BIOLUMINESCENCE DESIGN diagnosing the influenza virus using genetically modified bioluminescent bacteria

JAN VAN DER ASDONK



This thesis is dedicated to my parents, Jan and Marleen.

Thank you for supporting me all this time, both mentally and financially.

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ABSTRACT

Influenza is an illness hard to visualize for human beings. Numerous symptoms of influenza are also found in many other influenza-like illnesses. Furthermore, people are mostly not aware of the infection while suffering from influenza or any other kind of illness with pandemic threats. They choose to go on about their daily lives, possible infecting their surroundings. Diseases such as this should be made diagnosable at home, before they are offered the opportunity to spread.

Using a fascination originating from bioluminescence - nature's method for making organisms display luminescence - a unique theoretically-sound concept was created. By genetically modifying bioluminescent bacteria to become sensitive to strains of the influenza virus, a novel biosensor is created to visualize illness.

With the detailed design of the product and interaction, people are now able to use this diagnostic tool to test their saliva for traces of influenza during times of physical discomfort. The product offers people the ability to test their illnesses with the ease of a thermometer, using small liquid capsules of genetically modified bacteria stored in their freezer. With this technique people can make the right decision, concerning their illness, with the right motivation.

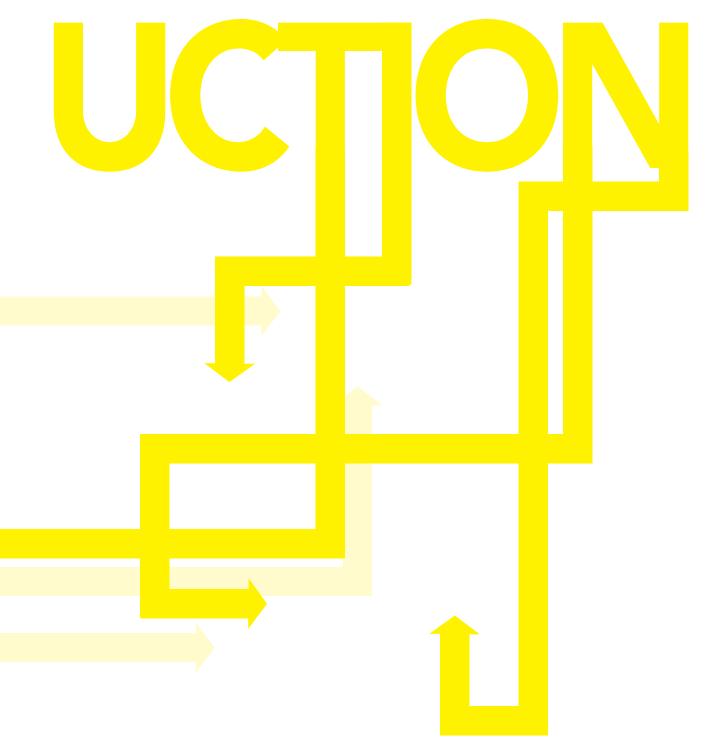
Even more, future developments might create the possibility of testing not only influenza, but many other diseases. Instead of trying to solve a pandemic with vaccines, the public can be diagnosed at home with the government sponsoring the distribution of the needed capsules.

Background

The background of this project resonates through the notion of using new technologies for the purpose of innovation. The goal of this project is to find a fascinating technology and apply it to a design context. Using this foundation, a unique product and interaction will be designed using an iterative design process with a mix of creativity, intuition, reflection, and various academic skills.

The first view will be a diverging one, where the identity and vision on the world are presented.

Next, a converging look will search for the subject of the graduation project, where later on a diverging approach will create the necessary creative input. Finally, the project will center on converging all these elements into a final design prototype. Upon completion, the project will take one last diverging look with an eye towards the future.



Goals

For this graduation numerous goals were formulated. The most important personal goal in this graduation project is to materialize a project worthy of the showcased design identity. It should present a creative and innovative concept with a certain fascination combined with a functional piece of design.

This brings us to the second goal: showcasing the author's creative design skills. For the graduation project the importance was felt to put a little bit more effort in the design aspect of the product as opposed to conventional projects at the Department of Industrial Design. The motivation for this decision originated from the fact most graduates spent less time on designing their prototypes than on making a working model. It is in the opinion of the author that a lot of design details and choices are often made carelessly, resulting in an unfinished design. This projects aims to create not only the most feasible working prototype possible, but also a very detailed and thoroughly iterated design form. This skill can ultimately be applied to future projects where such an in depth and detailed design approach is desired.

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...a creative and innovative concept with a certain fascination combined with a functional piece of design.

With the idea in mind of the multi-disciplinary designer, this project also tries to add some knowledge outside the scope of a traditional industrial designer. Practices such as microbiology, virology, laws and regulations, and the costs and benefits involved in the actual fabrication of the product offer more insights in the various fields accompanying this project. All of this to improve the communication with experts from other fields.

One of the more notable feedback points given by prof. dr. Loe Feijs on the graduation proposal was the fact that a lot of wisdom outside the faculty was going to be used. He therefore commented that the usage of experts from our own department would bring the needed balance concerning the utilization of outside expertise.

And finally, the bar was raised to a level as high as possible within the permitted frame of time. Mostly because this is the final opportunity to present the author's work at the Department of Industrial Design.

Introduction

Before the subject of this graduation project is elaborated upon, an identity and vision will be presented. They offer the diverging look at the world, albeit design inspired. The identity will determine the design character of the author, while the vision will reflect on the view of the world and time to come.





Identity

For as long as I can remember I have been searching for creative outcomes.

For some reason my character has always revolved around the rebellious act of creativity. During my years at the Department of Industrial Design

I have honed my creativity and added a tremendous amount of knowledge and skills to my repertoire.

My design identity revolves around showing people new things, centering on differentiating myself from other designers, by innovating on all possible aspects of a design process. I use this intuitive skill in conjuring ideas to create new and exciting products which not only alienate themselves from their competitors, but also raise a discussion on out-of-the-box thinking. They have a way of serving food for thought.

I strive to be original and do not hesitate to venture astray from conventional design practices. And in seeking to design such unfamiliar products I often throw myself in the deep end of the pool, working with new materials, approaches and fabrication methods. I enjoy this challenge and can easily work with experts on the subject at hand. I like diving into the deep end, ultimately the rewards are bigger.

"Jan has his head in the clouds, his hands in the mud, and his feet on the ground."

- dr. Koert van Mensvoort



...aiming to innovate into new and uncharted areas.

Vision

It is in my believe that there are an infinite amount of exciting things in the world around us, waiting to be discovered. With the help of a creative and design-thinking approach, these things can be formed into innovative and unique products to enrich our lives.

Most of these interesting things involve new technologies just waiting to be tapped and placed in a design context. While it can be relatively easy to take a mature technology and apply it into a product, it offers less challenge. The real challenge, accompanied by significantly more innovation, lies within the adoption of infant technologies. Not all the best solutions are found within our current world of electronics, and I prefer fields outside this present-day scope for purposes of potential innovation.

In order to come up with new and exciting innovations, these infant technologies need a push into maturity. This can either be done by aiding the development of the technology, or by the use of a speculative design. An example of such an approach is Tobie Kerridge's Biojewellery project. This undertaking mixes the bone tissue of a couple to be wed and grows new artificial bone tissue. This material is used to create two wedding rings, used by the couple^{Ref: 01}.

What I would like to do is create such exploratory speculative design products utilizing infant technologies, aiming to innovate into new and uncharted areas.

Introduction

The first step in creating the needed focus for the graduation project is the search for a suitable subject. During one of the many night-time hours of watching documentaries on the wonders of the natural world, bioluminescence was discovered. Its fascinating nature and mesmerizing effects were stunning to observe, as is the idea that nature can create such a wonderful phenomena.



ÖLOGY'

Introduction

Bioluminescence is a form of "cold light" emission, or luminescence. This means that less than 20% of the light generates thermal radiation. It is commonly confused with fluorescence (the emission of visible light by absorption of light at a different wavelength), phosphorescence (similar to fluorescence yet without the immediate emission of light), or refraction of light.

Currently the list of bioluminescent life is quite large. Ranging from almost 90% of deep-sea marine life to various insects, worms, and larvae. Even numerous fungi are known to exhibit bioluminescent properties.

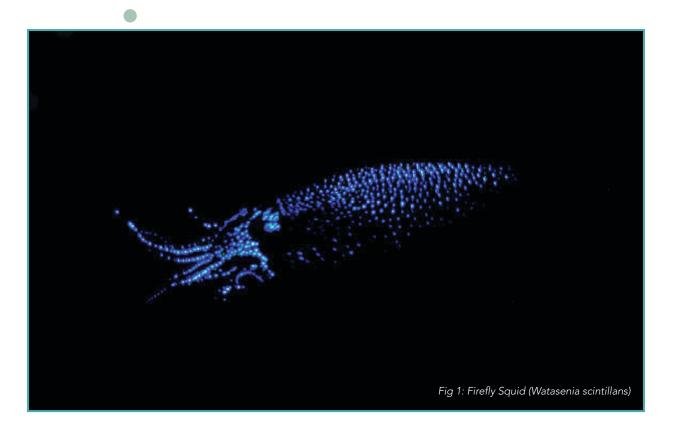
One can wonder how a property such as bioluminescence came to evolve and what its purpose is to the organism sporting this ability. At the moment there are five accepted theories for the evolution of bioluminescence traits:

1. Counter-illumination camouflage

Certain squid species are known to use bioluminescent bacteria to match the overhead environmental lights as seen from below. Photoreceptive vesicles are used to create the contrast of this illumination Ref: 02.

2. Attraction

Bioluminescence is often used to lure or attract prey. This property is most common among deep-sea marine life. A popular example is the anglerfish. A dangling appendage extending from the head is used to attract small fish within striking distance. Besides drawing in prey, this theory also covers the attraction of mates. The most well known bioluminescent example are fireflies. With periodic flashes of their light organ they charm mates during mating season.





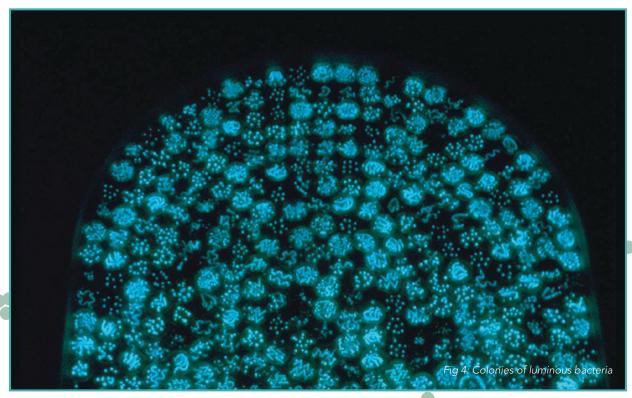
3. Repulsion

Similar to a squid using ink as a repellant, small crustaceans excrete a bioluminescent chemical mixture to ward off potential predators.

4. Communication

One of the most researched theories is the communicational aspect of bioluminescence. It is thought to play a role in colony aggregation of certain bacteria.





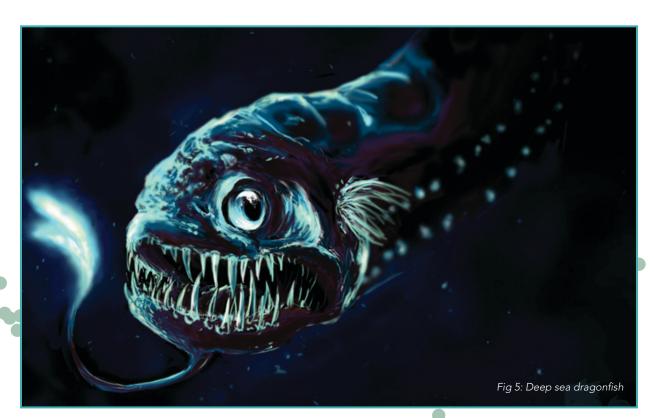
5. Illumination

Although bioluminescence is about the creation of light, not many species merely use it to illuminate their surroundings. While most marine bioluminescence is green to blue, the Black Dragonfish produces a red glow. This allows the fish to see red-pigmented prey, which are normally invisible. This is due to the water column filtering out the red wavelengths Ref: 03.

Growing a bioluminescent organism is not very complicated, and can be accomplished using the bioluminescent algae species Pyrocystis fusiformis. All that is needed is a clear container, sea salt, a grow light and timer, nutritional ingredients for the algae, and finally a starter culture of the algae themselves Ref: 04.









With the discovery of bioluminescence it was just a matter of time before we took control into our own hands and started working on artificial counterparts.

Chemiluminescence

Next to all the bioluminescent organisms, there is more to the luminescence story. With the discovery of bioluminescence it was just a matter of time before we took control into our own hands and started working on artificial counterparts. Enter chemiluminescence. As the name implies, it is the chemist equivalent of bioluminescence, tailored for a wide variety of products. Without going into all the chemical details, this technology is based onmixes two chemicals which result in a chemically-based luminescence.



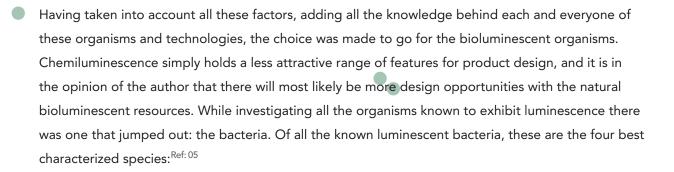




Vibrio fischeri

Before a choice was made on which bioluminescent organism or chemiluminescent technology to use, an exploration on all the available materials was done. All organisms known to express bioluminescent characteristics and chemicals known to obtain chemiluminescent properties were investigated on their usage for the graduation project. Factors weighing in on the decision which organism or technology to select are:

- Longevity or life-span of the illumination.
- Input required to create the illumination.
- Brightness of the illumination.
- Opportunities of the material in different design contexts.
- Availability of the material.
- Price of the material.
- Potential chemical hazards.



- 1. Photobacterium luciferum.
- 2. Vibrio phosphoreum (formerly Photobacterium phosphoreum).
- 3. Vibrio fischeri.
- 4. Vibrio harveyi.



What these bacteria need to grow is a culture medium called agar. Agar is basically a gelatinous substance derived from seaweed used in the growth of microbiological organisms. Furthermore, the bacteria only require oxygen to create the necessary energy for a bioluminescent reaction. In a nutshell: it is a constantly glowing liquid in colors ranging from yellow and green to blue, with the color being dependent on the species.

Because these species offer very similar characteristics a specific choice at this point in time is not vital for the continuation of the project. However, due to the availability, as described later on in this thesis, the choice was made to use the Vibrio fischeri species.

The Vibrio fischeri bacteria species, with its bioluminescent properties, is predominantly found in marine environments around the world. Planktonic Vibrio fischeri are found in just about any ocean in the world, albeit in very low quantities. This rod-shaped bacterium lives in symbiosis with numerous marine animals. An organic-based form of life, they move around using flagella; a tail-like protrusion at the back of the body^{Ref: 06}.

When the population of the bacteria species reaches a certain density, luminescence becomes visible. The bioluminescence is caused by transcription (the process of creating an identical RNA copy of a sequence of DNA, also called RNA synthesis) induced by population dependent quorum sensing Ref: 06. The bioluminescence follows, what is known as, a circadian rhythm. This means it is brighter during the nighttime than daytime.







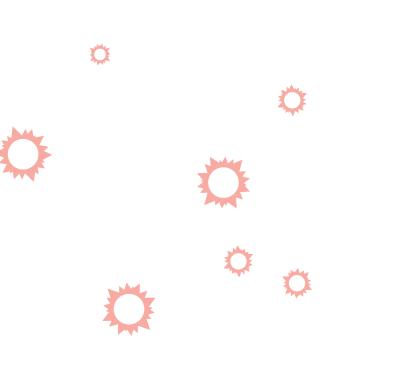
Introduction

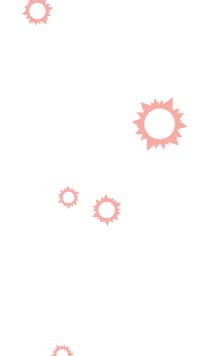
When thinking of the most obvious application when dealing with luminescent organisms something as simple as a lamp springs to mind. But with a lamp all you do is design a container for bioluminescent organisms. And the standards of this graduation project and of the faculty are far beyond merely making a lamp.

What this graduation aims to accomplish is designing a meaningful application using bioluminescent creatures. An application which uses the unique qualities of the chosen organism, offering more than just illumination.

The innovation would be to find an application wherein artificial light, such as LED's, cannot replace the bioluminescent organism providing the same functionality. Moreover, to obtain something truly innovative and unique, the project should result in something which is, to this day, not yet available or possible to the general public as a consumer product.

A preliminary creative session spawned a variety of concepts, yet none of these seemed to obtain the innovative appeal as stated above. So more points of view were investigated.





Pollution

The process of finding interesting and fascinating directions for incorporating a bioluminescent organism has been a challenging one. With a bioluminescent organism it can become quite challenging to see beyond the light aspect. A jar of fireflies is, obviously, not the preferred direction here.

During the quest in finding a vendor for the Vibrio fischeri bacteria species, a contact was made with a small company specialized in river water pollution detection. This company, microLAN, uses the bioluminescent bacteria species Vibrio fischeri for the detection of water contamination.

As microLAN's website states: "It still is impossible to analyze all chemical substances, which are brought into nature by man. Scientists suggest there are around 100,000 dangerous chemical substances and even with the most advanced instruments it is still not possible to detect them all. With the help of bioassays a much broader view of the possible dangerous effects can be analyzed there where it is most important: nature itself! With analytical / chemical testing only 5% can be detected,



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...where our artificial counterparts cannot match what this nature-based technology has to offer.

specially in waste and river water" Ref: 07.
microLAN uses Vibrio fischeri by mixing it with
the river water they want to test. If any pollution
is present the bacteria will react, leading to a
loss in quality of life, as they are being affected
by the pollution. And since the quality of life is
directly linked to the luminosity, the bacteria
glow less or not at all when polluted. And all of
this is detected by a sensitive light sensor. After
evidence of pollution has been found, resulting
steps are undertaken to find out the kind of
toxins that have been located.

This results in a very simple, yet broad net for pollution detection. Something which has not been artificially reproduced. In a way, these bacteria are a sensitive copy of human beings, being exposed to and finding the very particles that contaminate our waters.

This technique showcases a unique application for bioluminescent bacteria, where our artificial counterparts cannot match what this nature-based technology has to offer. A technology purpose such as this points itself into an interesting direction.



Influenza

Illness

In finding a new innovative application using the bioluminescent bacteria, the idea of creating something which is not artificially reproducible as of yet has be major strong point in the creative process.

In seeking things which are hard to visualize and hold meaning for us, people, the concept of illness emerged. Although there are numerous diseases, one has been notoriously hard to visualize, affects thousands of people every year and has been the backbone of many pandemics across the centuries: influenza.

Influenza, or mostly referred to as the flu, is an infectious disease infecting birds and mammals. Caused by RNA viruses (using RiboNucleic Acid as its genetic material Ref: 08, symptoms include chills, fever, sore throat, muscle pains, severe headache, coughing, weakness/fatigue and general discomfort. More serious cases could include pneumonia, which can be fatal particularly among the elderly and children Ref: 09.

The virus is spread through the air, mostly by coughs or sneezes, with small aerosols containing the virus. Next to that the virus is spread through direct contact with bird droppings or nasal secretions, or by coming in contact with contaminated surfaces^{Ref: 10}. An estimation on the deaths caused by influenza during seasonal epidemics range in between 250,000 and 500,000 each year, and millions more in pandemics^{Ref: 11}. It is estimated that the total economic costs of a severe pandemic such as Avian Influenza A (H5N1) could ramp up to 675 billion dollars. And this only counts the consequences of such a pandemic in the United States. Global figures will be off the chart^{Ref: 12}. Inactivating the virus can be achieved by applying sunlight, disinfectants or detergents, and frequent hand washing reduces the risk of infection^{Ref: 13}.

The problem with influenza is that it is easily confused with other influenza-like diseases.

Symptoms resulting from having caught a common cold, side effects of various drugs and signs from a diverse range of other diseases can all appear as an influenza infection Ref: 14. Combining the number of influenza-like illnesses with the actual cases of influenza, each adult and child can average 3-6 and 6-9 cases of possible infection each year Ref: 15. This would create the opportunity that a product detecting influenza, on average, will be used around the same amount of times per person per year. Of all these cases, roughly 20% will actually be infected with influenza during a regular season. During an epidemic, this number is estimated to increase to around 60-70% Ref: 16.

Behavior

Nonetheless, the problem does not stop with the mere existence of the influenza virus. Another predicament lies with the way people deal with influenza.

In most of western civilizations, people experience the need to perform and can be under severe work pressure. When faced with a cough or a little feeling of physical discomfort, they tend to ignore these feelings and continue their ordinary lives. Who wants to be perceived as weak in such a strong and driven world?

Now this demonstrates the root of the problem. If these people, infected with the influenza virus, continue their day-to-day operations they might contaminate their surroundings and infect other people. And this is exactly how easy pandemics spread. The problem is in knowing when you are ill or not. The right choice comes afterwards, based on a better understanding of one's physical state.

What if you could create the possibility for people to find out if and when they are actually carrying the influenza virus and are in danger of infecting other people around them? With such a tool people could make the right choice before they start spreading the diseases they might be infected with.



Conceptual Process

Private or public versus active or passive

One of the first things to consider when dealing with a product able to monitor the infection of influenza with people is whether it is a private or public artifact. One can imagine that your illness or infection is not something you involuntarily wish to share with others. It might put a stamp on how you are perceived by others, or deny access to public places or even countries.

Second, there is the question if this product ought to incorporate an active or a passive interaction. In other words: should you actively test yourself or could the device measure illness by merely sitting in a room?

A first creative session was done, creating various concepts and placing them inside a diagram comparing their individual characteristics on a scale of active to passive and private to public.

It became obvious that all of the *public* concepts held too much of a control-type functionality, wherein they might create undesirable communal situations. Also, the *private* concepts would create the opportunity to design products in a desired size constraint. So in this case the *private* concepts have a preference above the *public* ones.

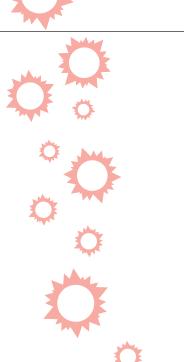
When comparing the *active* versus the *passive* concepts there is a certain predilection towards *active*. The main motivation for this is getting people to actively become aware of the fact they can measure their illness. The idea is that the active interaction creates awareness on their wellbeing and the status of this well-being, and adds a little bit more value as compared to a passively monitoring device: you have to choose to use it.

Comparison study

In order to provide a better insight into how the product might be used, similar diagnostic products were examined. These tools all focussed on visualizing something normally invisible to our naked eye. The four items investigate were: the pregnancy test, your tonsils, the weighing scale, and an electric toothbrush.

- *Pregnancy test:* something you use only occasionally, and only buy when needed. Using it takes little effort and produces almost an immediate result. The result is absolute, either yes or no.
- Weighing scale: something you buy once and always have. The usage is a couple of times per week (which varies greatly form person to person) and provides you with something to reflect upon.
- *Tonsils*: something on your body, they are always there. You are not aware of their existence until they tell you something has changed, like when you are getting or are ill. They blend into your life.
- *Electric toothbrush:* you use it daily and have to monitor the results yourself. It does tell you however when it thinks you have brushed your teeth good enough, though this is only based on time. It trusts you use this time to brush your teeth in an orderly manner.

This analysis was taken into account when conceptualizing the final direction for the project.



Collecting tissue

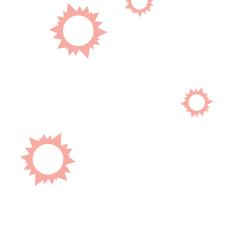


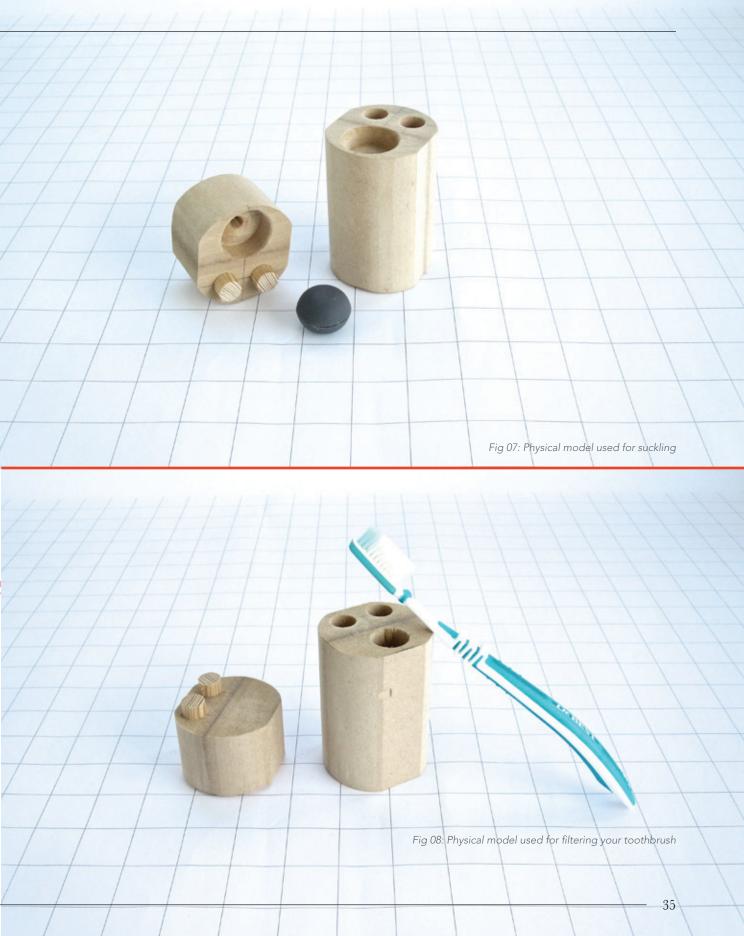
CONCEPT

Iteration 1

While there are numerous ways of collecting the necessary tissue to use for the detection of influenza, not all methods will be suitable in a product for all ages. To discuss this iteration with other designers, a series of physical models were made. These models illustrated the activity required to take the tissue for analysis in various methods. These methods are:

- Using a small liquid capsule to suckle on, gathering saliva.
- Rinsing your toothbrush in a cavity after having used it to brush your teeth, collecting saliva.





The other two methods are:

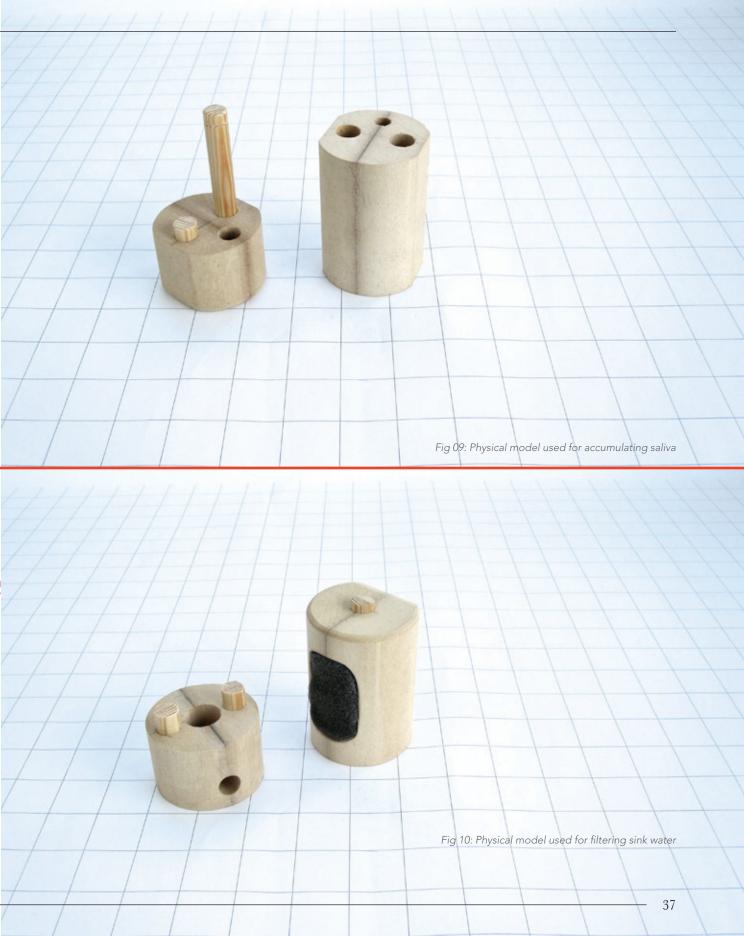
- Suckling on a small stick, accumulating saliva.
- Filtering all the necessary tissue from your sink by applying a product strainer.

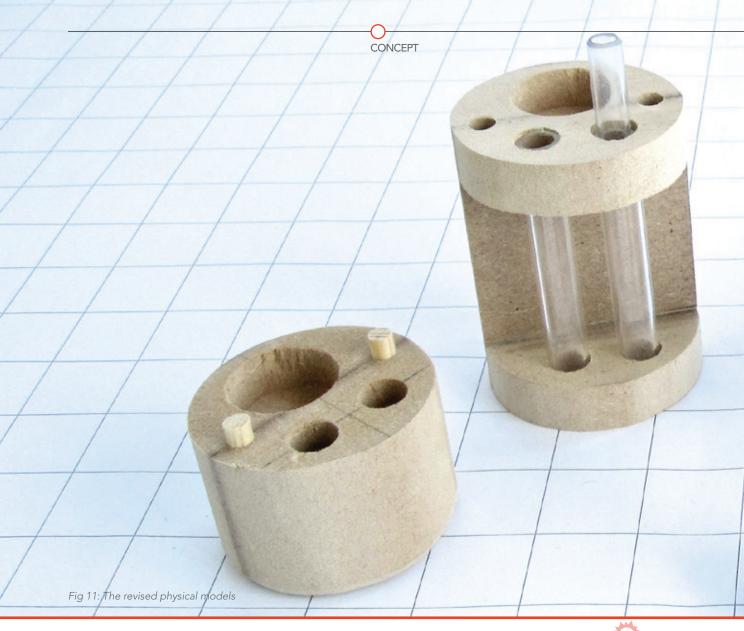
By confronting people with these models and an explanation of the functionality, some qualitative results were acquired. Using a small question and answer approach, the people were triggered to explore and discuss the models. The most valuable findings were based around the five basic questions used in the confrontational session:

- 1. What do you think are the strengths and weaknesses of these models?
- 2. Can you think of reasons why you or any other individual would not adopt or use this kind of functionality?
- 3. Do you have a preference towards any of these models? If so, how come?
- 4. Would you change anything considering this model? If so, what and why?
- 5. Do you have any further remarks?

Based on the discussions with twenty fellow designers, conclusions were drawn on the feasibility and suitability of each of the methods. The results were used in the next iteration.



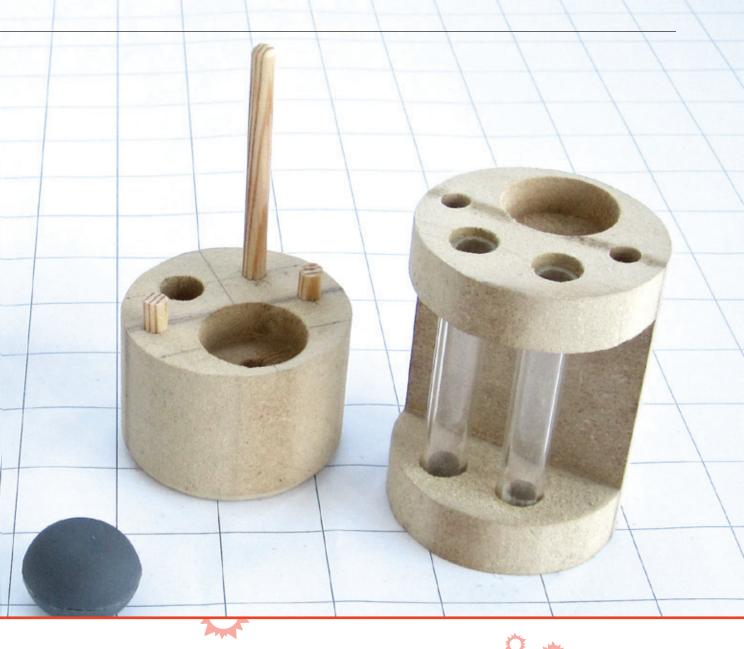




Iteration 2

Using the results from the first iteration, a second iteration was done. The most promising and suitable functionality was explored using more in-depth physical models. After the user confrontation of the first iteration the conclusion was drawn that the physical models exploring the functionalities of using your breath and saliva are the most suited ones for the further exploration of the concept.

In the second iteration another set of MDF models were made to explore the functionalities of breathing and collecting saliva. In these models glass was used to showcase the bioluminescent bacteria compartments, making it slightly more clear for the observing users in the upcoming confrontational session.



After a second confrontational session it became quite apparent that the model where saliva is collected using a protruding tool will be most suited for the broad target group. This conclusion is based on the assumption that the youngest and oldest people will have some trouble using a device where a deep breath is needed to obtain a quantifiable result. Besides, infants might not understand the question to provide a deep breath, and the geriatrics might lack the strength to provide this deep breath. Also, people of a very young or old age are easily admitted a saliva-tool by a second aid. Furthermore, influenza viral particles are present in the saliva when infected with the virus of offering a good theoretical method for measuring the illness^{Ref: 16}.



Liquid capsules

With the choice made to incorporate the bioluminescent bacteria, a method for inserting these bacteria suspended in liquid will have to be devised. A discussion with Joep Appels, managing director of microLAN, and hands-on experience with the Vibrio fischeri bioluminescent bacteria species resulted in some more insights. According to Joep Appels, the bacteria can only survive for about 14 days at room temperature. However, when frozen, these bacteria can be stored almost indefinitely. Making this the ideal storage solution for home usage: liquid capsules filled with Vibrio fischeri, stored in your freezer.

Final concept

The product

The final product uses your saliva to detect possible traces of influenza. The intended use is for people to test their illness in times of physical discomfort. A tool will be designed to capture saliva and mix it with the bioluminescent bacteria.

These bioluminescent bacteria will be genetically altered to become sensitive to strains of the influenza virus. If there is not biochemical reaction, the bacteria will keep on glowing bright green. If disease is present, the bacteria will die and change into a darker, non-illuminating liquid. It is this change which notifies the user of the present illness.

Small liquid capsules will be stored in your freezer and used when a diagnosis is needed. These capsules can be purchased externally, while the main product is only acquired once.

Name

Obviously a product needs a name. Listing the various attributes of this product created a small list:

- Test.
- Diagnosis.
- Influenza.
- Doctor.
- Personal.
- Private.

Using these words the choice was made to go for an amalgamation of influenza and doctor.

Influenza, because it is the illness diagnosed and doctor, because the products acts as a personal doctor for the home environment.

The name had to be short, simple, and to the point. It should be catchy and have a certain "medicinal" feel to it. Shortening influenza to "flu" and doctor to "doc" and combining both resulted in "fludoc." To add a little bit more distinction between both words the choice was made to display the latter in caps: "fluDOC," at it is the more dominant factor to display for a product. Working with a little font design resulted in the following name:



Fig 12: The Logotype

To add a more visually representing trait to the logo, a symbol will have to be added. Using the already iconic top view of the product, this symbol was easily found.



Fig 13: The entire Logo

Also, this symbol can be used as the new token to indicate a human virus, replacing the symbol commonly used for biological hazards. It might even be pushed as the form for viral testing.



Fig 14: The biohazard symbol



ACGTCAGTAL ACAGCALL TCALL ATCGGATAT AGTALACA TAI ACGTCAGTAL ACAGCALL TCALL TCA

Introduction

One of the emerging fields which potential interest to designers is the discipline of synthetic biology. This new field of biological research merges science and engineering in order to design and construct biological functions and systems.

Nature holds a vast and untapped potential for designers. New discoveries are made all the time, some offering new creative inspiration for emerging designers, some providing the world with technological improvements outgrowing their artificial counterparts. Synthetic biology aims to use these natural processes to create improved products and technologies to enrich our times to come. In the opinion of the author, it is one of the great emerging fields for future-minded designers to consider and even master.

GTACTATCAGTCGACCAAGTTCAGTCAGTACTGCA
TACTATCAGTCGACGTCAGTACTGCA

CTATCAGTCGAGCTAGTACTAGACGAAGTACTGC

AGESTIGICA GAS

CGACGTCAGTACT

IATCGAGTAGTAACA

GCGGATATATATA

GTACTATCAGTCGACGTCAGTACTGCATGCGTA

AGTACTGCA

Project assumptions

A research study was done in order to provide the necessary validation for the proposed genetic modification. The motivation behind this study was to ensure assumptions made regarding the subject of genetic modification were not made carelessly.

From here on we reach the two assumptions necessary to make this project feasible, and possibly successful in the near future. One, the brightness of the bioluminescence emitted by the luminescent bacteria - in this case the species Vibrio fischeri - should be genetically altered to produce enough luminescence so it is viewable under regular in-house lighting conditions. And two, the fact that a bacteria can be made sensitive to influenza virus types, which will diminish its quality of life. Ultimately resulting in a bacteria species which will exhibit less light when in contact with influenza.

GTACTATCAGTCGACCAAGTTCAGTCAGTACTGCA

TATCAGTCGAGCTAGTACTAGACGAAGTACTG

The origin of bacterial modification

The basis for the assumptions originate from the work of the J. Craig Venter Institute^{Ref: 17}, or JCVI. The origins of this institute date back to the earlier work of Dr. J. Craig Venter, a genomic researcher, also known as the "*Richard Branson of biology*" Ref: 18. Together with his team he started decoding organisms by a new revolutionary technique called Expressed Sequence Tags (or ESTs). Using this procedure, genes could be rapidly discovered and analyzed.

By using their new computing and computational tools, including a new DNA sequencing technology, the team sequenced the first free living organism, Haemophilus influenzae^{Ref; 19} in 1995. After sequencing and investigating 50 microbial genomes, and various important mammals, the ultimate goal would be the sequencing of the human genome. In 2001 the entire human genome was mapped by Dr. Venter and his team and published at Celera Genomics^{Ref; 20}.

In sequencing all these genomes and researching all the DNA encountered, a Registry of Standard Biological Parts was founded in 2003 by MIT^{Ref; 21}. Founded by Ron Weiss of Princeton, Michael Elowitz of Caltech, and Drew Endy of the Massachusetts Institute of Technology, this gigantic library currently houses around 3200 genetic parts that can be "mixed and matched to build synthetic biology devices and systems" Ref; 22. The registry has been growing even since, and offers compelling insights into the future possibilities of genetic modification. A quick search using the query bioluminescence shows 21 examples of genes that deal with bioluminescence, a promising insight in future genetic alterations.

Finally, in 2006 the JCVI was formed through the merger of several affiliated and legacy organizations: The Institute for Genomic Research (TIGR), The J. Craig Venter Science Foundation, The Joint Technology Center, and the Institute for Biological Energy Alternatives (IBEA). At the moment the JCVI houses more than 400 scientists at various locations in the United States of America and is a world leader in genomic research^{Ref: 20}.

STACTATCAGTCGACGTCAGTACTGCATGCGTA

Present day, the JCVI is exploring the creation of a synthetic chromosome and organism having successfully transformed one species of bacteria into another. Also, teams have sequenced a variety of important infectious disease agents and are hard at work understanding the evolution of several viral genomes such as influenza and coronavirus^{Ref: 20}. Next to that there are also plans underway to create microbes that produce hydrogen for use as fuel, for which the company Synthetic Genomics was founded^{Ref: 23}. Furthermore, on Thursday the 24th of January, 2008 a JCVI team announced they made a significant step toward the creation of synthetic forms of life. The team reported they had manufactured the entire genome of a bacterium by stitching together its chemical components^{Ref: 24}. Having previously constructed the complete DNA of viruses, this was the first time for a bacterium, as they are far more complex.

This opens up the exciting possibility of custom-made organisms. The ultimate goal, envisioned by synthetic biologists, is being able to design and print an organism on a computer, with the resulting DNA ready to be implemented into a cell to produce a custom creature. As Dr. Venter states: "What we are doing with the synthetic chromosome is going to be the design process of the future."

While definitely on a quest of synthetic biology, JCVI is not the only player in this exciting field of bioengineering. George Church, a professor of genetics at Harvard and a leader in the field, is pursuing the design and manufacturing of complicated biological circuitry. The earlier work focussed on grabbing the media attention via creations such as blinking bacteria and light-sensitive bacteria^{Ref: 25}, in collaboration with Stanislas Leibler of Rockefeller University. But now a variety of experts are hard at work in making a major impact on medicine and industry. For example, Christina D. Smolke, as assistant professor at the California Institute of Technology is "trying to develop circuits of biological parts to sit in the body's cells and guard against cancer" Ref: 25. Jay D. Keasling at the University of California, Berkeley, is "trying to take up to 12 genes from the wormwood tree and get them to work together in E. coli bacteria to produce artemisinin, a malaria drug now extracted from the wormwood tree" Ref: 25.

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Nonetheless, there are still some great challenges in the field of biophysics before we can actually start making fully-functioning organisms. As quoted from LingChong You, lead researcher at Caltech and assistant professor of biomedical engineering at Duke; "You write the same software and put it into different computers, and their behavior is quite different. If we think of a cell as a computer, it's much more complex that the computers we're used to" Ref: 25. And it is for that reason that some scientists state it might be a quite the test to get biological engineering as predictable as for example bridge construction. Additionally, an expert on the matter, professor Arnold from Caltech says that even getting the most simple bioengineered application to work in any environment is complicated: "There is no such thing as a standard component, because even standard components work differently depending on the environment" Ref: 25. And there are safety factors to mind when dealing with such an unpredictability.

But it must be said that with all these wonderful notions of modification, it is nothing compared to what nature has already accomplished with cell design. "We have micro-organisms that live in such a strong acid or base solutions that if you put your finger in, the skin would dissolve almost instantly." Dr. Venter goes on saying: "There's another organism that can take three million rads of radiation and not be killed. Its chromosome gets blown apart, but stitches everything back together and just starts replicating again" Ref: 22. Four billion years of evolution has most certainly brought us a lot to contemplate. And with all of this information published originating from earlier years, one can only imagine how far these scientists have come at this point in time, when publication has not yet occurred.

As can be concluded form the above dissection, the field of biophysics or bioengineering is a fast-growing one, and with promising future expectations. When observing these results, it can be deducted that nothing seems out of reach.



Validating the assumptions

More luminescence

From the two, the first one seems easier to accomplish. One can imagine that by synthetically engineering the bioluminescent organ from a bioluminescent bacteria species, a brighter bioluminescence reaction is achievable. Furthermore, research done in the field of chemiluminescence has already concluded the possibility of much brighter chemical reactions in the development of synthetic bioluminescence.

Sensitivity to influenza

The second part of this validation, and the most complex, involves the creation of a synthetic bioluminescent bacteria species sensitive to a strain of the influenza virus.

Local development

Although this concerns an industrial design graduation project, time was spent in understanding basic microbiology and virology. The motivation behind this short study was not only to enhance the level of communication towards experts and specialists regarding the subject, but also to search for possible directions for the actual creation of the synthetic bacteria species sensitive to influenza.

During this brief study three possible leads where identified. The first of these concerns a virus type that infects bacteria, called a bacteriophage. They are among the most common and abundant organisms on our planet^{Ref: 26}. One of the problems with infecting a (bioluminescent) bacteria with a virus like influenza is its target. Influenza does not contaminate any bacteria specifically. The idea behind using bacteriophages is bridging the gap between influenza and a bacteria species. It might be possible to have influenza make an impact on a bacteriophage which is specifically designed to target a certain species of bacteria. This would eventually also create the needed sensitivity with the (bioluminescent) bacteria.

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Another approach would be to incorporate the technology behind BioDetection Systems' CALUX cells Ref: 27. These cells are engineered to produce light when in contact with specific chemicals. The option here is to adapt the CALUX cells to detect strains of influenza and react accordingly by producing light visible to the naked eye.

Finally, another possibility would be to incorporate the signaling characteristics of the Green Fluorescent Protein, or GFP^{Ref: 28}. This protein exhibits bright green fluorescence if exposed to blue light and the GFP gene is used in the creation of various biosensors and acts as a reporter gene^{Ref: 29}. This substance could be used to trigger luminescence instead of having to genetically adapt an organism to exhibit bioluminescence. Unfortunately, GFP is used in the medicine industry and is quite hard to gather. At this point in time it is priced at around 5,000 euros for 1 milligram^{Ref: 30}.

Conclusion

Based on the recent developments in the world of synthetic microbiology the conclusion can only be drawn that making bioluminescent bacteria sensitive to strains of the influenza virus is a goal reachable within our near future. However, this will still be a tall order to accomplish, even for the experts of the field. The actual realization of such a technology will most likely involve a lot of money, experts, and time before comes to fruition.

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...a tall order to accomplish, even for the experts of the field.



DESIGN

Introduction

With a personal preference towards design and, as stated in the chapter dealing with the graduation goals; this is an area explored to great depths. Successfully shaping a product's form is a powerful yet complicated skill to acquire. However, it is also a vital ability to obtain as a designer.

The problem with designing a product sporting a new functionality is the perceived functional appearance of the product. For example, the shape and design of a phone tell you it is a phone. This is based on your cognitive memory of what phones look like and their respective functionalities. Yet what will a product which diagnoses your illness in a unique and new method look and feel like?

In order to overcome this difficulty the design was dissected into perceptive elements. Each of these elements was designed to provide a different awareness on its functionality and emotion. These perceptions were based on moodboards visualizing products with correlating expressions. Finally, these design details are divided into two domains: the exterior and interior, each of these with their own guidelines.





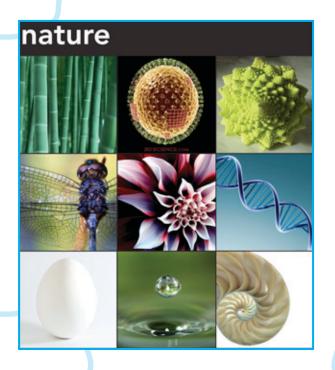




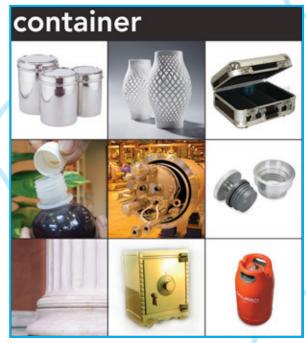


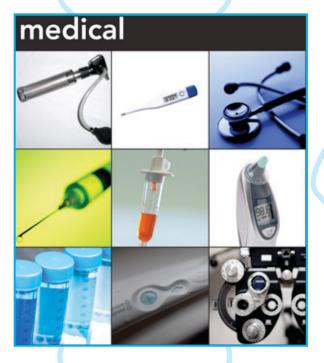


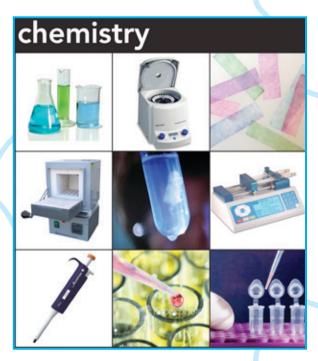
Fig 15 - 22: The moodboards used as inspiration for the design process.

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Exterior

Hygiene

Hygiene is one of the most important expressions of the exterior of this product, not only with the visual appearance but also with the qualitative measurement capabilities; nothing should contaminate the reaction between the modified bioluminescent bacteria and the influenza particles.

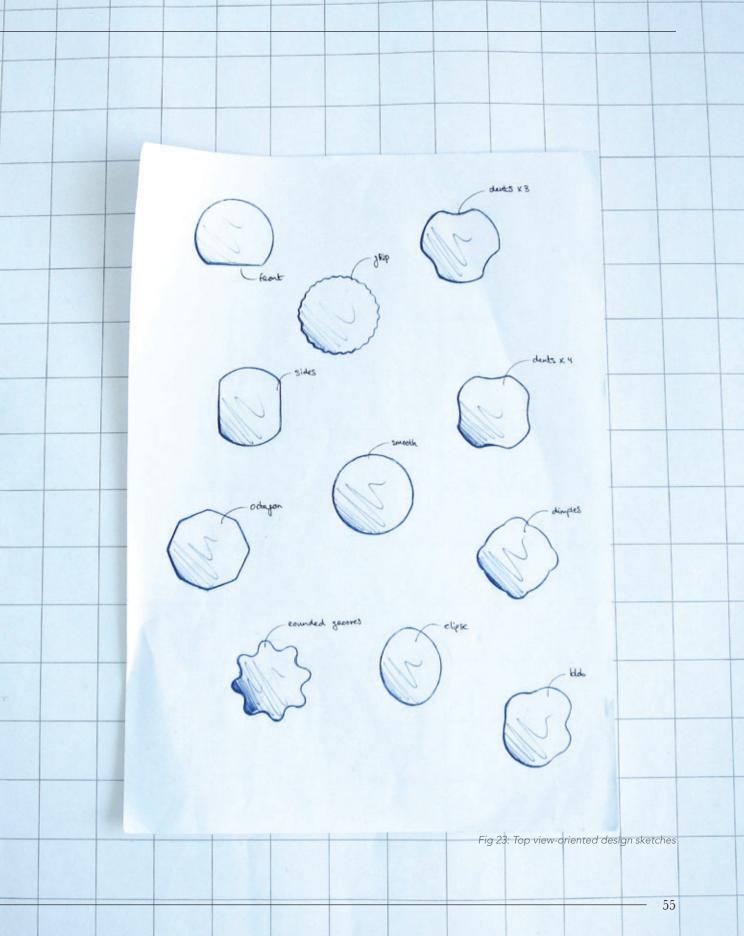
With hygienic products it is important to not use many horizontally-placed lines for dirt and other unhygienic material to gather. The usage of a more vertically-oriented design is favored.

Inconspicuous appearance

The reason for a less detectable form is rooted on the possible growth of mysophobia. When confronted with the product's appearance and the knowledge it offers the option of detecting illness, it is possible a person might question his or her physical state, resulting in a usage far above what is considered to be necessary. While this might increase sales of the liquid capsule containing the bioluminescent bacteria, it is far from a preferred induced behavior.

This conclusion results in a clear guideline considering the exterior design: it is vital to provide the exterior with a very minimalistic look, blending into the bathroom environment. Also, because this product will most likely be observed from the side when placed on a bathroom cabinet, it is favorable the design has a subtle side view. Having said that, to express the uniqueness of the product in an iconic matter the top view can be used.

When combining this guideline with the one dealing with hygiene, the conclusion is drawn that the design should be an extrusions from a top-view oriented shape.



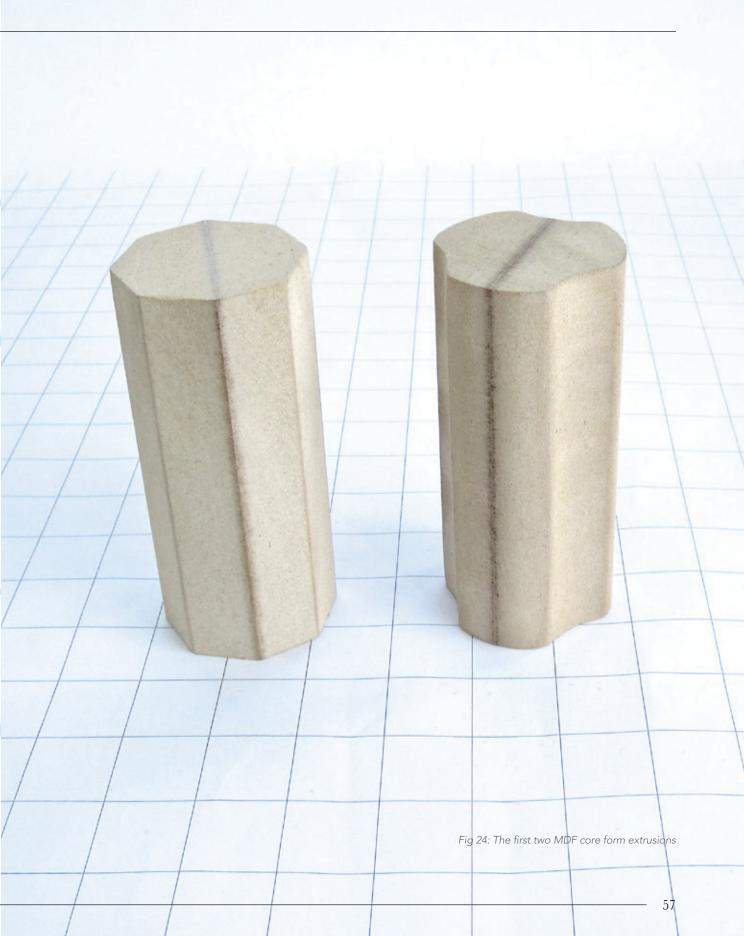
Size

With this product being destined for your bathroom cabinet or shelf it is easily sized against its fellow bathroom products. With the goal in mind to keep a discreet expression with the exterior design, size-wise it should also not stand out. Size comparison with similar bathroom shelf products yielded approximate dimensions.

Sketches

Using the preceding design guidelines various top view sketches were made. While sketching, one shape jumped out based on visual appearance and preference. To experience this shape first hand, a preliminary 3D model was made out of MDF together with another top view with a more rectangular appearance.

Both models measured in at 120mm tall and 56mm in diameter.





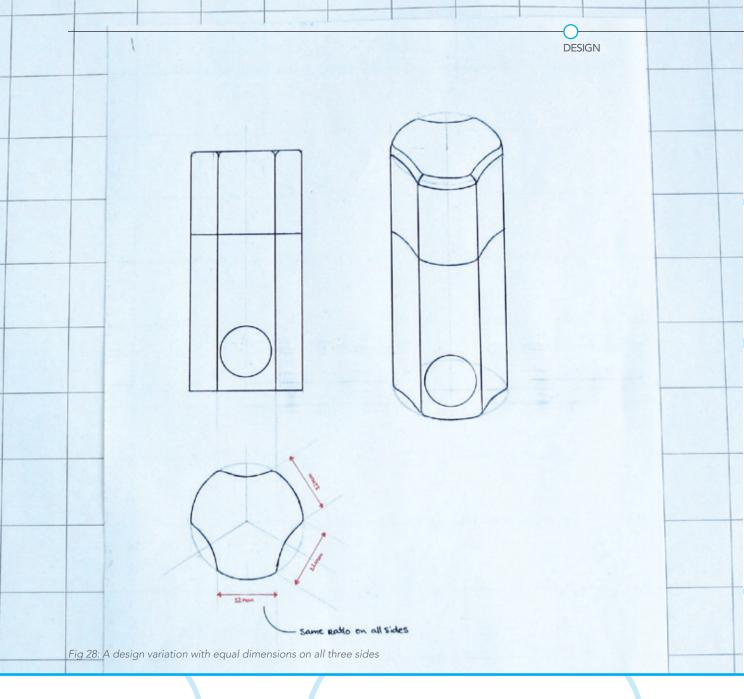


...a perfect fit, for smaller and larger hands.

Using these two models some confrontational sessions were done. Discussing these shapes two things became obvious. First, although the more rectangular form expressed a rather "precise" and "accurate" feeling, it felt out of place for the intended application. A preference was directed towards the more organic model. Second, despite the fact that the diameter afforded for an easy grip, it was still slightly oversized for hands of all ages and sexes.

With a clear personal preference towards the organic form, a third model was made, this time only 100mm tall and 46mm wide. This proved to be a perfect fit, for smaller and larger hands.

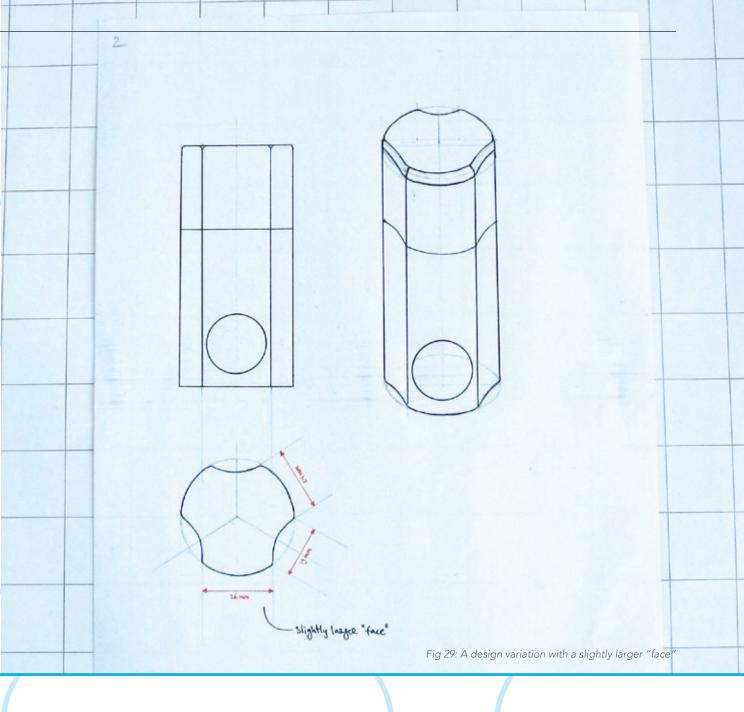




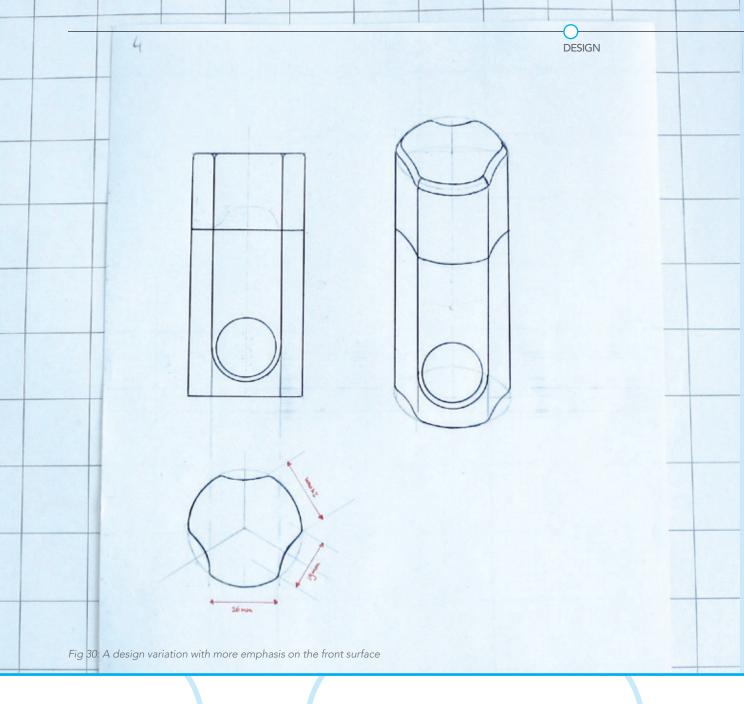
Design details

With the basic shape completed, time was spent on the design details surrounding this core form. With the help of form expert Lucian Reindl, attention was given to working out all the different radii, lines and surface treatments. During this process a multitude of sketch and model iterations were made to explore and support the design decisions.

One of the more direct changes was a slightly



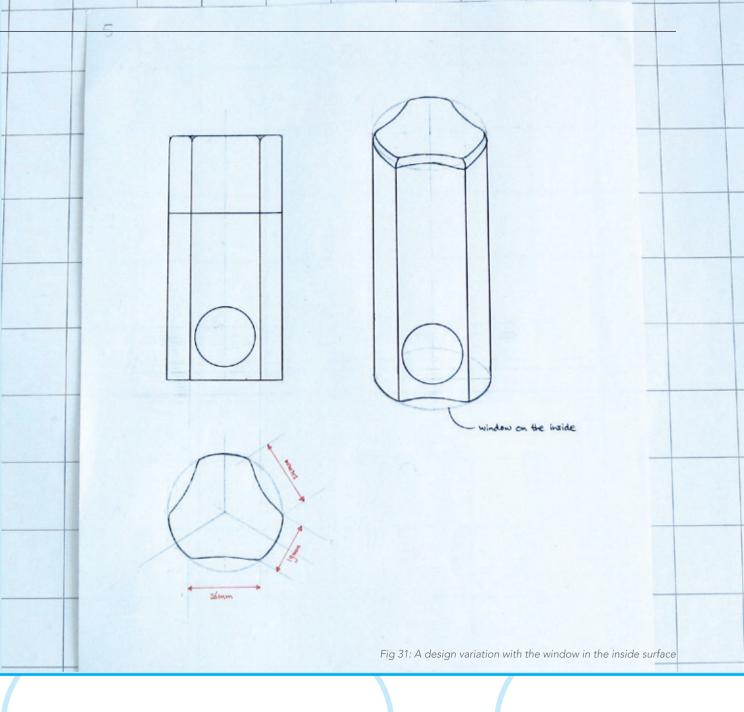
convex top surface. There are three reasons for this design change. One, a convex top is more hygienic and less dirt will congregate on the top surface. Two, a flat surface is, in combination with the lines of the product, perceived as a slightly concave surface, where a convex surface is preferred. And finally three, the convex surface will make sure the product is not placed upside down, as it wobbles.



A less apparent revision involved the proportions of the three sides. To provide the product with a more distinct "face" the choice was made to make the front side slightly broader than the other two sides. This also yields more space for

the glass diagnostic window.

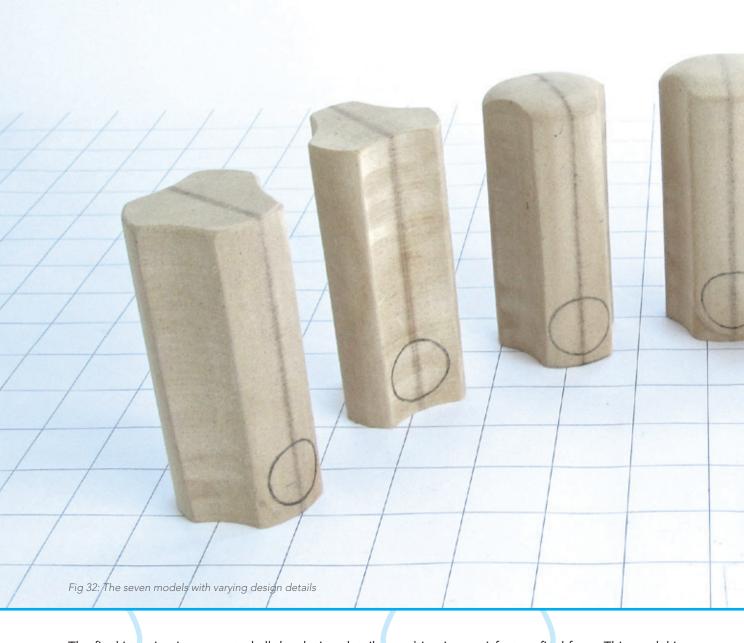
Another change involved applying different radii to all the different angles. As mentioned above, the biggest radius is obviously located on top.



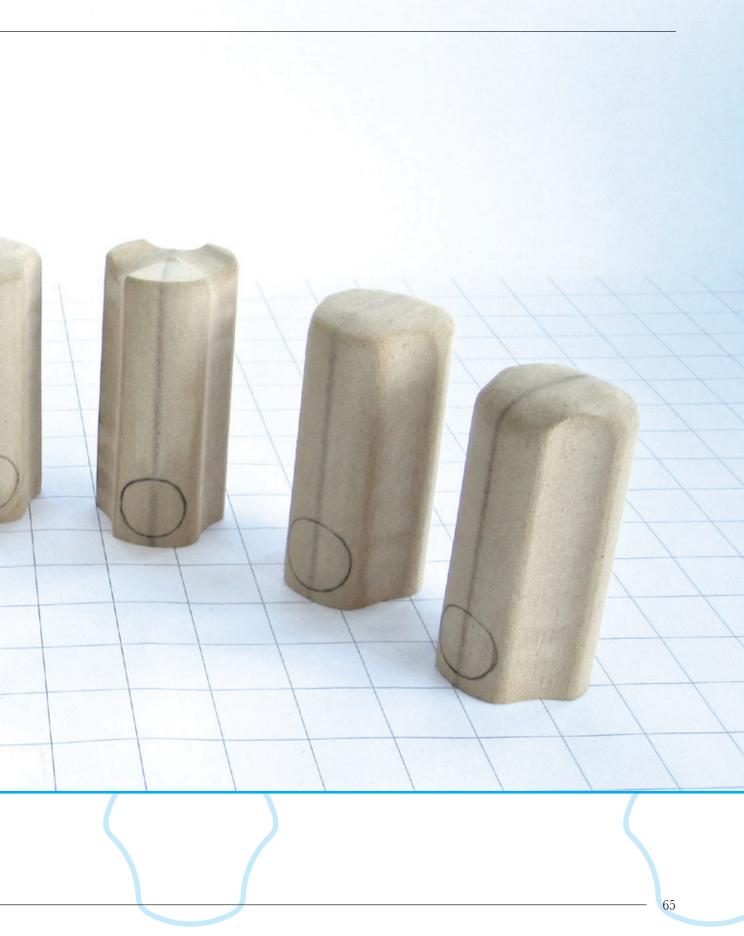
The other noticeable radius is the one between all the vertical edges. It is right in between the feeling of a comfortable grip and the perception of a more toy-like product for children.

Lastly, the top surface blends very uniformly

into the three protruding vertical shapes while the indented vertical shapes have but a slight radius. This is done to direct the eye away from the top surface down to the side, where the glass window is found.



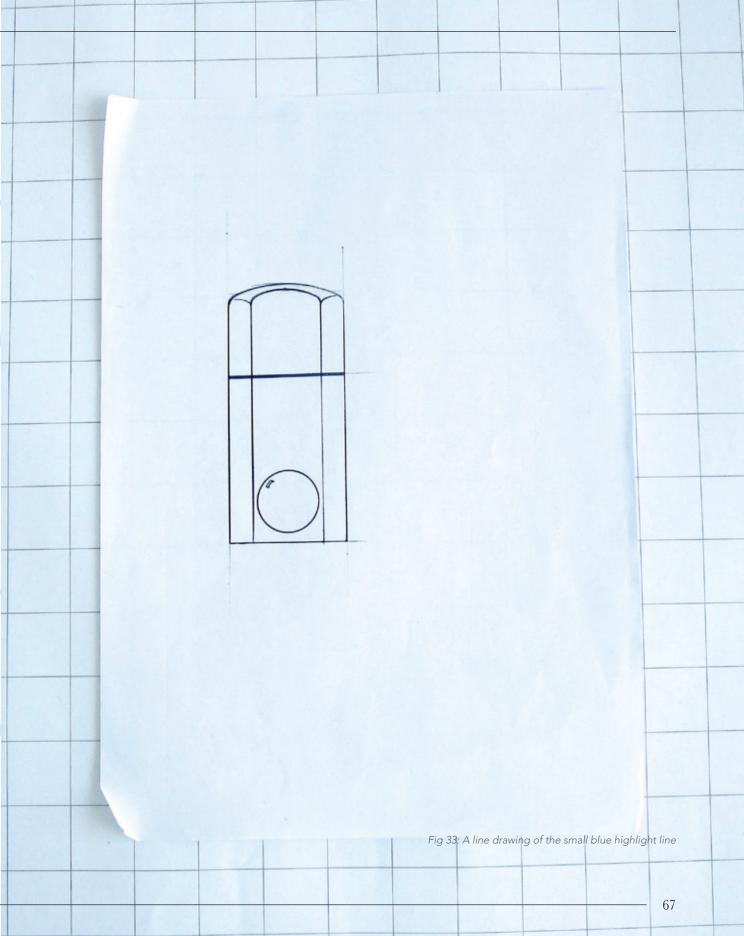
The final iteration incorporated all the design details, resulting in a satisfactory final form. This model is the model on the right in the above picture.



Color

When looking at the moodboard covering hygiene, the obvious conclusion would be to make the entire product white. Not only to blend into the average bathroom environment, but more importantly to express the perception of hygiene.

To provide the product with a bit more medical character and to support the pre-interaction of opening the product, a small thin blue line was painted on both the top of the body and the bottom of the cap. This color was depicted from the moodboard titled medical. Also, to avoid confusion between both cavities, the liquid capsules and the capsule shaft will be colored green. Both the blue and green colors are ranged within the medical tints as seen on more medical products.



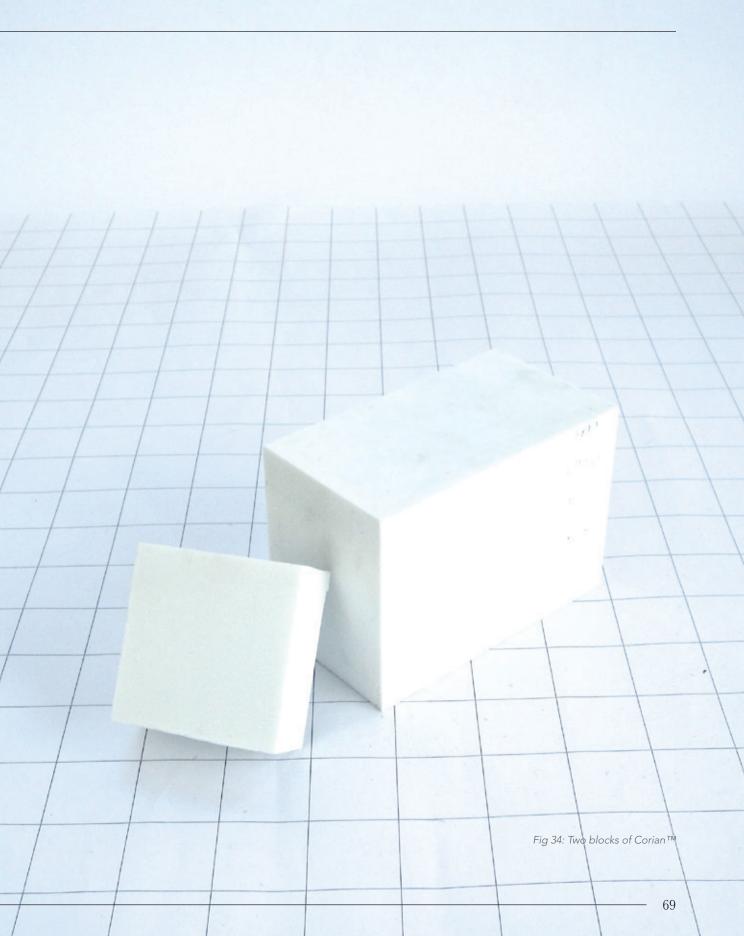
Material

With most of the exterior design guidelines decided upon, one remained: the material. With regard to the bathroom and hygiene, the preference goes towards a white and homogenous material. Although there are various plastics which fit this description, only one material comes close the desired richness for this graduation project: CorianTM.

Corian™ is the brand name for a material constituting of acrylic polymer and alumina trihydrate created by DuPont. It is used in kitchen and bathroom counter tops and was first sold in 1969^{Ref: 31}. The most noticeable attributes of Corian™ are the homogenous properties and the high density. These make it a very suited material for hygienic products, offering a little heavier feel to it adding to the perceived quality of the product.

The result of the high density is needless to say, a high weight. For something resembling a standard plastic, it is surprisingly heavy when first lifted. This weight gives the product a little more stature. And this is exactly what this product should express: a doctor-like product with prominence.

To add even more hygiene to the picture the Corian[™] a nano-coating could be applied. Such a coating could make sure no bacterial cultivation can stick to the Corian's[™] surface, both the outer as the inner surface of the product^{Ref: 32}. This way it will become even harder for other bacteria, viruses, or contaminations to corrupt the qualitative measurement capabilities of the product.







The shiny character of the glass provides another cognitive link to a lollypop, while presenting a rather hygienic appearance.

Interior

Saliva stick

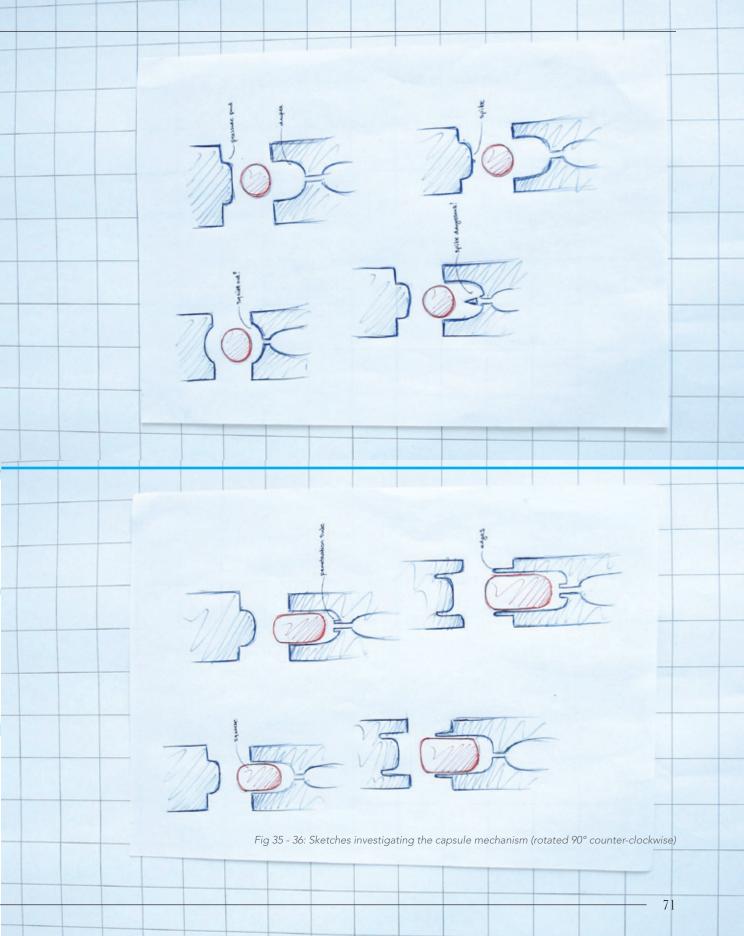
Based on the moodboard dealing with oral products the choice was easily made to go with a lollypop-oriented design for the saliva stick. Not only does it offer a larger surface for saliva to gather on, it also is not easily mistaken for a product to insert in any other cavity than the mouth.

The shiny character of the glass provides another cognitive link to a lollypop, while presenting a rather hygienic appearance. Also, it distinguishes itself from the Corian™ used in the body and cap.

Liquid capsule plug and cavity

To empty the liquid capsule a plug was fitted to the bottom of the cap. Numerous sketches explored variations on this subject.

The plug has a slightly smaller diameter than the cavity, and a small rubber o-ring for a good liquid-proof seal. Additionally, the cavity is connected directly to the glass window and via the saliva cavity by means of two small canals. When closed, the plug punctures the structurally-weakened bottom of the liquid capsule by applying pressure, emptying the capsule into the canals. Besides, the capsule's membrane will also close the two canals from any contamination or runaway fluid.

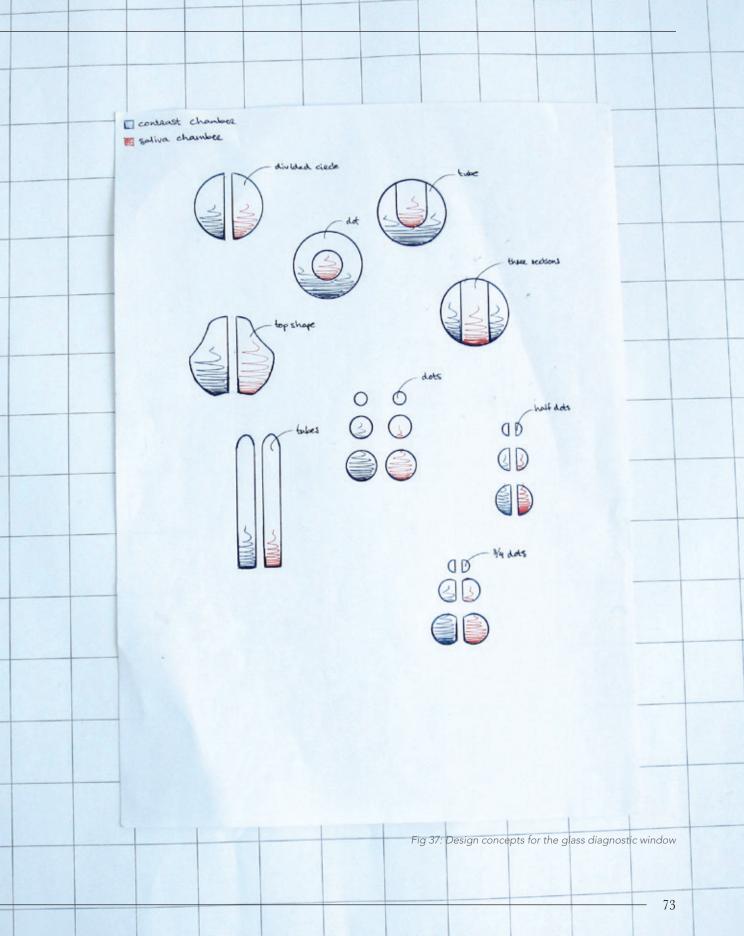




Glass window

For the diagnostic tool two compartments filled with the same bioluminescent bacteria were going to be compared for a lack of luminescence. One of these would come in contact with the saliva of the subject.

Earlier sketches denoted a problem with comparing two separate forms next to each other; there might be a problem in presenting the outcome as either a "you are ill" or a "you are not ill." People might questions the luminescence and color difference.





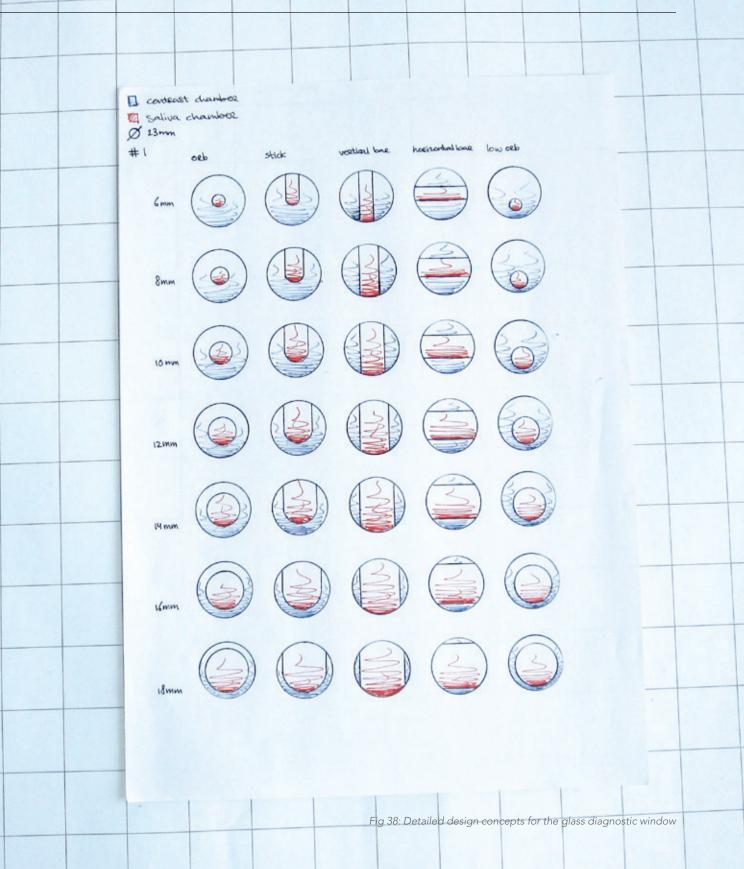


In a sense, this is a biological diagnostic tool.

A design which could trounce this problem is a chamber within a chamber, both made of a transparent material. When not ill, both compartments will stay evenly lit, looking like a single chamber. However, upon infection, the inner compartment will house the bacteria infected by the illness. They will exhibit less luminescence and color, resulting in the emergence of the inner compartment's form. In a sense, this is a biological diagnostic tool.

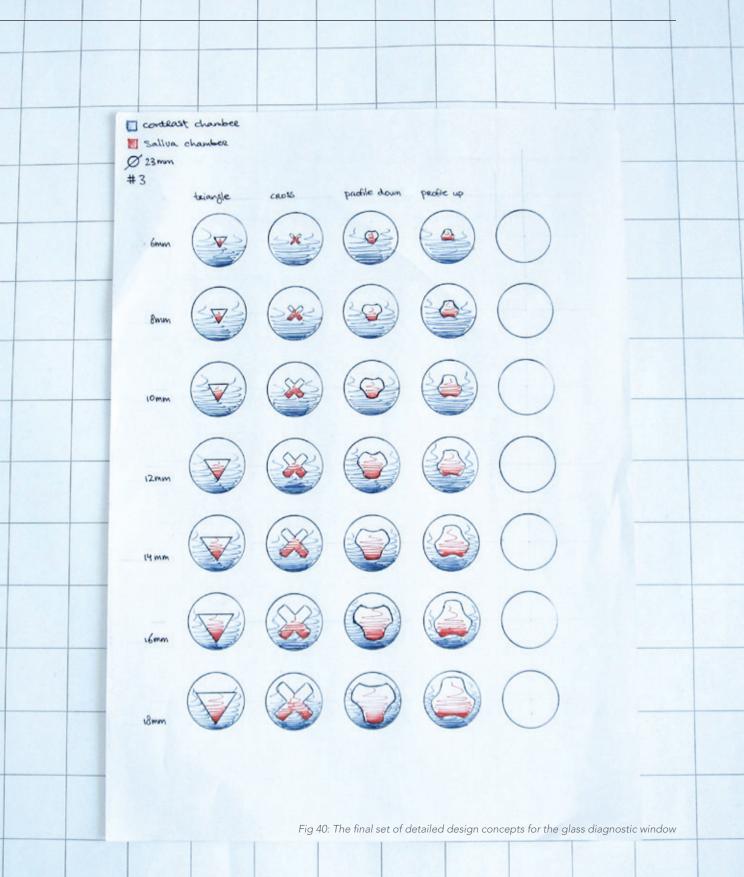
In addition, the novel solution does not contribute too heavily on the separation of the mind and body by presenting the output in a less meaningful way such as a number.

Using the same form as the top view of the product for the inner compartment enhances this analogue diagnostic tool. This shape was chosen after conceptualizing numerous different shapes and sizes, investigating the form needed to communicate illness.



DESIGN

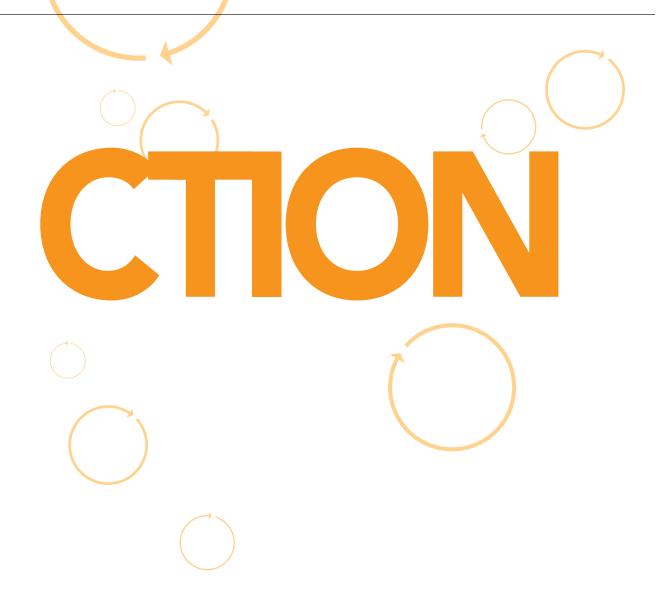
Fig 39: More detailed design concepts for the glass diagnostic window





When dealing with the interface of the product there are six main interactions to consider. Each of these interactions is carefully designed to provide the user with the right expression. In chronological order, the six main interactions are:

- 1. Opening the product by removing the cap.
- 2. Inserting the liquid capsule containing the bioluminescent bacteria.
- 3. Gathering the saliva by using the saliva-stick.
- 4. Closing the product by securing the cap and puncturing the liquid capsule.
- 5. Waiting and observing the test's outcome.
- 6. Cleaning the product.





Locking system

In searching for something which would enrich the first four interactions, a fluent and unique interface was conjured. With a product working with delicate bacteria and measurement system it is vital to provide the user with a feeling of a firmly sealed cap when closed. And when dealing with product destined to arrive in the hands of both the very young and the very old, it is crucial to create an interactive system which will work for all ages.

While there are numerous methods for closing a cap onto a body, some have a preference above other due to their simplicity and design possibilities. Early on, the choice was made to experiment with magnetism. Not only do magnets guide the closing interaction, they also afford for that feeling of a firmly locked cap as stated before.

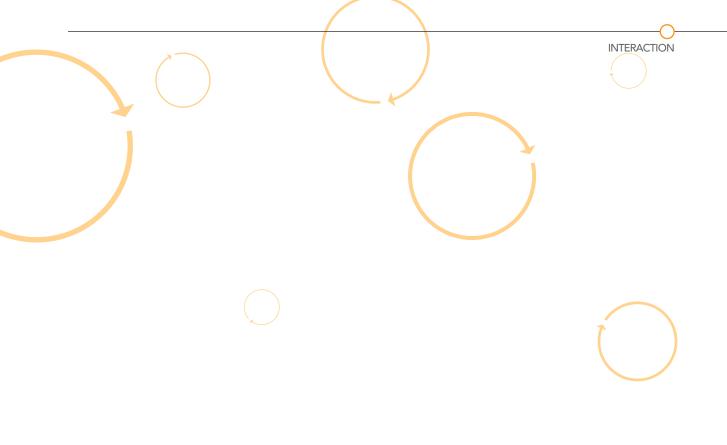
Another aspect of this magnetic locking system is the direction in which the product is opened. It would be more than logical to use the magnets in a vertical orientation, thus opening the product by pulling the cap vertically. Nonetheless, to avoid confusion and add

more interactive affordance, a rotational method for opening was also added.

A MDF model was incorporated with two magnets; one in the cap and one in the body. By using small spigots protruding from the cap and holes in the opposite vertical position in the body, both halves always end up in the same locked orientation. However, when rounding off these spigots' ends the cap is lifted slightly when rotated. This ultimately results in the magnets coming out off alignment, making the cap easy to remove from the body. When closed, the magnets guide the cap automatically into the right orientation and position.

Putting all these details together culminates into a product with a diverse interactive locking system. Not only is the cap lifted in a vertical direction by pulling, it is also lifted by rotation. When closed, the magnets and spigots guide the cap into the one and only position suited for closure, providing the user with a feeling of a firmly sealed cap.





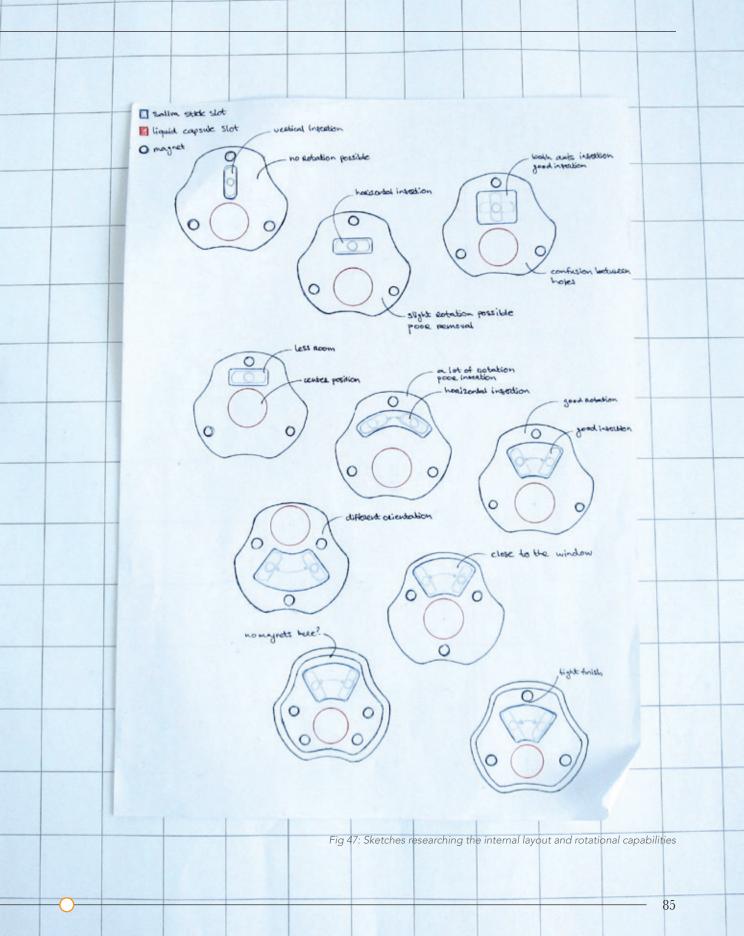
First hand experience with this first model provided some useful feedback. Hygienic-wise it is better to have the spigots' holes in the cap instead of in the body. This decision makes sure no possible unhygienic material can congregate in the holes in the body. And secondly, these spigots' holes need to be slightly smaller in diameter than the actual spigots, since the rounded ends have a little smaller size. This is done to ensure a tight fit and no end play is left on the rotational axis between the body and cap.

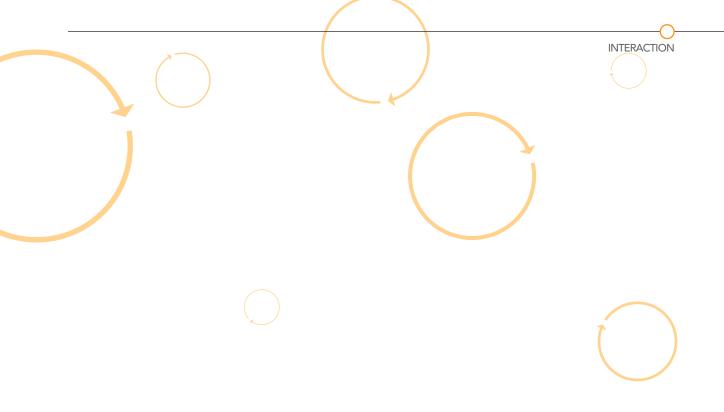




While this model contained only one shaft for the stick, the final model will incorporate a second protruding cylinder to push and close the liquid capsule into its own shaft. Now this presents a small problem: creating the rotation needed is now not possible.

To overcome this problem, one of these protruding shapes - either the saliva stick or the liquid capsule cylinder - has to have an opposite shaft in the body with more end play along the rotational axis.



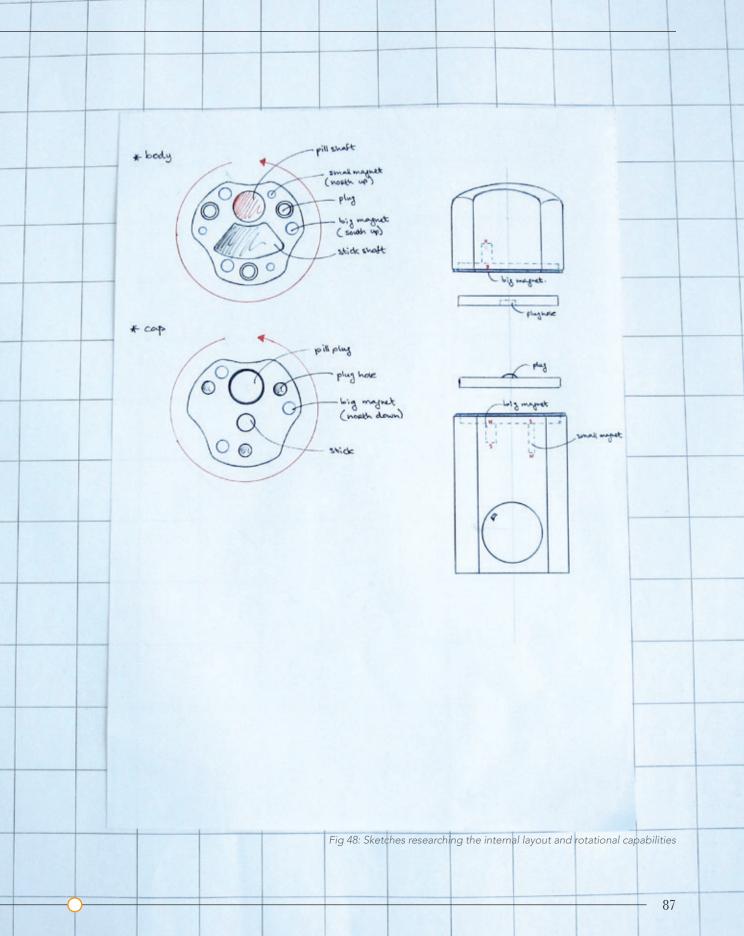


Playing with these layout versions and the allocation of the smaller magnets resulted in various sketches showcasing these options. It became apparent that the shaft for the liquid capsule would become the center point for the rotation. The shaft for the saliva stick would be made broader to facilitate this rotation.

Because the saliva stick has a lollypop-inspired end, the shaft where it is inserted should not obstruct the rotation, or this end might brake off. Also, this shaft should afford for the stick to be entered at any angle and rotation.

Sketching variants concluded the most suitable location of the magnets, liquid capsule shaft and saliva stick shaft.

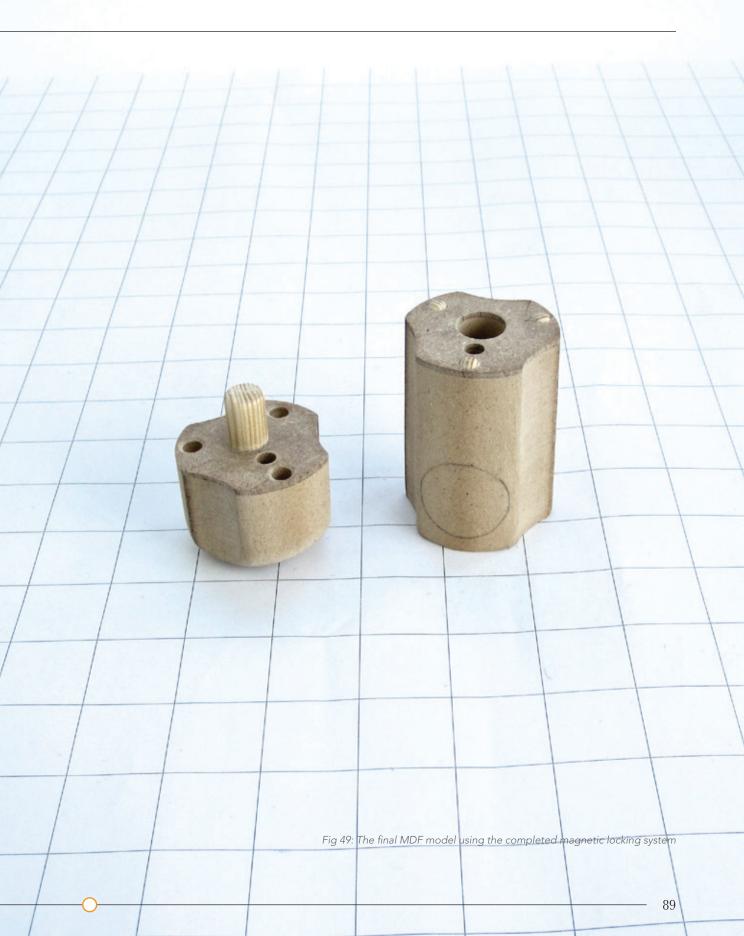






This subtle feeling enriches the already present magnetic interaction.

Finally, even more interactiveness was added by the inclusion of a second set of magnets in the body only. These magnets are placed with repelling poles as supposed to the magnets located in the cap. This meant that upon rotation, the cap is pushed upward first by the spigots, and later by the smaller magnets. This subtle feeling enriches the already present magnetic interaction.





The six main interactions

Interaction 1: opening the product by removing the cap.

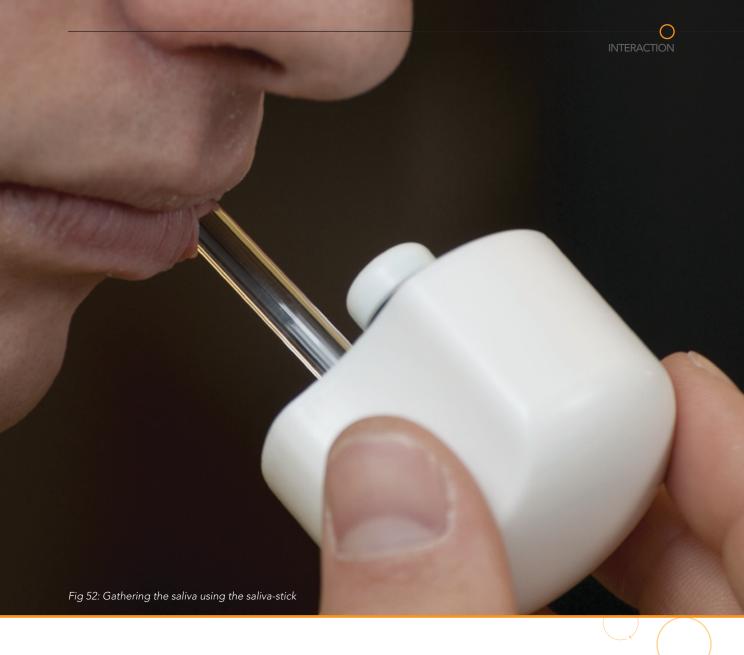
The opening interaction should be easy to understand for anyone without prior knowledge of the product. The opening interaction supports affordance by not only providing the user with the ability to pull the cap away from the body along the vertical axis, but also by turning the cap along the rotational axis.





Interaction 2: inserting the liquid capsule containing the bioluminescent bacteria.

After the product has been opened, the first step in performing the test is to insert the liquid capsule. With a considerable volume, the capsule is easy to hold in once's hands. To exclude any confusion as to which shaft it is inserted, both the capsule and the shaft are colored green. The actual insertion aims to communicate a medical sensation.



Interaction 3: gathering the saliva using the saliva-stick.

Next up is gathering the tissue. The lollipop-shaped stick attached to the cap is inserted in the mouth to collect the saliva. To collect enough saliva, the stick should be rotated and moved inside the mouth for about 10 seconds. The length of the stick allows for good penetration inside the mouth and the cap affords for a good grip inside the hand. By using glass, the stick obtains a more medical and hygienic character. The lollipop-shape affords towards oral usage.



Interaction 4: closing the product by securing the cap and puncturing the liquid capsule.

While both the opening and closing interaction in combination with the magnetic locking system provide the sense of a well locked product, the closing interaction is thoroughly guided by these same magnets. In addition, the magnets aid in the pressure needed to puncture the capsule and empty it into the reservoirs. The entire interaction is perceived as an easy one to perform.



Interaction 5: waiting and observing the test's outcome.

During the time the product needs to fully complete the biochemical reaction, the user can perform other bathroom activities. After 15 minutes, the product ensures a completed reaction. To observe the outcome, the user can either watch the product's observation window with the product standing on its feet or by picking it up.



Interaction 6: cleaning the product.

The last interaction in the process of using the product is the cleaning. Although a thorough rinsing with hot water will be sufficient, users might wish to use their dish washer to ensure an even better disinfection. This is easily accomplished by placing the opened product inside the dishwasher. Beforehand, the liquid capsule's shell and bioluminescent bacteria will have to be disposed of in the sink.

PROTO

Introduction

One of the finishing touches for a graduation project is the fabrication of a professional final prototype. Especially since it is often overlooked to create not only a working prototype, but also an aesthetically-pleasing one.

With the financial support of the Department of Industrial Design and approval by the director of education, Dr. Caroline Hummels, the model will be machined by a professional milling shop. Also, she wanted to use the entire process consisting of all the sketches, models, and visualizations for the new Frame of Reference Exhibition. This FoR exhibition showcases qualitative reference projects for visitors and future students.

The Corian™ was acquired via leftover parts from recent fellow graduate student Jasper Dekker. Who, in turn, received the material from CoproNed; a Dutch specialized and certified DuPont seller.

With all the parts designed a list of fabrication elements can be constructed. The main body and cap will be milled from a solid block of Corian™. These parts will incorporate various canals and holes to accommodate for all the magnets, glass components, stainless steel plugs, and plastic surface plates. The glass items will be custom blown by a glass expert and the stainless steel plugs will be machined and polished on a lathe. And finally the plastic plates covering all the holes for the magnets will be laser-cut from 1 millimeter plates of polystyrene.









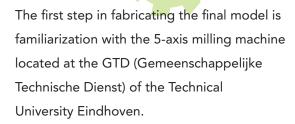








3D model



A mock-up 3D model was created using the Rhinoceros NURBS modeling software. This model incorporated the main shape and curves including all the inner channels connecting the shafts with the glass window at the bottom.



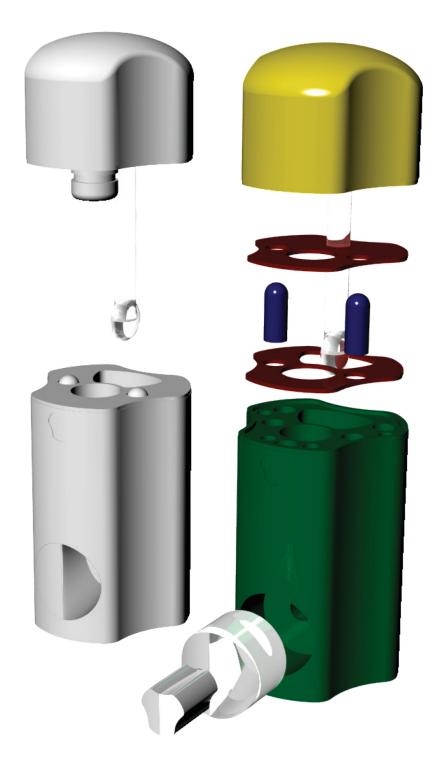


Fig 56: A 3D render of the entire selection of parts for the final prototype





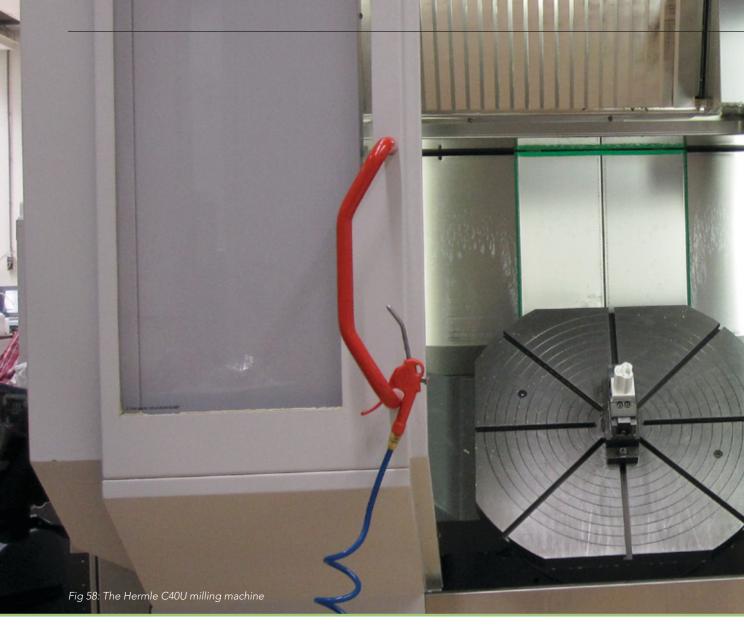
Harry de Laat, group leader at the GTD, was consulted with the mock-up 3D model. Using his knowledge of the milling machine, small revisions were made to the final 3D model. Most of these changes dealt with margins, radii and drilling depths.

With the GTD's milling machine having a preference towards the STEP file standard (Standard for the Exchange of Product model data) for 3D models, Solidworks was used to export the Rhinoceros model to the required STEP format.





Fig 57: A 3D render of the final model sent to the milling department



Milling

With the model completed the next step would be creating the program for the milling machine. With the help of Paul de Laat, 5-axis milling expert at the GTD, the milling machine was programmed to create both the body and cap.

Programming a milling machine is done to arrange the order in which all the milling steps are executed



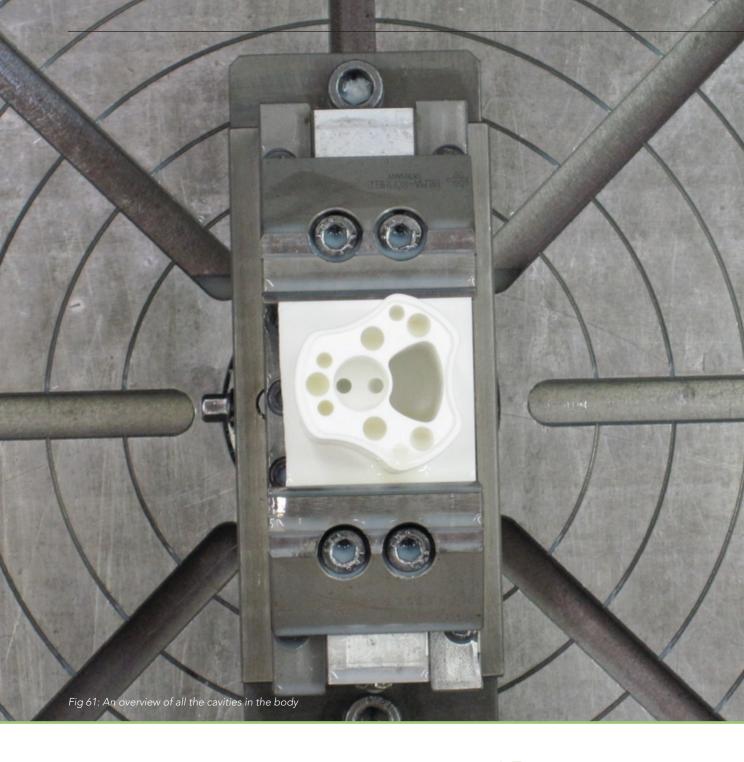
and to create the best possible aesthetic outcome. Examples of this process is a choice in milling direction, drill size, rotational movements, and milling speed. The machine used for the occasion is the Hermle C40U 5-axis Vertical Machining Center. Able to mill simultaneously along five axis up to 1400 kilogram, this machine is priced, including various drills and milling cutters, at around 400,000 euros.



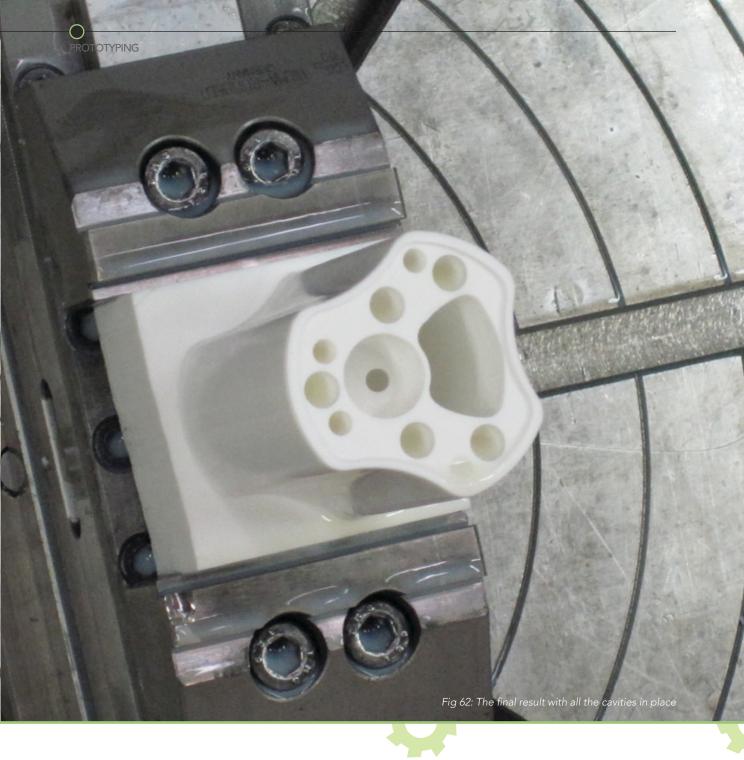
The milling procedure was done in two major stages. First, the body's main profile was cut from a solid block of Corian™. Next, the cavities for the liquid capsule and saliva stick were milled. Subsequently, the entire top surface was milled down 1 millimeter to accommodate the laser-cut plates covering



all the magnets. A small rim was removed along the top edge where paint will be applied later. After which the holes were drilled to house the various magnets, plugs, including the canals guiding all the liquid bioluminescent bacteria to their respective compartments.



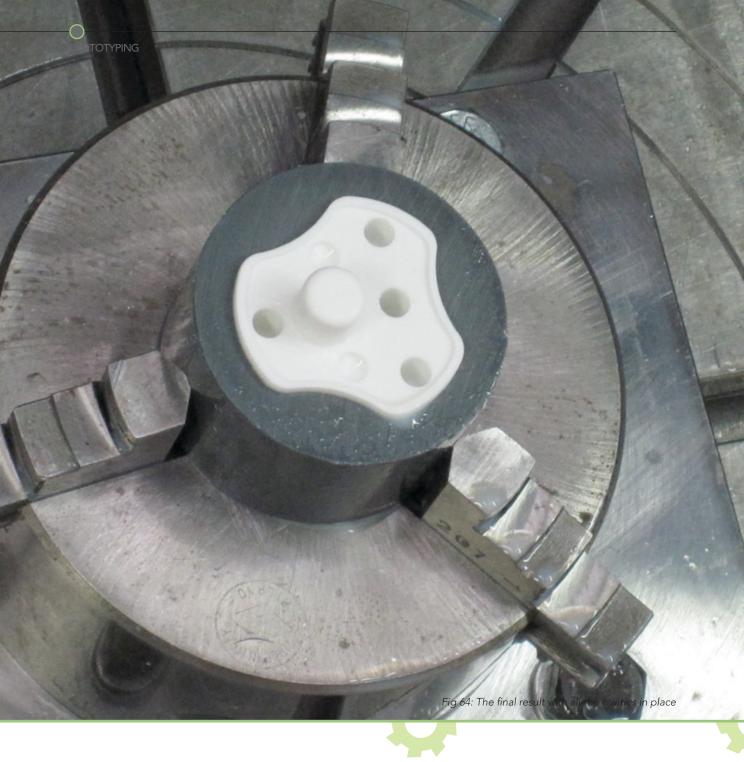
Next up were the front-facing hole to incorporate the glass window and the logo inscription. Especially the logo required some intensive programming since it is carved along a curved surface. This meant instead of moving the milling cutter along the fixed model, the model would be moving along a fixed milling cutter.



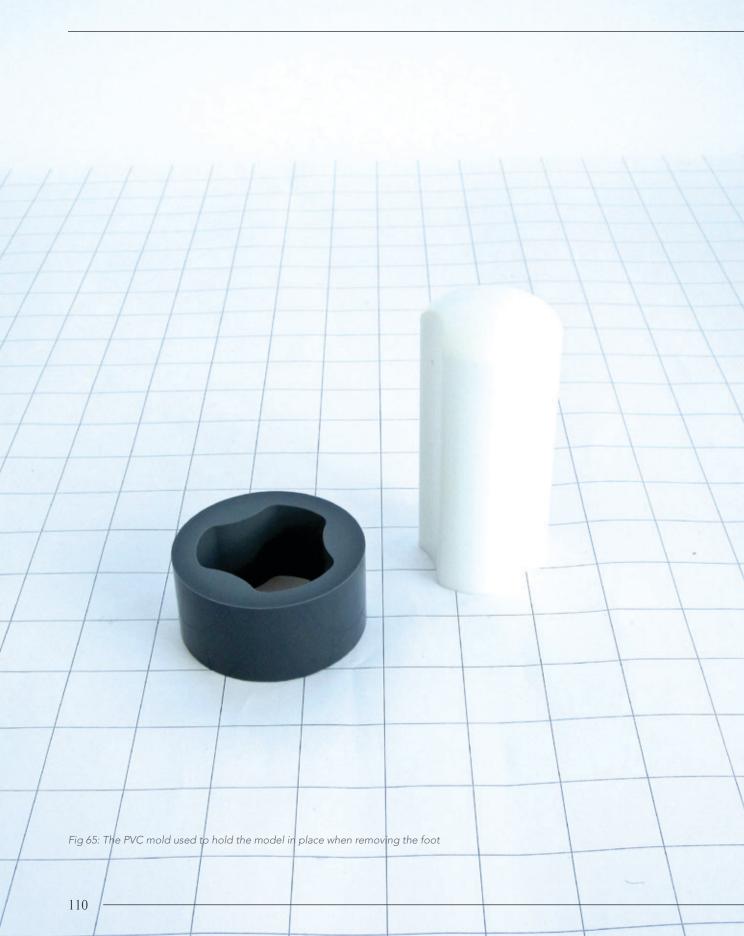
Finally, the foot left to clamp down the body was removed with a saw and shaved down with a lathe. The body was held in place by the same mold used to clamp down the cap when the bottom end was milled and drilled.

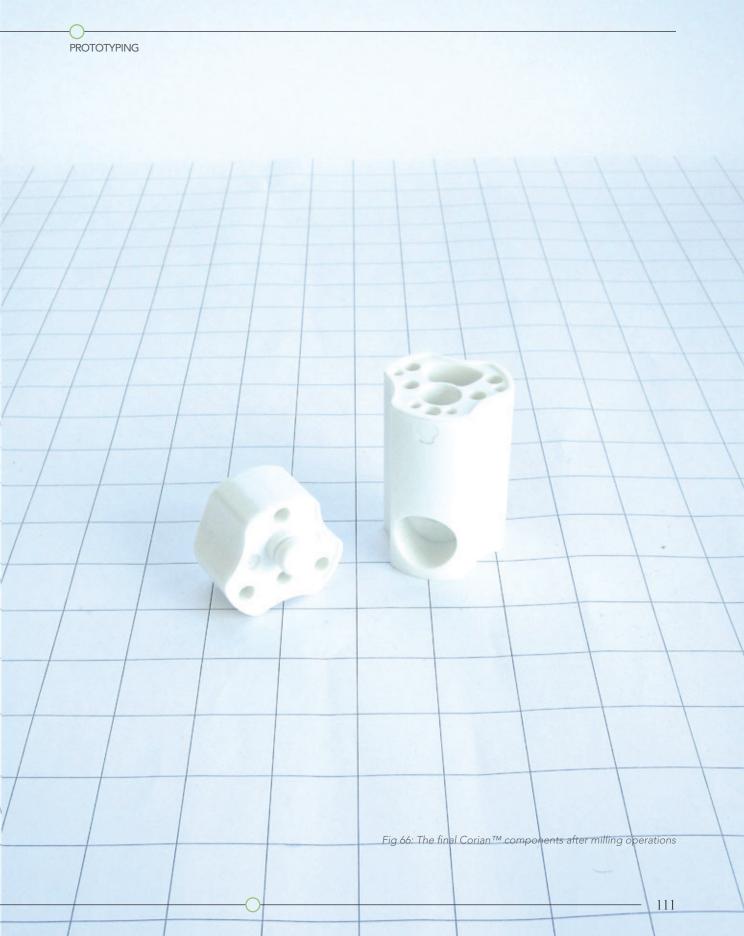


The curved section of the cap was easily cut in a downward spiral motion. To mill the bottom of the cap a negative mold was made using some solid plastic. The same iconic tri-shape was milled from the plastic and the cap was inserted. By tightening the clamp the mold was press-fitted against the cap, offering a tight seal during milling operations.



First the shape was cut down to create the plug. Next, the surface was milled down 1 millimeter to accommodate the laser-cut plates covering the magnets. Finally the holes were drilled and an edge was removed from the plug for the rubber seal. The final results fitted perfectly on the body.





Glass parts

Besides the complicated milling procedure, a two pieces of glass will have to be constructed: the glass saliva collector and the glass window housing the two compartments. Tasked with this arduous job is the GTD's Glass Lab.

The first step in the fabrication of the glass models is the creation of detailed constructional plans. While the saliva stick offers no problems in terms of creation for the experts of the GTD Glass Lab, the window is a whole other point. Both the compartments have their respective "fabrication challenges." The bigger compartment (seen in red) has a challenging curve on its face. The smaller compartment (seen in yellow) is made of the same main shape used throughout the design, and is in its scale complicated to construct without warping the glass during treatment.







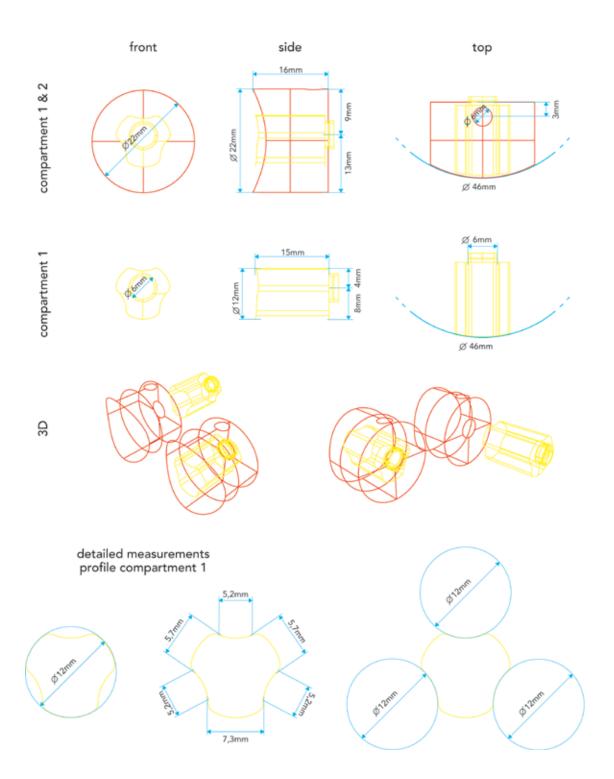


Fig 67: The 2D detailed construction plans for the glass components



ould then be filled wit

Using the constructional plans above, the models were discussed with Frans Kuijpers and Ad Waterschoot, experts at the GTD Glass Department. They figured it would be doable to create, yet quite a challenge. The smaller compartment was constructed using a new method proposed by the author. A twelve millimeter tube was heated and small dents were pushed in to create the iconic tri-shape. This worked out considerably well compared to having to assemble the entire form out of separate curved three millimeter sheets of glass.

The best results with such complicated glass shapes is making a graphite mold. This mold

would then be filled with a thin sheet of glass, ultimately resulting in the desired design.

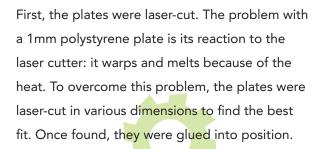
However, a graphite mold will have to be milled. And graphite is quite harmful for milling and tooling machines. Therefore, the choice was made to not take this direction and burden the milling facilities with the possible damage caused by making graphite molds.

Also, the glass window could have been replaced by a 3D custom milled form out of a solid block of acrylic. However, with a tight schedule at the milling department of the GTD there was simply no time to pursue this direction.



Assembly

The assembly of the model involved fitting and applying the laser-cut polystyrene plates covering the magnets, and placing the saliva stick.



The glass saliva stick was also glued into place and positioned carefully in the correct orientation.

To provide the prototype with a bit more medical allure, a touch of blue was added along the rim between the body and cap.

Using a COPIC B04 "Tahitian Blue" marker, the lines were applied and smoothed with a damp cloth.











The decision was made to not incorporate the stainless steel plugs. The motivation for this decision is based on the fact that they increased the effort needed to rotate the cap and offered no improvement in the ficture of the cap onto the body.

BUSINE

Introduction

With the introduction of a new product utilizing genetically modified organisms there is a vast range of aspects to deal with when looking at it from a business perspective. The goal of this chapter is to investigate all the factors dealing with the introduction of such a product, making sure no key aspect is overlooked.







Funding and research

The first step in getting the project off the ground is gathering the necessary investments to get the research and development phase under way. Capital will most likely come from either a governmental organization, a pharmaceutical company, or a biotechnology company.

When the finances have been acquired the research and development phase can commence. First, the theoretical feasibility of the genetic modification of bioluminescent bacteria will have to be examined. When finally a method for making bioluminescent bacteria sensitive to strains of the influenza virus has been accomplished, the next step is obtaining the approval for mass production and distribution.

Approval, Laws, and Regulations

Approval

When the technology has been proven to be feasible, it will have to pass a wide variety of trials in order to be deemed "safe." During these trials the technology is investigated by institutes such as the Dutch RIVM (Rijksinstituut voor Volksgezondheid en Milieu) or the United States' FDA (Food and Drug Administration). These organization research the potential hazards involved with the introduction of such a technology on public health.

Laws and regulations

Now with the technology approved by the general health and safety institutions, there are certain laws to abide to. The most important ones are the GMO Regulations: "The GMO (CU) Regulations provide for human health and safety and environmental protection from genetically modified micro-organisms and contained use, and additionally the human health and safety from genetically modified plants and animals (GMOs). The key requirement of the GMO (CU) Regulations is to assess the risks of all activities and to make sure that any necessary controls are put in place. The GMO (CU) Regulations

provide a framework for making these judgements, and place clear legal obligations on people who work with GMOs." As stated by the Health and Safety Executive Ref: 33.

The basis for these laws originate from the Protocol of Cartagena Ref: 34. This regulation was enforced in September of 2003 and describes the earlier directives concerning the "living organisms originating form modern biotechnology" and their particular effect on the biodiversity. In a sense, this statement can be seen as the predecessor of current GMO's. On the 12th of May 2004 the Netherlands adopted the European Union's regulation 2001/18/EC Ref: 35, regarding the intentional introduction of genetically modified organisms (GMO's) into our environment. This directive states that anyone wishing to commercialize a product containing GMO's should apply for a permit which is valid for a period of 10 years (and extendable). After said introduction an inspection will be performed by the Commission tasked with GMO's. After the introduction of the above regulation, various revisions have been enforced, the latest being from 21-03-2008 Ref: 36.

This commission will consult the necessary scientific committees concerning any aspect dealing with our health and environment. Also, the Commission has the right to consult ethical committees concerning the proposed product. The entire process is carefully documented for future reference.

Every three years this commission will publish a summary of the measures taken regarding the enforcement of this directive. This summary also contains the experience of previously adopted GMO's and their respective effects on the health and environment. Furthermore, each year a report concerning the ethical questions is published. One of the outcomes of these reports is a new directive involving the border crossing relocation of GMO's: regulation 1946/2003/EC^{Ref: 37}.

Regulation 1946/2003/EG declares the differences between purposefully introduced GMO's and GMO's used as nutritional supplement, animal fodder, or destined for agricultural uses. Since this product falls within the first category - purposefully introduced GMO's - it requires an additional set of

approvals for shipment to other countries. The directive issues the application of a written notification to the authorized national agency regarding the introduction of the product. The goal of this order is to notifying the importing government to decide beforehand if the product in question is approved or not. When a reply is not been given by the importing country within a time frame of 270 days, the product's vendor will have to send a reminder letter to the authorized national agency, and a duplicate to the aforementioned Commission. The national agency is obliged to reply within 60 days. If everything is approved, the technology can be scaled to fit a global distribution pattern.

Mass production and fabrication

The technology

For the mass production of the genetically engineered bacteria special growth farms will have to used or constructed. Although this might seem as a gigantic step, when the technology is completed the bacteria are easily cultivated. Elements needed for the production include: agar, fresh oxygen, a climate control system, a sterile environment, and freezer for storage before transportation.

The product

Besides the technology there is also the production and fabrication of the designed product. Using Joris van Gelder's experience in the production and fabrication of his own Master graduate work at the Department of Industrial Design, thought was spent in estimating the cost-aspect of the product's fabrication.

Before making such approximations, some changes will have to be made to the product and chose materials. For one, the usage of Corian™ and custom blown glass will heavily increase the costs involved in the creation of the product. Therefore, the choice is easily made to use a homogenous

plastic-basis for the body and the translucent parts. Using injection molding will decrease the necessary costs for production without a major loss of design quality as opposed to the Corian™ and glass model.

Based on his knowledge with the production of his Kitchen Remote^{Ref: 38} and the revision of the final design, Joris estimated that the first step was making a mold for the injection molding of all the parts. This mold would range in between 1,000 and 2,000 euros. This would bring the estimated costs for each product in between 1 to 3 euros excluding shipping and handling.

On a side note, it can even be imagined that a low-cost alternative design can be created for decreasing the production costs. This version could be specifically targeted at developing nations. However, this presents other challenges to overcome, such as freezer to store the capsules with the bioluminescent bacteria.

Product placement

When placing the product in the market its competitors will have to be known. Although this is a new method for diagnosis illnesses such as influenza, it is by no means the only one of its kind.

A similar, more familiar tool is the thermometer. Tasked with measuring the body's temperature, it can be a decent indicator for illness when detecting a fever. Nonetheless, the weakness of a thermometer is its inability to detect a specific illness, as fever is a common symptom for many medical conditions^{Ref: 39}. Another approach is using vitamins not as a diagnostic tool, but as a preventive or treating method. Still, just as the thermometer, vitamins do not diagnose illnesses and offer no direct treatment.

However, a point of difference for both the thermometer and vitamins as compared to the fluDOC is general acceptance. People believe and accept their thermometers and vitamins usage and functionality, which offers these tools an edge to the lesser known fluDOC product.

Unique selling point and benefits

The unique selling point of the fluDOC is its ability to accurately diagnose influenza with the ease of using a thermometer. And, in the near future, possibly also a vast range of pandemic threats.

Benefits of the fluDOC include:

- Provide people with the right foundation when having to make the decision to go out or stay in bed.
- Lowering the run to the physician during times of pandemics, no longer can people doubt their illness: they can test it immediately, at home.
- Making sure infected people will not infect more people while visiting a physician, gathering medicines, or just going out of the house to public places.

Business models

At the right an overview of two business model are visualized. The first and top one illustrates the creation of trust needed to get the consumers to adopt the new technology in a product form. The second model showcases the revenue flow on a basic level to all the parties involved.



...its ability to accurately diagnose influenza with the ease of using a thermometer.

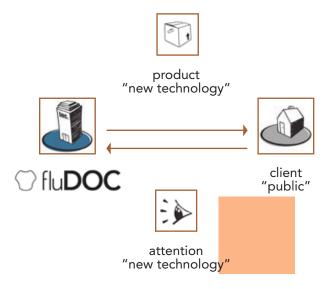
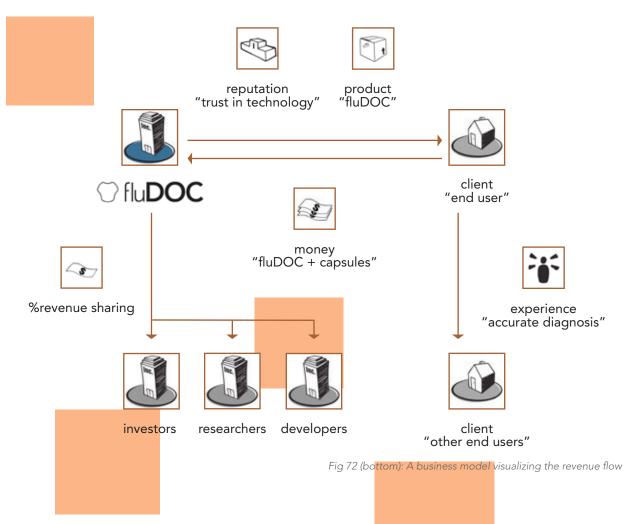


Fig 71 (top): A business model visualizing the creation of trust in the technology



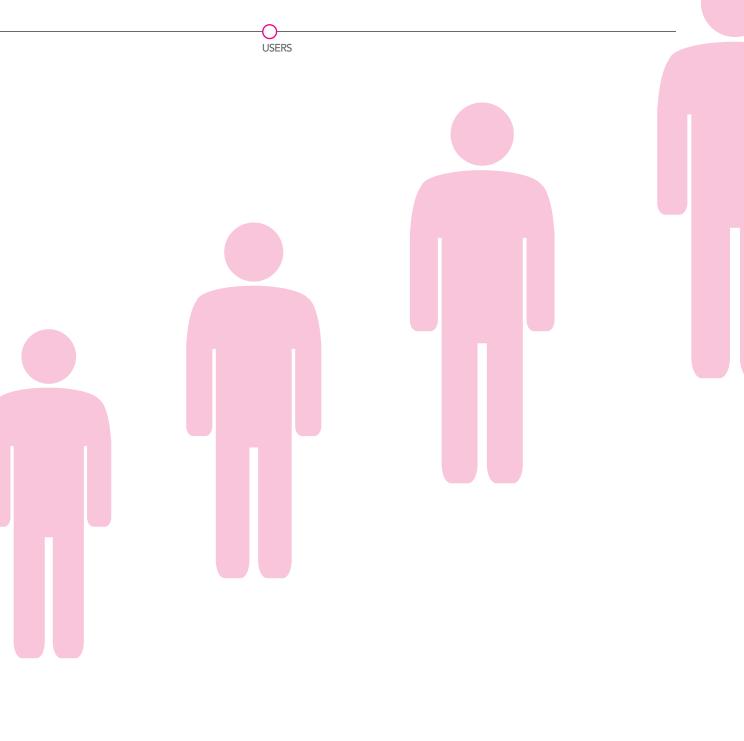
USERS

Introduction

When a product could invoke this much of an impact on the daily life of people, it should not be excluded to any particular group of people. Therefore, it comes as no surprise to make this product available to the masses, of all ages.

Having said that, there are various hurdles the product will have to overcome in order to be accepted and adopted by the general public. With the cooperation of Dr. Lu Yuan, business expert at the Department of Industrial Design, the adoption and introduction of the product was investigated.

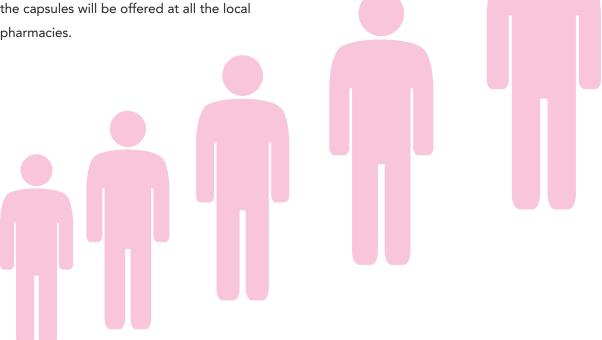




Service model

With a product destined for an entire family, there is no need to purchase the entire product multiple times. The product is acquired once, for the entire home. After each handling, it can be cleaned. This means the liquid capsules will be purchased when needed, stocked in the freezer.

To provide the product with medical allure and a more serious nature, the capsules containing the bioluminescent bacteria will not be sold at your local grocery store. Also, to lower a potential threshold, the capsules will not need a prescription by your physician. Instead, the capsules will be offered at all the local pharmacies.





Adoption and confidence

The main goal is creating the awareness and confidence to stimulate the mass adoption of the product. According to Dr. Lu Yuan this is best achieved by first introducing the technology and functionality on a more public scale. Using this order the required awareness of the product can be demonstrated to the public, increasing the appeal to purchase similar technology for one's own house.

This would mean incorporating the technology in for example air fields, at the borders, with doctors, and other public places. Together with promotional backing from governments and research agencies, such a approach would create the imperative belief needed for the fluDOC's adoption.

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With a product destined for an entire family, there is no need to purchase the entire product multiple times.

Environment

Environment selection

A suitable environment would have to be found in order to provide the concept with a context and guidelines for the design process.

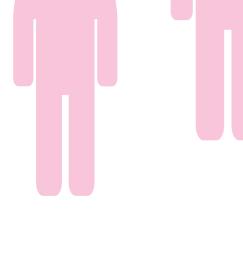
With a product destined to be used in a home environment, the choice can always be made to not lock it to a certain space in the house so the user can decide where to use it. However, because this product deals with a rather private diagnostic tool a more secluded space could be desired.

When observing the spaces in a house, one area springs to mind when it comes to dealing with private healthcare-like products: the bathroom. This location offers the hygiene and privacy which would match a product of this kind. Therefore the choice was made to use the bathroom as the main environment for the utilization of the product.

Bathroom rituals

Another aspect to look at are existing bathroom rituals. This might help in understanding the how people deal with products located in the bathroom and how the ritual designed for this product could be placed there.

During the project various bathroom rituals were observed in taken into account during the development of the product.





DISCUS

Introduction

As might be expected, there are points of discussion. After having finished the project, process, and product it is time to discuss the results and findings. And even offer some future revisions along the way.











Discussion

Project timing

One of the main points of discussion is the selection of the technology at this moment in time. It can be criticized that the genetical modification of bioluminescent bacteria is a technology not ripe to be included into products just yet.

However, as a designer this is the push that should originate in order to stimulate the technology into fruition. In 1994 James Cameron decided not to initiate his latest film titled "Avatar" as he believed the necessary technology was not yet available to achieve his vision in the film. In 2005 he decided the needed 3D film technology could realized if it was pushed Ref: 40. What materialized was a blockbuster movie winning three Academy Awards and grossing more than 2 billion dollars; a world record.

His success story is one of many, and it showcases that in order to innovate, one should not wait for a technology to be fully matured. Instead, at the right and opportune moment, a well placed concept and design can stimulate the growth of a technology. This eventually resulting in new and unique technological innovations and products, systems, and services.

Exorbitant product

Another subject up for discussion is the exorbitant use of materials, design details, and rich interaction for a product of such stature. It can be concluded that these factors heavily increase not only the cost price of the product, but also raise the question if the author was unable to create a suitable design for the product in question.



As stated before, the choice was deliberately made to showcase the author's creative design skills. With this being the Master graduation project of a design department and with the a personal preference towards form design, this sure is a vital aspect of the project.

Nonetheless, another argument for the use of more expensive materials and methods is the premiere distribution of the product. With the basis of the product relying on a technology requiring vast amounts of funding, the choice can be made to design a product for a market segment where more money is spent on similar products. This way the product can be introduced into the market using a top-down approach, starting with the wealthier communities.

However, it can be noted that the product allure can also go the opposite way. A low-cost alternative can be designed using cheaper materials and less of a rich interaction. This product could accordingly be sold in more developing nations, where consumers have less money to spend.



Design revisions

After having completed the final prototype and having discussed it with other designers and experts some, design revisions emerged. These adaptations are illustrated below.

Cotton swabs

It was questioned by some experts that a better quantifiable result of possible influenza particles could be reached using dry cotton swabs. This adds another component to the product, possibly making the product slightly more complex. However, it might be solved by incorporating a orifice where standard cotton swabs can be inserted. Another approach would be to add some more texture to the glass for a better adherence to the saliva without destroying the preferred oral usage.

Saliva hairs

While the gathering of the saliva is an easy task, getting the saliva to properly mix with the liquid bioluminescent bacteria is more difficult assignment. In the current prototype the saliva is mixed by running the bioluminescent bacteria over the saliva stick.

An option to improve the mixture of saliva and bacteria is by adding small hairs inside the shaft for the saliva stick. With this method the saliva is spread across the hairs, increasing the target surface for the needed biochemical reaction between the saliva and bacteria, when the capsule is punctured.

Glass components

When dealing with custom blown glass the accuracy can and will never

reach that of a professional milling machine. In order to overcome fitting problems between custom glass components and a milled form, it is best to design and construct the glass first. Measurements from the actual glass piece are taken into consideration when designing and fabricating the milled parts to ensure the best possible fit.

Another approach would be to replace the glass parts by the same proposed 3D form milled from a solid block of acrylic. This will also result in the desired fit with a bit more precise finish.

Timing the biochemical reaction

A method for timing the biochemical reaction between the saliva and the gentically modified bioluminescent bacteria could be to include a chemical strip. Similar to the ones used in pregnancy tests, they can provide a indication of when the test has finished its diagnosis, without the addition of a battery-powered timer.



Expert knowledge

Throughout the earlier research phase of the project contact was made with various institutions, research departments and universities, regarding the feasibility of the creation of a synthetic bacteria sensitive to influenza. In the course of this correspondence these experts were asked to provide their adept opinion on the matter. The question asked was: "will it be possible (some time in the future) to genetically alter a (bioluminescent) bacteria to become sensitive to the human strain of influenza? If so: what are the difficulties to overcome? If not: where lies the problem?" Of all the experts contacted several replied with detailed ideas regarding the feasibility.

Prof. John Glass from the Synthetic Biology Group at the J. Craig Venter Institute remains positive on the potential success of such an adaptation, yet had some serious questions regarding the amplification of the signal originating from the bacteria: "This seems doable but hard. You must also consider viral titer in saliva, which I do not know, as part of this construct. For this to work I think there must be a massive amplification of signal. Meaning a few virions interacting with a few bacteria are sufficient to cause those bacteria to begin growing and to keep growing even if there are no further virus-bacteria interactions."

Prof. Vincent Racaniello of the Department of Microbiology and Immunology at the University of Columbia also had some great input on the potential hurdles to overcome. All of these comments focussed on engineering the bacteria to be infected by the virus, similar to how the it infects humans. This, however, presented a rather biased view as this is most likely not the only method for creating the connection between virus and bacteria. He concluded by saying: "My view is that whatever is biologically possible is selected by evolution, which does a much better job at designing systems than we possibly can."

Dr. Martin Welch, Department of Biochemistry at the University of Cambridge, took a more critical note to the genetic modification task at hand. In his words: "This is potentially possible (nearly everything is if you put your mind to it) but there are serious hurdles to overcome and probably easier

ways forward. Influenza is an RNA virus which has evolved to subvert the function of eucaryotic cells..... it will not enter through the cell envelope of gram-negative bacterial cells and would probably not replicate there even if it could be introduced directly into the cytoplasm. Easier would be to transfer the genes encoding bioluminescence (luxCDABE - these have been cloned long ago) into an influenzasensitive eucaryotic cell line, then tinker with the genetics to make it "report" on the presence of flu viral particles (or flu gene products). But even this is a tall order and would require much thinking-through even to come up with a theoretically sound reporter system (which may not work when put into practice)."

Prof. Marc Zimmer, specialized in chemistry and the Green Fluorescent Protein, responded he had little knowledge in the actual genetic modification of bacteria to respond to influenza. He wondered if "one would find a general acceptance to using genetically encoded bacteria as monitors for human influenza."

Concluding, it can be stated that of the response give, the overall view is positive on the possibility that such a technology can be realized in the years to come when provided with the needed funding and expertise. Still, based on the knowledge and view of the experts, it is concluded they find it hard to see beyond the scope of their profession and education. Most ideas focussed on the "traditional" infection of a bacteria by the influenza virus; coding his own mRNA, instead of finding other methods for bridging the gap. Further communications were hard to sustain and yielded no additional insights or response.

Influenza 2.0

With a product relying on such an undeveloped technology there are bound to be potential opportunities. If genetic modification can make a bioluminescent bacteria sensitive to influenza, a lot more will be viable in the future. What if you could choose between innumerable capsules to visualize not only basic influenza but also make a distinction between the different serotypes leading to the pandemics we know today? During these pandemic times, the government can support the diagnosis of pandemic cases by providing the public with the needed capsules, free of charge.

As Dr. Larry Brilliant states in his TED Talk^{Ref: 41}: "We need early detection and early response to counter pandemics before they spread." His talk illustrates the danger of pandemics, and how something as dangerous as SARS can spread across the entire world within three weeks. The problem is not curing the disease, but to contain it. Organizations such as GPHIN, the Global Public Health Intelligence Network, hunt down cases of pandemic illnesses and contain them locally^{Ref: 42}. They require vast amounts of local data to keep track of important events for such an early response.

One can imagine how the impact a product such as fluDOC can aid in the early identification of pandemics. The most common approach is spending a lot of funding on the development of vaccines. But why create a solution which might solve your pandemic problem after it has already spread? And what if there is no cure? Why not detect the disease before people get a chance to spread it?

Networked diagnosis

And what if the results of pandemic-sensitive illness could, after being diagnosed by a product such as the fluDOC be wirelessly communicated towards a central hub? This system would maintain a profile and count of every case of diagnosed illness, reporting it to institutions such as GPHIN and the World Health Organization (WHO) who might utilize this information for sake of public health.

For such a product version, some changes will have to be made. Besides an obvious power source and wireless transmitter, the product would require two internal light sensors. One to measure the luminescence of the contaminated bacteria, and one to take the ambient light into account. Moreover, a hub system will have to be constructed, handling all the data on illness, location, time and all other relevant information, displaying it in a meaningful way.

However, a possible method for overcoming the battery problem would be to incorporate a kinetic apparatus able to provide the wireless antenna with enough power to send a signal to a local internet hub. This kinetic energy can be gathered during the obligatory shaking of the product to properly mix the saliva with the bioluminescent bacteria. The major focus for such a technological addition is making sure the user does not have to perform any extra task for the completion of such an incorporation.

Other illnesses

And this might not even stop with influenza, but go on to provide home-diagnosis for any kind of disease detectable by saliva? Even for the sicknesses which require blood a product variation can be designed. Can you imagine a world wherein illness is easily diagnosed and contained at home? A time where we no longer have to wonder what it is we are suffering from? A place where the doctor is in your house instead numerous kilometers away? But this is a considerable challenge, involving a new set of hurdles to overcome. But someday in the future we might.

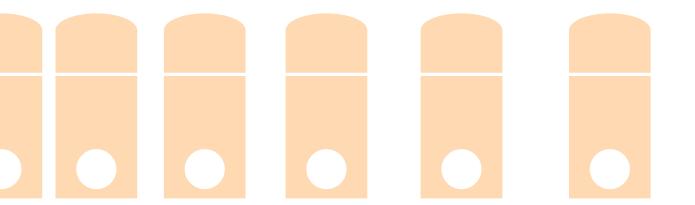


What if you could choose between innumerable capsules to visualize not only basic influenza but also make a distinction between the different serotypes leading to the pandemics we know today?

Introduction

Finally, after having served the necessary food for thought, there is the conclusion.

It is divided into two sections: a project-and a personal conclusion. The first takes a look in bringing the final prototype into a final set of user confrontational sessions, while the latter focuses on any personal reflections on the project, process, and final prototype.



Project conclusion

To conclude the project process, twenty people from different genders, age groups, and occupations were confronted with the final prototype. During these confrontational sessions, they were explained the background story behind influenza, its invisibility, and pandemic threats. Also, information was shared regarding the theoretical genetical modification of bioluminescent bacteria. Finally, the prototype was showcased, explained, and handed over.

Of these sessions there were some interesting conclusions. During the discussions following the explanation of the project, almost all of the people reacted positive on the impact such a product could have on their lives. Some of them wondered if they would actually deploy the product, asking themselves the question of wanting to use a product housing genetically modified bioluminescent bacteria.

Furthermore, some participants had some uncertainty regarding the feasibility of the proposed technology of the genetically modified bioluminescent bacteria. As Dr. Lu Yuan stated, this trust will have to be earned through the introduction of a more public awareness application.

Some questioned the amount of times they would use the product, thinking their average usage would lie far above the intented average usage. This is one of the difficulties of the product, wherein it is hard to control the usage amount for each specific user. This will have to be investigated into more detail, with possible design revisions to increase the usage threshold.

With regard to the form design and interaction, all of the participants experienced them in a very pleasant way. They enjoyed playing around with the magnetic locking system. Although this proves the richness of the interaction, it is by no means a favorable behaviour for such a product.

Overall the reactions are positive, with complimentary remarks towards the uniqueness of the concept and the detailed form design and interaction, as well as the choice in materials.

Personal conclusion

As is the case with all of my projects where I search for fascinating technologies, the difficulty lies in finding a valuable application where the user is not only confronted by a possibly temporary fascinating technology, but also a valuable product able to enrich their lives. The turning point in each of these projects is always the creative phase were an application will have to found and developed. With the pressure to create something so beneficial it can be quite a challenge to find this meaningful application.

However, at this point I can honestly say I did not only cross that creative point and found my significant application but also managed to create a very purposeful final design. Especially for the last couple of weeks of this project I have been smiling constantly. The moment all the pieces of the puzzle were in my hands I knew they only needed to be assembled for me to successfully complete this project.

Looking back at my goals, I can conclude I got to finish a project worthy of my design identity. Furthermore, I did get to showcase my design skills not only in a thorough design process, but also with an interesting interface and interaction. Moreover, I got a chance to work with experts outside the scope of traditional industrial design, working on microbiology, virology, biochemistry, genetics, glass experts, milling experts, business cases, and much more that further developed my knowledge on design-related substance. Concludingly, my goals are all checked, delivered, and in the mail.

I believe that, within the given frame of time, I have accomplished as much as possible based on the tasks and quality levels bestowed upon me by myself. And I have never been so satisfied with a project and its outcome, and I see this as a befitting end to my years at the Department of Industrial Design.

I think my smile will have to be surgically removed...

- Jan van der Asdonk

Introduction

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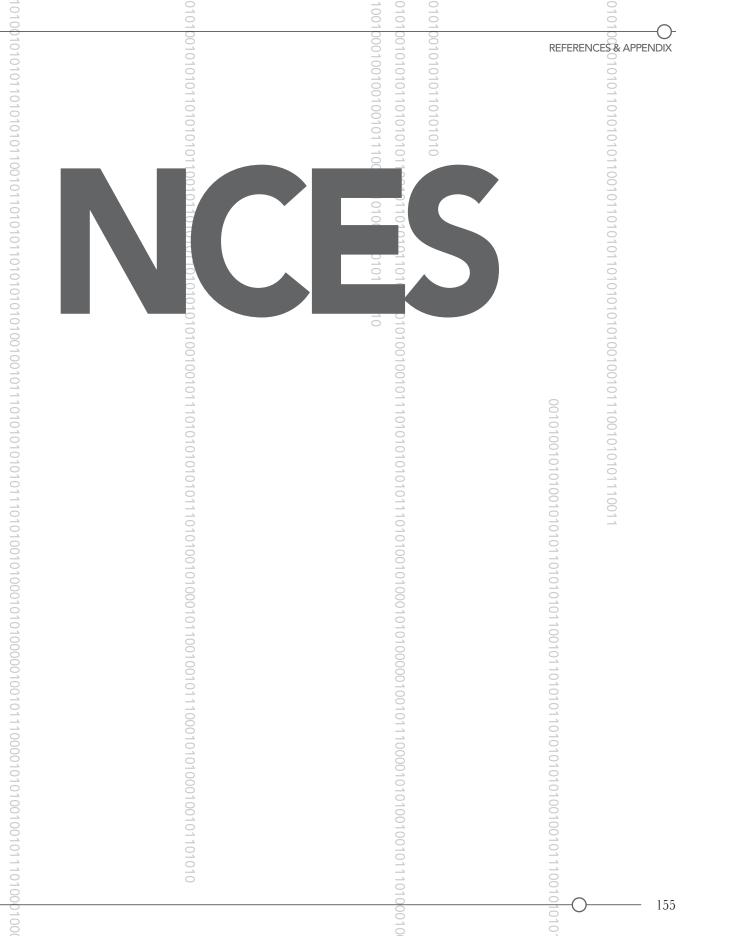
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Thank you for taking the time to read this thesis, I hope you enjoyed it.

You can find more of my work at www.janvanderasdonk.com

