bacteria. In general students valued the speed of the visualisation as all right. Most male respondents stated this could go a bit faster. One interviewee mentioned the form and was enthusiastic about the characters like the professor. The information that was provided during the virtual lab was found clear for most interviewees, but they noted that the text presented itself slow.

Feasibility

Survey. The information and feedback from the professor in the virtual laboratory was vague and students did not find it helpful. Students did not know they had to put a ribosome binding site between each gene. Most of the time, the tip to read the information of this BioBricks was enough to complete the construct.

The students differ in reading the amount of information given. Most given feedback from the researcher and teacher is about the ribosome binding sites (field notes and recordings).

> S 62: [6d] “Not all questions were answered, while you were wondering if you were right.”

> S 43: [6d] “Failure professors of the professor were sometimes vague.”

On the speed of the text or visualisations the students said for example:

> S 4: [7e] “I read faster than the letters were sometimes on, so that was disturbing.”

> S 26: [7e] “The text came too slowly.”

> S 37: [7e] “Yes, it's a lot of text and it's annoying when it appears in each case.”

> S 64: [7e] “Animations could have been faster, clear.”

And some quotes on the level of this virtual laboratory were for example:

> S 66: [9] “Not too hard, only just too long for 45 min.”

> S 42: [7e] “Sometimes difficult, for example, when a cDNA had to be made strict, there were more and more genes everywhere.”

> S 49: [9] “Only making DNA was difficult.”

> S 34: [9] “Lack of [prior] knowledge”

Interview. Finally the interviewees were questioned on the feasibility of this virtual synthetic biology laboratory. Frequently the students mentioned the interaction during the interviews. With this they meant the amount and the form of the actions they had to perform and the questions they had to answer. The amount of questions was all right and the construct making was an activity most students found fun and challenging. The activities during the technique phase (LA 5) however were found repetitive. One example of such a comment can be read in quote 10.

> *Quote 10:*
>
> *S 41: "And on the rest of the part it was like clicking on the pipette, clicking on the pipette, clicking on the pipette and at some point you had such an ok click, click .. So then ..."*
>
> *I: "Frequent repetition?"*
>
> *S 41: "Yes exactly."*

About the level of the questions, teaching and learning activities of the virtual lab the students did not agree completely. Some interviewees thought the overall level of the virtual lab was all right for them (quote 11). Nevertheless some students stated the questions were not very difficult or too much information was already given, as can be read in quote 12.

> Quote 11:
>
> *S 41: "I thought it was good at everything we learned and I could understand everything. Uhm, yes, I think it's just good."*
>
> *Quote 12:*
>
> *I: "Okay what did you think of the level of the virtual lab?"*
>
> *S 68: "By doing this [virtual lab] you got more information and had to think about how you did it, but I thought the questions were not very difficult. It's a bit of a mix in between."*
>
> *I: "Would you do anything else to make it easier or more difficult?"*
>
> *S 68: "Uhm yes you can make these questions a bit more difficult, but it's more difficult when you give less information and then the questions are less easy, but I think it was, yeah, ok"*

The level and therefore the feasibility also depends on the connection to prior knowledge. The information and visualisations have to be recognisable for the students, however similarly provide new concepts and insights.

> Quote 13:
>
> *I: Did it connect with your level?*
>
> *S 60: "Yes, I think, especially because we are now doing the whole theme of DNA now, at least you have learned what I've been doing now, because just to learn to study DNA is of course very different from that You think, okay, this will be done, we can do this in the future. So I found that very fun."*

As can be read in example of quote 13 this students stated that the subject connects to the prior knowledge, this because the student already learned about DNA before starting this virtual lab. The student also mentioned it enriches his/her knowledge because it shows different information and an (modern) application of DNA.

One last aspect of the feasibility is the feedback from the virtual laboratory. This feature is very important because it is about the amount of support the students receive. Quote 14 shows an example of the thought of a student that is shared with most of the other interviewees.

> *Quote 14:*
>
> *I: "And what did you think of the piece that your DNA was checking for it worked?" S7: "Yes, I was a little sorry and if that did not work, he said "sorry, try again" but he did give a hint or [explained] why it did not work. So, for example, if you tried to combine all combinations, I still would not know.*

Like this example a lot of students mentioned that the feedback was vague and could be more specific, especially with making the DNA construct. The professor only mentioned it was wrong or incomplete, but did not tell the students what their mistake was, did not give a hint or helped them with the next step.

Conclusion

This design-based study aimed to discover if and how the teaching and learning activities can be used to foster students' conceptualisation of synthetic biology using a virtual synthetic biology laboratory, using visualisations and problem based learning strategy. Therefore the following research question and sub-questions were formulated: **How can a virtual synthetic biology lab foster students' conceptualisation of synthetic biology?**

1. What teaching and learning activities are helpful in conceptualisation of synthetic biology?

Most importantly is to note that the problem based strategy fostered a logical order of learning activities for the students. They mentioned that the pathway, information and goal of the virtual lab and different learning activities was clear. Besides making the DNA-construct was the learning activity that was valued most challenging and educational learning activity. It was found that the learning activities about the different techniques were clear, however valued less educational by the students. From the results it can be concluded that these learning activities can foster conceptualisation on synthetic biology, however there are some guidelines on usability and feasibility that can be further developed and improve this virtual synthetic biology lab.

2. What are guidelines for the usability of a virtual synthetic biology lab?

Firstly it is important to mention that the information provided by the virtual lab was clear for the students. It was found that the visualisations and text fostered the conceptualisation and were valued as clear and helpful by the students. Moreover this study also showed that the visualisation and text appearance could be faster, and the amount of information could be reduced. Although the program was valued primitive by some students, it was found the students could control the program without much difficulty.

3. What are guidelines for the feasibility of a virtual synthetic biology lab?

First of all the time that was set for this virtual lab was not reached within the given lessons, therefor some students did not finish the virtual lab. Therefore it cannot be concluded that 45 minutes is enough. However it is found that some students can finish the virtual lab with a lesser amount of time. Overall the students that were able to complete the virtual lab did not get stalled somewhere and were able to finish the virtual lab without any or much help of the teacher/researcher.

Within this study it was found that the virtual laboratory and its learning activities could be more challenging for students with pre-university level. Besides, it was found that the learning activities about the different biological techniques have to be more interactive. Moreover the visualisation and text connected to these learning activities could go faster. In addition the feedback given by the virtual lab was valued helpful, nevertheless sometimes too vague or incomplete.

Discussion

Conceptualisation

The design of the virtual laboratory was based on a problem-based strategy providing the students a problem to solve using synthetic biology and different biotechnology techniques to foster their conceptualisation (Chen, 2014; Graaf & Kolmos, 2003XX). The virtual lab provided different learning and teaching activities with moving and static visualisations. Most important finding is that the designed learning activities do foster conceptualisation of synthetic biology. The problem based strategy provided a logical sequence of learning activities and created a clear pathway and goal for the students. Making the DNA-construct was the learning activity that raised a feeling of understanding and learning with most students, because it was an interactive challenging hands-on activity (Marbach-Ad, Rothbain & Stavy, 2008). All students managed to complete a working DNA-string, which is the main goal of this virtual laboratory. They used the right BioBricks in the right order to accomplish this learning task. However this task was found challenging and difficult for most students, because they had to use prior knowledge, read provided information and apply these bits of knowledge to create a product that could help solve the problem. Because students can decide which information they read, this learning activity scaffolds between different levels of the students and their prior knowledge (Scalise et al., 2011). Some students have more prior knowledge and read less, some students read everything and also completed the construct.

The following learning activities were simulations of different techniques which tested the constructed product of the students in different ways. The students had to answer questions about what they were doing and had to click on different objects on the screen to set the techniques and visualisation in motion. The pathway of these learning and teaching activities were clear for the students, they knew what to do and where to click, however these activities were found less educative. Because the students were not able to manipulate materials these hands-on activities were less interactive (Klahr, Triona & Williams, 2007). Therefore, these activities were less supporting in conceptualisation of synthetic biology. For example the third question was answered correctly by most of the students as was shown in the results, so the students understood what the function of the restriction enzyme was and they understood how it operates. The fourth question was already answered correctly by fewer students. Still most students answered correctly and showed they knew the purpose of exposing to ampicillin. This fourth question was not to check whether the students understood something of the virtual lab but to activate their prior knowledge, so the information given after the question was asked gave the students the right answer (Edelson, Gordin & Pea, 1999). Despite the clarity and the informative purpose the students thought the interactions from this part of the virtual lab were repetitive, especially the clicking motion. This repetitiveness made it slow and less interesting for most students.

The questions that were asked during the virtual laboratory were answered mostly correct, therefore the students showed they knew what they were doing during the different learning activities. It was also found that more students thought these question were too easy, moreover most of the students thought this virtual laboratory was not too hard. The activity in which the students have to make a DNA-construct was found the most challenging.

Usability

Based on this study a few guidelines for the usability of this virtual synthetic biology laboratory can be formulated. First the control of this virtual lab. The students found no difficulties in controlling and managing the different tasks within this virtual laboratory. It was clear for them what they had to do and what was expected from them during the different learning and teaching activities. Moreover they also had an idea of what the goal of the virtual laboratory should be. The information that was provided during going through the different activities was clear for most students. Some students thought that the amount of information and techniques was too much, this could overload the working memory of the students (Scalise et al., 2011). Moreover the information they had to read was moving in on the screen and it was found this was too slow for most students. This was also found for the visualisations. The visualisations facilitated a lot of students on the conceptualisation of synthetic biology, it was found these visualisation were valued as clear and helpful. However it was also found a lot of students found the speed of these moving visualisation too slow. Therefore some students mentioned the interactions were sometimes boring, repetitive, less challenging or less interactive.

Feasibility

Guidelines on feasibility for this virtual laboratory can also be found from this study. As mentioned before the speed of the provided information and moving visualisation could go faster. As well, this could be helpful to decrease the time spend on completing this virtual lab. Although there are no hard time measurements it was found that a lot of students did not complete the virtual lab within the amount of time set for solving the problem. It is also a possibility to increase the amount of time students can use to complete this virtual task. In addition, the level of the laboratory could be increased when it is used with pre-university students. The construct making activity was found challenging but the other activities could be more difficult. It was found that the students thought the teaching and learning activities on the techniques could be more interactive. They found the clicking motions were repetitive and the questions too easy. Some suggested to implement another construct making activity to alternate the exercises. Another possible way to increase the difficulty is to leave out the modules as an introduction and let the students work out this virtual lab with only prior knowledge on common genetics and molecular biology. In this way students are able to manipulate materials more and therefore get more actively engaged (Klahr, Thriona & Williams, 2007).

Besides the easy level of the different activities and questions it was found that the students could work with the feedback given by the virtual lab. Sometimes the feedback was not literally given, but implemented in the information afterwards, besides students did not always have to do something with de feedback. But when the students had to implement the feedback they could work with the given response, however some say the feedback was too vague or too little. To prevent confusion and lack of motivation the feedback should be more consistent, clear and precise (Klahr, Triona & Willams, 2007). Furthermore there was one point within this virtual laboratory where some students got stuck, this was with the activity where the students had to make the DNA construct. The students massively forgot to use a second ribosome for the second gene. This was mainly due to not reading properly, so encouraging reading that specific piece of information was the only structured feedback that the teachers and the researcher had to give to help the students to move forward within the virtual lab.

Methodological reflection

As described in the methods four different classes were used to test the virtual laboratory and there were three different teachers, who teach one class each. However one teacher had two classes, one of which was a class with students who were excellent at beta subjects. Although the differences between the answers and values of the students of the different cases were not statistically compared, there seemed not much of a difference between these cases. From the interviews and the pilot study it was noted that the teacher worked together very closely, so they agreed on the ability of the students finishing this virtual lab and having the same prior knowledge. Nevertheless each teacher has their own way of teaching genetics, DNA and molecular biology and therefore small differences in prior knowledge, learning strategies, recap abilities can still exist among the students.

Besides the differences in the prior knowledge due to different teaching strategies and methods, the students were introduced to the subject of synthetic biology using two different modules. These modules were focused on the moral aspect of synthetic biology. However the differences between the two modules was not the content, but the approach and order the content was represented. In the first modules different applications of synthetic biology were divided over groups of students, who had to figure out what the application was and how synthetic biology was used to accomplish this application, afterwards they have to discuss the ethical issues around this new field of science. The second module, used in the other two classes, was more classically orientated. The students first had to form an opinion about synthetic biology, discuss different arguments and then learn about the concept and applications of synthetic biology in more detail and see if their opinions changed. So the approach of the different modules were different, but the learning goals and the expected learning outcomes were the same. These differences were also not measured statistically, but qualitatively there was no outstanding differences in the answers or opinions of the students between the different classes.

Limitation of the study

Besides the reflection on the different cases there are also limitations of this study. Firstly this first design cycle is done in four cases, which is a total number of 75 students. These students are all at the same skill level, namely pre-university on a Christian Gymnasium. To get more reliable results different levels have to be included in the design cycles. This because the virtual laboratory will eventually be used for different levels of pre-university students and maybe even higher general secondary education (HAVO). Besides the students are all at the same skill level they also attend to the same school. This study or a next design cycle can be conducted at different schools to increase the generalisability and reliability.

Second, this virtual simulation used one case, namely the problem of a patient with an infected burn wound. It can be useful to see if there are different problems and contexts, which connect to the world of the students. This example is directed at healthcare and for some students very interesting. However it is possible that some students would prefer other contexts like programming algae to produce clean energy or programming bacteria to produce medicines like Artemisinin. This in order to reach as many students as possible in connecting with the matter, because this subject is very abstract.

Another very important limitation of this study was time. Because there was only one lesson of 45 minutes available for each class, a lot of students were not able to finish the virtual laboratory on time. Within these 45 minutes all the students had to walk to class, sit down, listen to a short introduction of the researcher about the program and then had to start the virtual laboratory. Despite the virtual lab and all the computers were set up, this took up to 10 minutes of each lesson. So the effective amount of time was around 35 minutes. To really have all the students to complete the virtual lab they have to be doing the virtual laboratory effectively for at least 45 minutes.

Finally the program that was used to create this virtual synthetic biology lab was PowerPoint. This program has a lot of limited options concerning programming and designing a simulation with interactions. PowerPoint is a very basic and primitive tool and does not provide all the options to let the virtual laboratory achieve optimally. The most important limitations of this program is the speed and smoothness of the visualisations and transitions. More importantly is the lack of ability to provide specific feedback. Since PowerPoint needs to make an alternative pathway for every possible mistake the students can make, it is impossible to give the students all the right and specific feedback they needed.

Implications for further research and educational use

For further research some recommendation can be made. First, only one design cycle was conducted during this study. So a next step would be to develop this virtual laboratory using the guidelines found during this research. Frequently design studies consist of multiple design cycles in which the results and feedback from each cycle is used to develop and improve the product. Therefore it is found that the learning activities, visualisations and information of this virtual laboratory can be used as a first concept for a virtual laboratory. Nevertheless as raised in the discussion, some aspects of this prototype has to be enhanced. Most importantly the second part has to be more interactive. For example by introducing a second construct or learning activity in which the students have to apply synthetic biology in a different setting, with less presented information. In this way there is also more room for scaffolding and to make it more challenging. And for pre-university students the speed of the text and visualisation could be increased. Furthermore the feedback has to be more specific when the students are dealing with the DNA construct.

For this study two modules on the ethical aspect of synthetic biology was used. However it is possible to implement this virtual laboratory in a different way in the curriculum. It is fruitful to test whether this virtual laboratory can be used without the modules. Moreover within this virtual lab synthetic biology is introduced.

Overall this research showed that this virtual lab contains learning activities that foster students' conceptualisation. Besides, guidelines are found to improve and develop this virtual synthetic biology laboratory even further. Future research and new design cycles should be conducted to establish a virtual environment in which students could experiment with synthetic biology and actively learn about this new field in biology.

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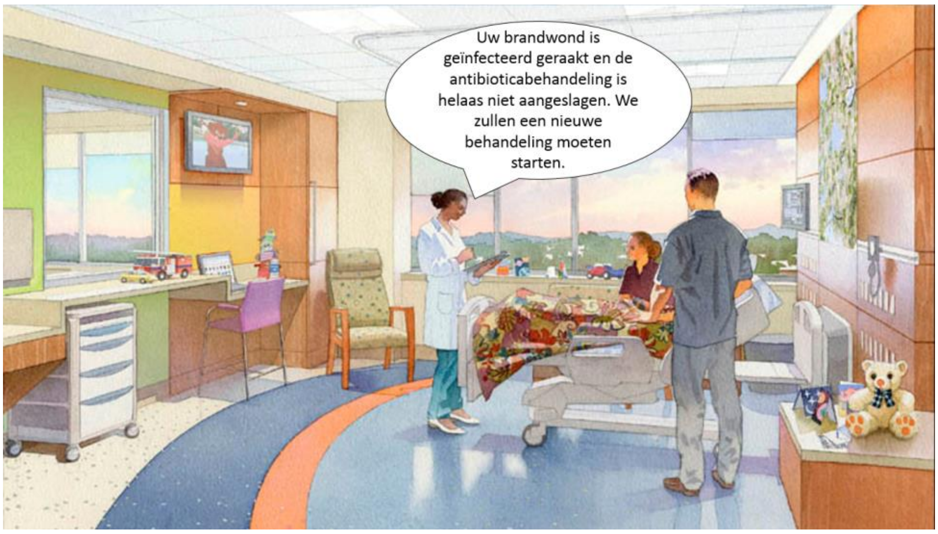
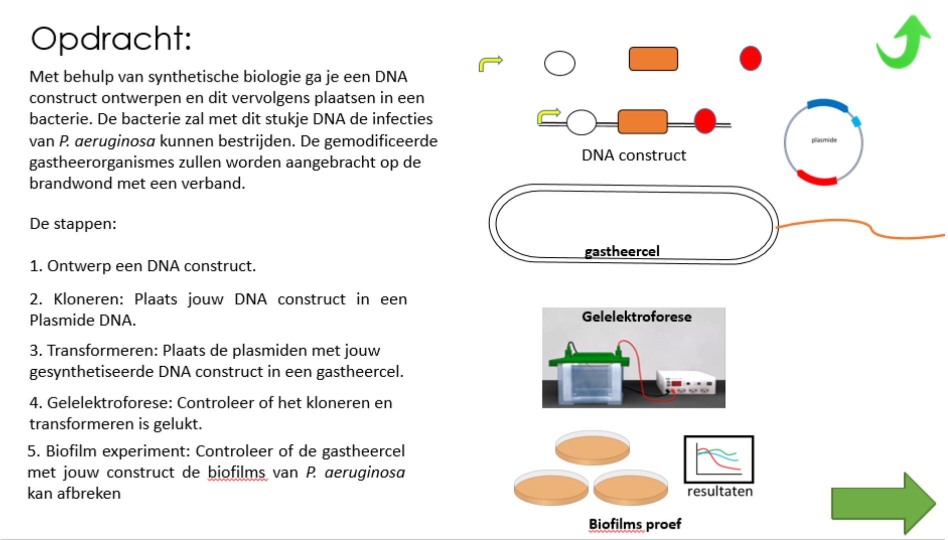
Appendix 1 Virtual lab screen shots.

LA1:

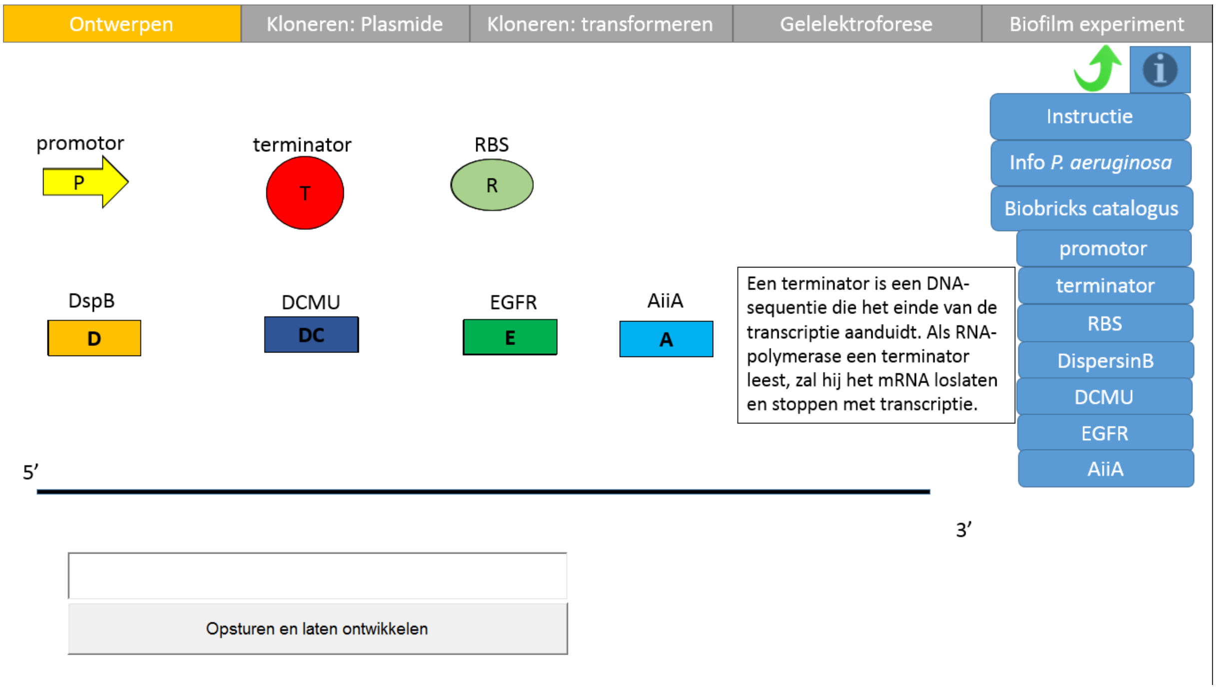


Introduction of the case.



Introduction of the assignment.

LA 2:



Making a DNA construct.

LA 3:

A feedback comment of the professor.

LA 4:

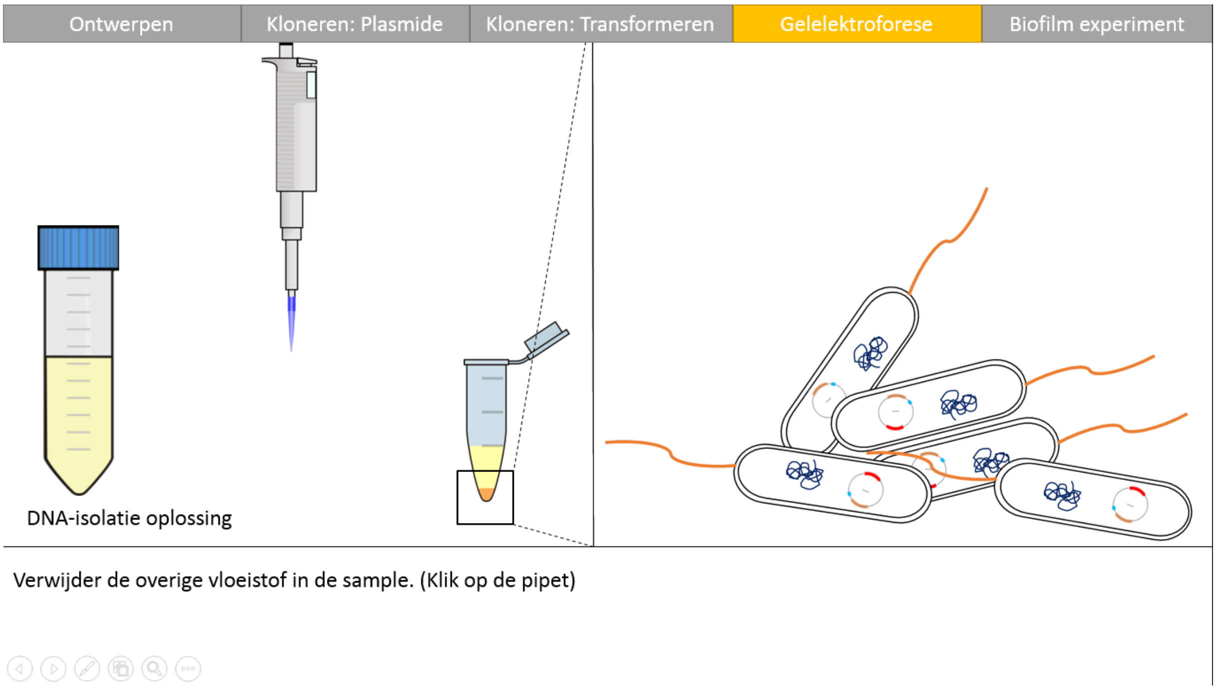
Het DNA construct moet nu worden geplaatst in een gastheercel. Hiervoor zijn veel mogelijkheden. Welke van de onderstaande gastheercellen zal het meest ideale resultaat geven? (klik op de naam van de gastheercel voor meer informatie)

Bevestigen

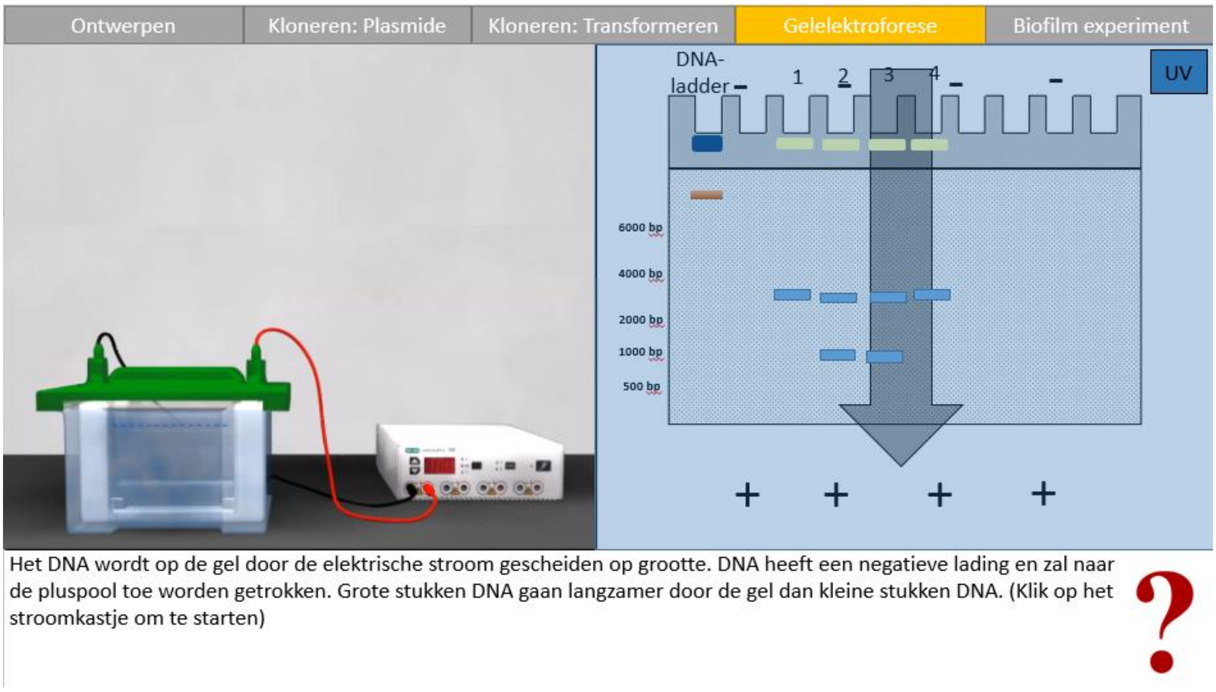
Pseudomonas aeruginosa	*Lactococcus lactis*	*Escherichia coli*	*Candida albicans*
			
P. aeruginosa is een gram-negatieve staafvormige bacterie, die bij de mens infecties kan veroorzaken. Doordat de bacteriën bij elkaar gaan zitten en zichzelf beschermen door het aanmaken van een biofilm kunnen antibiotica moleculen en afweercellen de bacterie niet bereiken. Communicatie tussen *P. aeruginosa* is mogelijk door middel van AHL-moleculen.	*L. lactis* is een gram-positieve bacterie, die leeft op de huid en het haar van dieren, dus ook bij mensen. *L. lactis* wordt ook gebruikt om melk of kaas te maken. *L. lactis* is een onschadelijke bacterie, maakt geen sporen en veroorzaakt zeer zelden infecties. Een bijzondere eigenschap van *L. lactis* is dat het goed kan overleven in zeer extreme omstandigheden.	*E. coli* is een gram-negatieve staafvormige bacterie, die voornamelijk in de darmen van dieren en mensen leeft. *E. coli* wordt vaak gebruikt als modelorganisme. Als *E. coli* op andere plekken in het lichaam terecht komt, door bijvoorbeeld een darmperforatie, kan het vervelende infecties veroorzaken.	*C. albicans* is een eukaryotische eencellige gist die leeft in het maag-darmstelsel en de urinebuis. Het leeft daar zonder nadeel of gevaar voor de mens. Echter onder bepaalde omstandigheden, zoals bij een antibiotica behandeling of een ernstige ziekte, kan deze gist soms 'overgroeien' wat leidt tot een infectie.

Choosing a host organism.

LA 5:

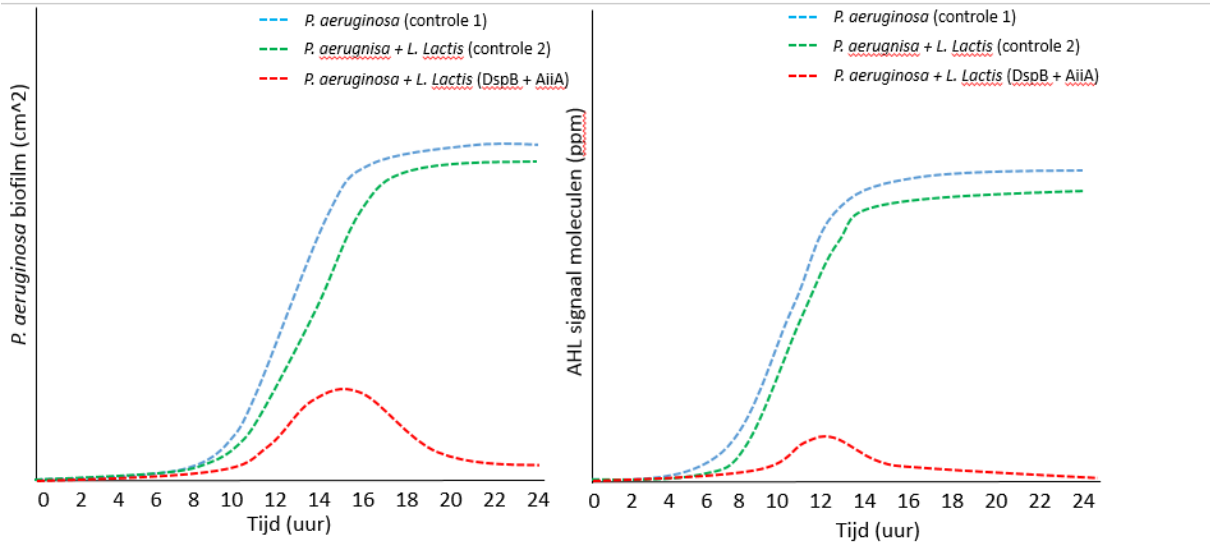


One of the techniques used in this virtual lab (isolating the plasmids).



Another techniques used in this virtual lab (gel electrophoresis).

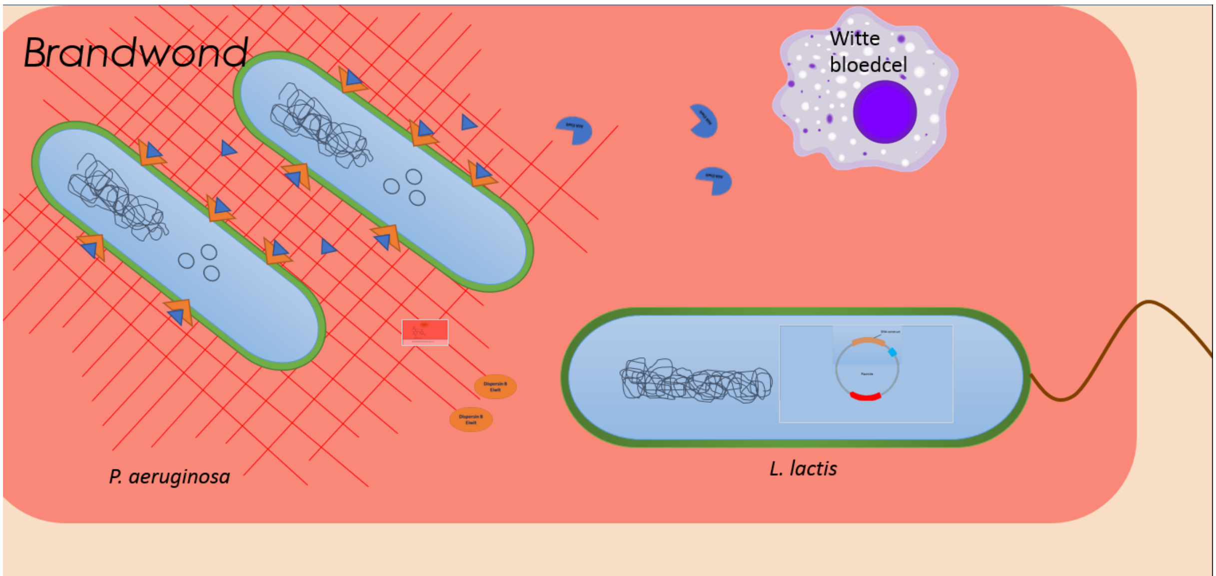
LA 6:



Om te kijken of het experiment succesvol is gebleken worden er twee factoren gemeten. De grootte van de biofilm en de aanwezigheid van AHL moleculen.

Interpreting the data.

LA 7:



Het Dispersin B eiwit breekt de biofilm af door de hydrolyse van N-acetyl-D-glucosamine polymeren te katalyseren. Klik op het Dispersin B eiwit voor een animatie.

Visualisation of the working of your designed DNA in a burn wound.

Appendix 2: Virtual lab question (translated from Dutch)

1. "Making the construct"
2. What is the difference between synthetic biology and synthetic biology?
3. What happens if the DNA-sequence CTTAAG/GAATTC is present twice within the plasmid and the restriction enzyme EcoR1 is added?
4. Why do the transformated bacteria get exposed to ampicillin?
5. About how many base pairs do the DNA-strings consist?
6. Which colonies are cloned successfully? Explain your answer.
7. Why do we make a petri dish with only a P. aeruginosa sample? (One word answer)
8. Why do we make a petri dish with L. lactis bacteria without the plasmids added? (One word answer).
9. What is checked when a non-modified L. lactis is added to the petri dishes with P aeruginosa?
10. Which effect does the DNA construct has on making a biofilm and which gene is responsible for this effect?
11. Which effect does the DNA construct have on the AHL-signal molecules of P. aeruginosa and which gene is responsible for this effect?
12. Are the results positive, and is with that this experiment successful? (Yes or no)

Appendix 3: Interview teacher for pilot study (translated from Dutch)

1. Name:
2. Date:
3. Class(es):
4. Years of experience as biology teacher:
5. Education:

De les

6. What did you think of the lab?

7. What did you think of the level?
   - For a 12th grader??
   - For a 10th or 11th grader after teaching genetics?

8. What did you think of the duration of the VL?

9. Where the steps as expected?
   - Would you like to change something? If so, what?

10. Do you think the learning goals are reachable with these learning activities? Why?

11. Do you have any other suggestions or comments on this VL?

12. Other questions?

Learning goals (extracted from the HLT fort his pilot study).

After using the virtual synthetic biology lab, students should be able to:

- Explain how DNA constructs are designed and synthesised by using BioBricks, like different genes, promotors, ribosome binding sites, terminators.
- Explain that these constructs are implemented via plasmids in organisms and tell which organisms are used, like bacteria, yeast and minimal cells.
- Name the different lab-techniques used for synthetic biology and explain their function.
- Explain that the newly designed and synthesized DNA is translated and transcripted within the organism to produce the desired products, like medicines, functional proteins (enzymes, antibodies, markers).
- Solve a biological problem using synthetic biology. (Therefore, choosing the right BioBricks, placing them in the right order, choosing the right host-organism and know which techniques to use and why.)

Appendix 4. Survey virtual laboratory (translated from Dutch).

To get more insight and develop this lesson on synthetic biology, we want to ask you to fill in the following questions. This data will be processed anonymously. Thank you.

General

1) Name (Pre- and last name): ……………………………………………………………………………

2) What is your age? ……………

3) What is your gender? …………………………………………………

4) Which profile do you have? ……………………………………………….. Subject of choice: …………………………………………..

The Virtual laboratory

5) What did you think of this virtual laboratory (pick one box)?

Totally not enjoyable	*Not enjoyable*	*Neutral*	*Enjoyable*	*Very enjoyable*
O	O	O	O	O

Additional notes:

………
………

6) Learning process

	Totally disagree	*Disagree*	*Neutral*	*Agrees*	*Totally agree*
The images, animations and visualisations were understandable/clear.	O	O	O	O	O
At the end of this VL I can explain what SynBio is to someone.	O	O	O	O	O
This virtual lab gave me feedback I could work with.	O	O	O	O	O

Additional notes:

………
………

7) Usability

	Totally disagree	*Disagree*	*Neutral*	*Agrees*	*Totally agree*
This virtual lab was too long.	O	O	O	O	O
This virtual lab was too short.	O	O	O	O	O
This virtual lab was controllable.	O	O	O	O	O
IT was clear for me what I had to do.	O	O	O	O	O

Additional notes:

……
……

Z.O.Z

8) Level

	Totally disagree	*Disagree*	*Neutral*	*Agrees*	*Totally agree*
This virtual lab connected to the prior lessons.	O	O	O	O	O
This virtual lab was hard to finish.	O	O	O	O	O
The information in this lab was clear and understandable.	O	O	O	O	O

9) If you found something hard within this VL, can you explain what and why?

……

……

……

10) If you could change anything, would you. If so, what would you change?

- O No
- O Yes, I would change:

……

……

……

Conceptualisation

11) Did you learn something from this lesson? If so, try to explain what you did learn. If not, try to explain why.

- O Yes, I have learnt:
- O No, because:

……

……

……

12) Try to write down, in your own words, what synthetic biology is:

……

……

13) Room for other comments:

……

……

Thank you for filling in this survey. Hand this in with you teacher or researcher of the University of Utrecht.

Universiteit Utrecht

Freudenthal Instituut
voor Didactiek van Wiskunde en Natuurwetenschappen

Appendix 5: interview questions (translated from Dutch).

Introduction:

About the interviewer: Eline Visser. Master Science Education and Communication. Utrecht University.
About this research: designing lesson material for synthetic biology, Synergene project.
The results will be anonymously processed. The interviewee has to agree.
This is not an oral test. So there are no good or bad answers. It is about your opinion and values.
Expected duration of interview: 15-20 min

General questions:

Date:
Name:
Gender:
Age:
Which class:
School profile:
How many years did you practise the subject biology:

Conceptualisation and understanding:

1. Can you give a description of synthetic biology in your own words?
2. Which problem had to be solved according to you?
3. How did you use synthetic biology to solve this problem?
4. Can you recall which BioBricks you needed or used to make the DNA-construct?
5. How did you handled designing you DNA-construct?
- Which steps did you take?
- Which information did you use?
6. Can you explain, in your own words, what happened with your DNA after you designed it?
- Which techniques did you see during the virtual lab?
- Why and how where these techniques used?

Usability and feasibility

7. Did you manage to finish the virtual lab?
8. Did you get stuck somewhere in the program? If so, where and why? Could the teacher or researcher help you getting further?
9. What did you think of the level? (Too easy/too hard?)
- What would have made it harder or easier?
10. What or which part(s) of this lab did you value educational? Why?
11. Were there learning activities that were less or not educational? Why?
12. What did you think of the instruction part or this program? (This is the introduction and the presentation of the problem and your assignment? Why?
13. What did you think of making the DNA-construct? Why?
14. What did you think of the part where you had to check your DNA in your chosen host organism? Why?
15. What did you think of the part where you had to interpret the results? (Why)
- Can you recall if you had the right genes? How do you know?

Connection to prior knowledge and lesson modules

16. Does this VL connect to your prior knowledge from your biology lessons?
- What did you think of the connection to the prior lessons on synthetic biology (so the modules)?
- Could you have done this VL without this module?
17. Is the example used in this VL a desirable application of synthetic biology? Why?
- Can you think of any pros and cons?

Concluding questions:

18. Would you want to change this VL? Why?
- If so, what would like to change? Did you miss something, or were parts unnecessary?
19. Do you have any comments or suggestions for this VL?
20. Do you have any other questions or comments?
21. Can I have your e-mail address so we can keep in touch if I have any questions about your answers?

Thank you very much for you answers and collaboration!