The Art of Antibiotics

Two residencies. Two artists. Two labs.

Biofaction

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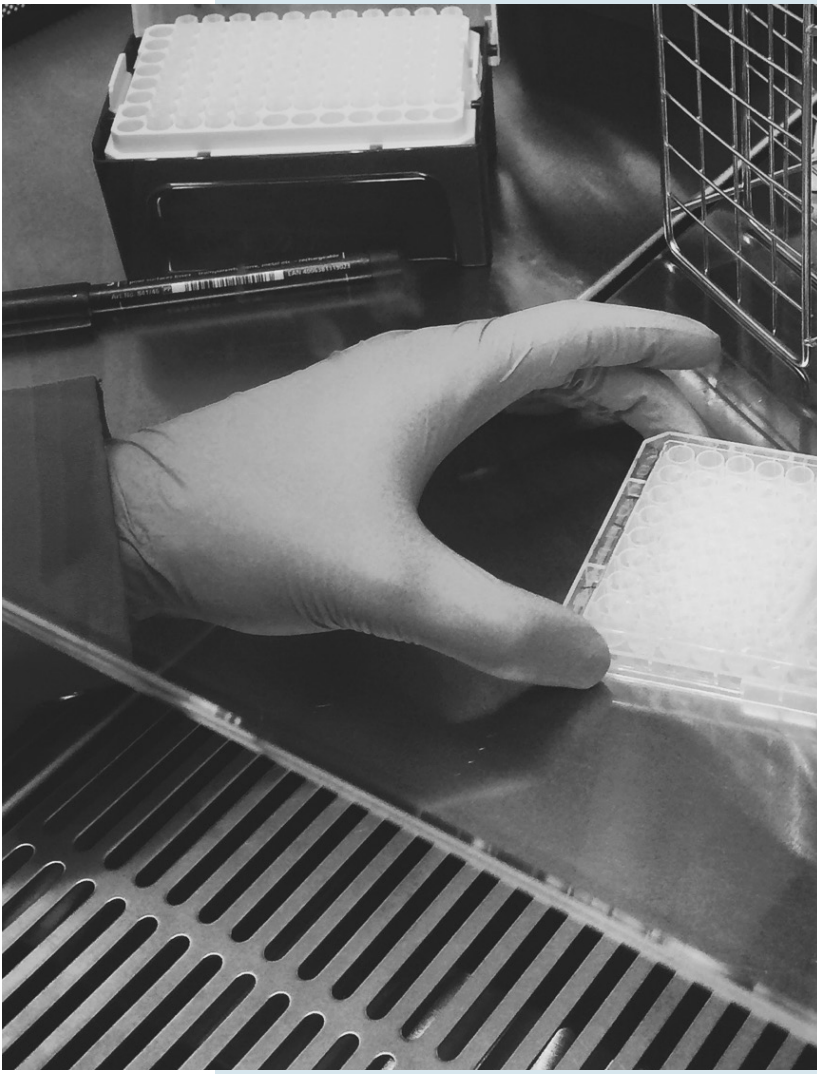

Image: Sarah Craske

Image: Camillo Meinhart

Table of Contents

The SYNPEPTIDE Art Residency

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by Markus Schmidt

The SYNPEPTIDE Art Residency

This booklet documents the artist in residency program we organized within the EC FP7 funded project SYNPEPTIDE. The aim of the project was to design and test novel types of peptide antibiotics. In recent years it has become all the more clear that we are entering a post-antibiotic age, where hitherto useful medicines against bacterial infections are losing their strength due to the build-up of antibiotic resistance in bacteria.

The global answers to the threat of resistant bacterial infectious diseases are manifold and range from better diagnostics, across alternative forms of treatment (such as phage therapy) to altered forms of industrial agriculture (especially in relation to livestock) - to name just a few.

The search for and development of novel antibiotic molecules, however, must remain a high priority, especially since the well-established large pharmaceutical companies no longer seem interested in the development of novel antibiotics, as the return on investment expected in such a venture is viewed as unprofitable. This situation, which has been described as a pharmaceutical "market failure", is a wake-up call for governments everywhere and clearly highlights the importance of publicly funded research and innovation.

Given the magnitude of our need for novel antibiotics, it is no exaggeration to state that a successful search for novel medicines will save the lives of thousands, if not millions, in the future. We see SYNPEPTIDE as an investment by the public hand into the future of public health.

While the precise scientific undertaking to understand, design, synthesize and test large amounts of combinatorial lantibiotics requires highly specialized knowledge and skill sets and seems very academic and abstract, the real world ramifications of this research are tangible, concrete and have a direct impact on society. This ambiguity between the abstract challenges in the quest for

novel drugs and the tangible societal implications make the SYNPEPTIDE project a prime candidate for an intervention from the field of art.
For that reason, we issued a call for artists to submit their CVs, portfolios and a letter of motivation to explain why they would like to take up a residency in one of the SYNPEPTIDE labs. Within a few weeks, we received 78 applications from all over the world representing highly diverse artistic backgrounds. Our short list of 8 artists featured individuals who we felt were well equipped to carry out their work within a laboratory environment and in collaboration with scientists. These 8 artists had already had some exposure to the natural sciences and work in the lab, but, moreover, they demonstrated their ability to take up inspiration from science and to transform it into their art.

After a series of interviews and consultations with the respective laboratories, we finally invited "artist without category" Sarah Craske (UK) to carry out her residency in Switzerland at the ETHZ Basel, in Sven Panke's Bioprocess laboratory, and composer/programmer Eduardo Miranda (Brazil and UK) to spend his residency in Germany at the University of Regensburg, in Ralf Wagner's group.

In discussions with the artists and scientists we highlighted the importance of not merely viewing the residency as a form of pedagogical variation of science communication, but rather as an opportunity to allow an unhindered exchange between art and science, between them personally, in the hope that the antibiotic research would in one way or another find its way into future artworks.

We were aware that a residency of 4-6 weeks in the respective labs might not be sufficient for the artists to produce a completely new piece of art, but we were confident that the selected artists would continue their work after the residency to eventually be able to show an artwork at a later stage.

It goes without saying that the artists were free to choose their own approach and topic, while our function at Biofaction was to offer support and feedback whenever necessary and needed. Each artist was also supported with a lump sum (to cover travel costs, materials and artist fees) of 7.000 Euros. However, the real opportunity for the artists (and scientists of course) was, without a doubt, the chance to interact in the lab, to learn from each other, and to reflect on the ramifications of the research from an artistic point of view.

The two artists are currently in the process of organising exhibitions and/or opportunities to premiere their work. For updates please check our website at:

www.biofaction.com/portfolio/synpeptide-art-residency

In this booklet, we offer an introduction to the problem of antibiotics resistance in pathogenic bacteria and the SYNPEPTIDE strategy to overcome that, using modularity and combinatorics of peptide antibiotics. Sarah Craske and Eduardo Miranda then offer an insight into their work by describing their experience with the residencies and the pathways towards their artwork. Finally, the involved scientists report their experience with the artists spending time in their lab.

We hope that the readers will be intellectually, emotionally and aesthetically stimulated by the contents of this booklet.

In case you would like to get back to us with any kind of feedback, please do so at: *art-science@biofaction.com*

An Introduction to Antibiotics

by Lei Pei & Markus Schmidt

Introduction

Antibiotics are one of the most successful medicines that have saved many lives and contribute significantly to the control of infectious diseases. The modern antibiotic era is usually associated with the discovery of syphilis treatment drugs by Paul Ehrlich on the one hand, who developed approaches to screen chemical compounds in order to find one that could cure syphilis in 1909, and on the other hand the discovery of penicillin by Alexander Fleming in 1928, who developed approaches to screen antibacterial compounds from other microorganisms (Aminov 2010). Until today, these two types of approaches continue as the main strategies in the research and development of novel antibiotics, which have led to obtaining antibiotics currently available in the market and have contributed greatly to improving public health all over the world. However, due to the limitations of the antibiotics themselves, the misuse of the drugs, as well as the emergence of resistance factors in bacteria, novel approaches are needed in order to find new antibiotics to control antibiotic-resistant bacterial pathogens, as shown in Figure 1 (Brown and Wright 2016).

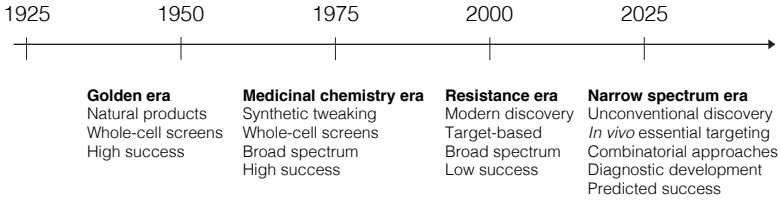

Figure 1. *Historical and future anti-bacterial drug discovery approaches (Adapted from Brown and Wright 2016)*

With the advent of antibiotics as well as other preventative approaches (such as hygienic practices, vaccines etc.), bacterial infections and related diseases became much less of a health problem. In contrast to the pre-antibiotic era over a 100 years ago, infectious diseases are not the leading cause of death in the developed world (see Figure 2) (Armstrong et al. 1999). Combining the amount of lives saved and the offspring of these "antibiotic" survivors, it is fair to say that a large part of the world's population today lives because of antibiotics.

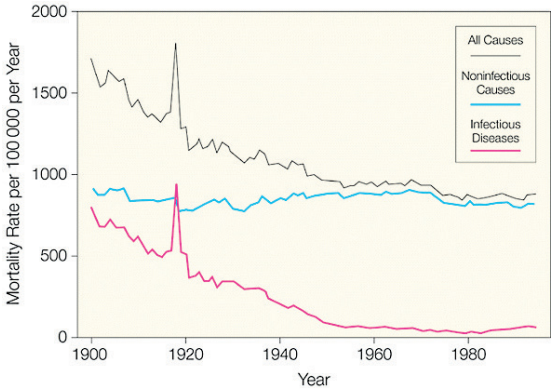

Figure 2. *Mortality rates for all causes (in grey), noninfectious causes (in blue), and infectious diseases (in pink) in the USA since 1900. The spike around 1918 was caused by the Spanish Flu. (Source: Armstrong et al. 1999)*

Antibiotics are only effective against bacteria (but not viruses) and can be classified based on their mechanisms of actions, that is the way the antibiotic molecule interferes with the bacteria to stop its growth or inactivate/kill it (see Figure 3).

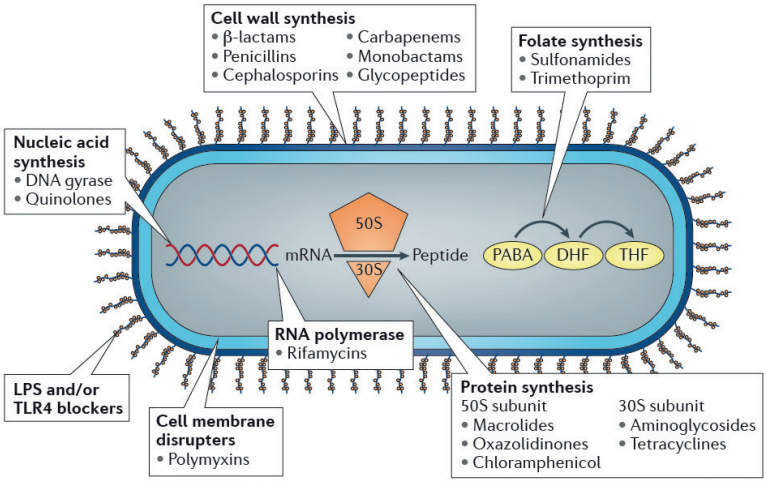

Figure 3. *Different antibiotics use different biochemical targets and mechanisms to attack bacterial cells (a schematic bacterial cell is shown here). Some antibiotics inhibit the synthesis of the cell wall, others block the synthesis of the DNA etc. (Source: Brown 2015)*

Antibiotic Resistance

Records and evidence of antibiotic resistance can be traced back before the antibiotic era, as herbal medicines and other ancient anti-infective treatments have been used to treat humans for a very long time (Aminov 2010). In fact, scientists have even found genes for antimicrobial resistance in ancient DNA from 30,000-year-old Beringian permafrost sediments pointing to the existence of antimicrobial weapons and their defensive mechanisms a time long before humans started to apply medicine (D'Costa et al. 2011).

There is a paradox existing for antibiotics: that "through their use, they not only inhibit an infection, but also select for the emergence and spread of resistance, directly counteracting their long-term efficacy" (Baym et al. 2016). Yet the increasing prevalence of antibiotic-resistant bacteria poses a great threat to primary antibacterial therapy (Davies and Davies 2010). The emergence and spread of multidrug-resistant bacteria poses a great burden on human health: increased mortality, morbidity, and expenditure (WHO 2014).

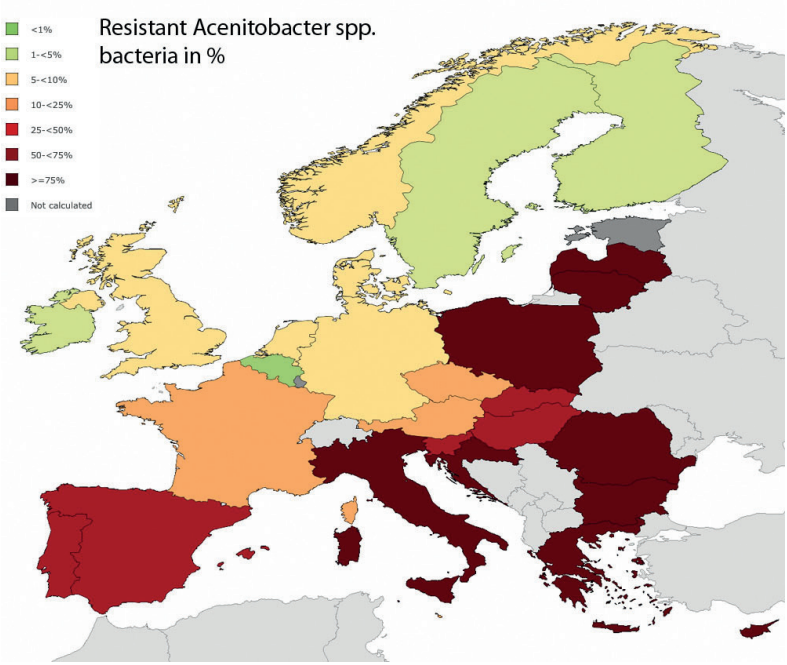

Figure 4. *Antibiotic resistance in various EU countries, Surveillance Atlas of Infectious Diseases, data for 2015 (Source: ECDC 2017)*

To combat antibiotic-resistant bacteria, the origins of these resistances need to be understood. From the point of view of the pathogen, several reasons for antibiotic resistances are known:

- Genetic mutations in the bacteria that cause (partial) resistance
- Exchange of existing resistant genes via so-called horizontal gene transfer between bacteria
- Inactivation of the drug before it can reach the target site.

From the point of view of human practices and their impact on ecosystems and evolution, the following factors contribute to the emergence of antibiotic resistance:

- Using antibiotics as "growth promoters" in livestock
- Treating sick farm animals with excessive antibiotics
- Feeding antibiotics routinely into aquacultures
- Unnecessarily adding antibiotics into household products
- Over- and/or mis/prescribing antibiotics in patient treatments

To make matters worse, there is not only an increase in the resistance to antibiotics, but also a lack of interest by large pharmaceutical companies to research and develop novel antibiotics. As WHO pointed out, hardly any new antibiotic drug has been developed in recent years or even decades, a situation that has also been described as a market failure (Figure 5 and 6). We are "now heading for a post-antibiotic era"(WHO 2014), which is calling out for urgent global action to tackle antibiotic resistance (Hede 2014).

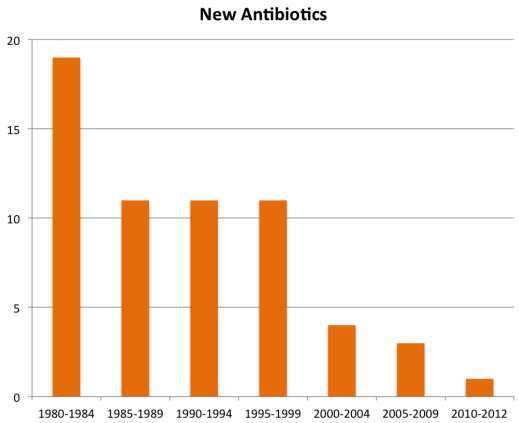

Figure 5. *Recent decades show a decline in the number of novel antibiotics developed (Adapted from US Centers for Disease Control and Prevention, CDC 2013)*

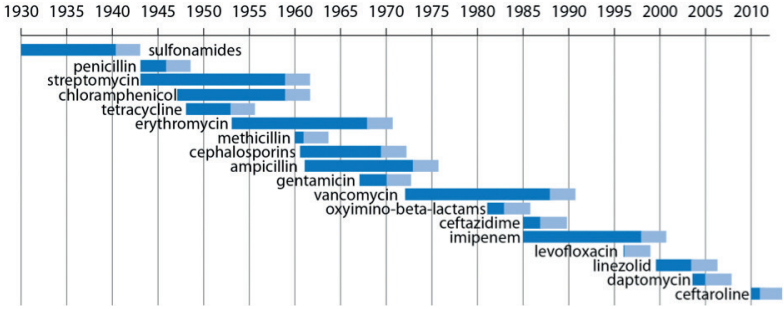

Figure 6. *Development of antibiotic resistance. Timeline of effective drug treatment for selected antibiotics. Dark blue bar: Time from first release of a novel antibiotic or antibiotic class to the market to time when first resistance was observed. Light blue: Time for which the antibiotic was continued to be administered after the first appearance of resistance. (Adapted from McClure and Day 2014)*

Strategies to Tackle Antibiotic Resistance

A global problem requires a global solution, which is why antimicrobial resistance is an item on the agendas of the EU, the G20 and the UN World Health Organization WHO.
The WHO is updating a priority pathogens list to facilitate the research and development of new antibiotics. The list contains the name of the bacteria and the type of resistance:

Priority 1: CRITICAL

- Acinetobacter baumannii, carbapenem-resistant
- Pseudomonas aeruginosa, carbapenem-resistant
- Enterobacteriaceae, carbapenem-resistant, ESBL-producing

Priority 2: HIGH

- Enterococcus faecium, vancomycin-resistant
- Staphylococcus aureus, methicillin-resistant, vancomycin-intermediate and resistant
- Helicobacter pylori, clarithromycin-resistant
- Campylobacter spp., fluoroquinolone-resistant
- Salmonellae, fluoroquinolone-resistant
- Neisseria gonorrhoeae, cephalosporin-resistant, fluoroquinolone-resistant

Priority 3: MEDIUM

- Streptococcus pneumoniae, penicillin-non-susceptible
- Haemophilus influenzae, ampicillin-resistant
- Shigella spp., fluoroquinolone-resistant

The EU has prioritized the problem high on its agenda, issuing for example a European One Health Action Plan against Antimicrobial Resistance (AMR) (European Commission 2017) with the following aims:

Best practices

- Better evidence and awareness of the challenges of AMR
- Better coordination and implementation of EU rules to tackle AMR
- Better prevention and control of AMR
- Better addressing the role of the environment
- A stronger partnership against AMR and better availability of antimicrobials

Boosting research, development and innovation of AMR

- Improve knowledge on detection, effective infection control and surveillance
- Develop new therapeutics and alternatives
- Develop new preventive vaccines
- Develop novel diagnostics
- Develop new economic models and incentives
- Close knowledge gaps on AMR in the environment and on how to prevent transmission

SYNPEPTIDE: synthetic peptides

While the AMR strategy contains a number of alternative tactics to fight pathogens, including better diagnostics and vaccines, amongst others, there is still a need to produce novel antibiotics.

The European Commission funded project SYNPEPTIDE is one of the few international research projects that aim to develop novel antibiotics. SYNPEPTIDE is a pan-European project bringing together 5 academic groups and 3 SMEs across Europe to identify and produce novel antibiotic molecules, focusing on lantibiotic molecules, which are peptides containing animo acids linked via sulfur bridges (Figure 7).

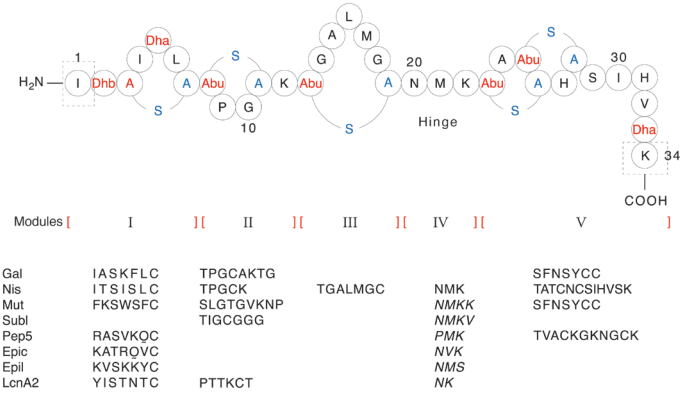

Figure 7. *(A) Schematic view of a lantibiotic peptide called Nisin. Note that some amino acids (circles) are connected by additional sulfur atom bridges (added after the translation from DNA to amino acids) that cause the specific shape of the molecule. (B) List of different natural lantibiotics, whereas each letter represents one amino acid (e.g. A= Alanine, C=Cysteine). The chain of amino acids can be broken down in different modules and rearranged in different combinations. (Adapted from SYNPEPTIDE)*

SYNPEPTIDE harnesses the methods of synthetic biology and high-throughput screening to discover novel peptides with antibiotic activities and then synthesize them via metabolic engineering approaches. The project has been conducted in a five-stage approach:

1. Define the standard building blocks of lantibiotics
2. Design a DNA library of new modules that incorporate non-canonical amino acids
3. Develop approaches to synthesize these novel lantibiotic molecules from the library
4. Synthesize new lantibiotics *in vitro* and screen them for antibacterial activities
5. Mimic the approaches of *in vitro* synthesis of lantibiotics via metabolic engineering design to overcome restrictions in cellular biosynthesis to enable their production by large-scale fermentation

The DNA library contains the information to code for the amino acid modules seen in Figure 7B. By combining the natural modules in new ways, SYNPEPTIDE was able to produce thousands of novel lantiopeptides not found in nature. Each of these new molecules is tested in a high-throughput diagnostic system to see if the new molecules are effective as an antibiotic. In a next step, SYNPEPTIDE attempted to add amino acids that are are not found in natural peptides. This is based on the fact that of the several hundred amino acids known to exist, only 20 to 22 are used to make proteins and peptides. The incorporation of some of the remaining so-called non-canonical amino acids is another goal of SYNPEPTIDE. The main goal of SYNPEPTIDE is the combinatorial design of lantibiotics using peptide modules, including the introduction of non-canonical amino acids and other modifications to further diversify the biochemical structure of the lantibiotics. The SYNPEPTIDE research project hopes to make a substantial contribution to the design of novel effective antibiotics not found in nature.

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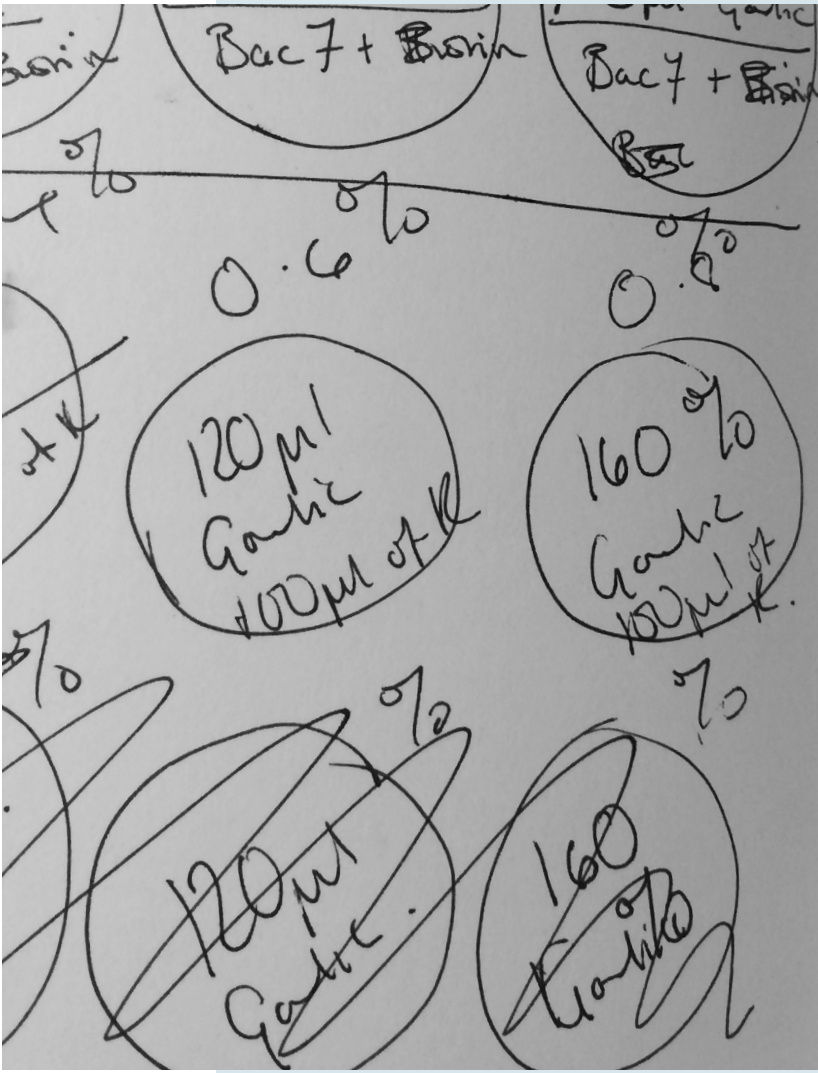
Image: Sarah Craske

Sarah Craske's Residency

Bioprocess Laboratory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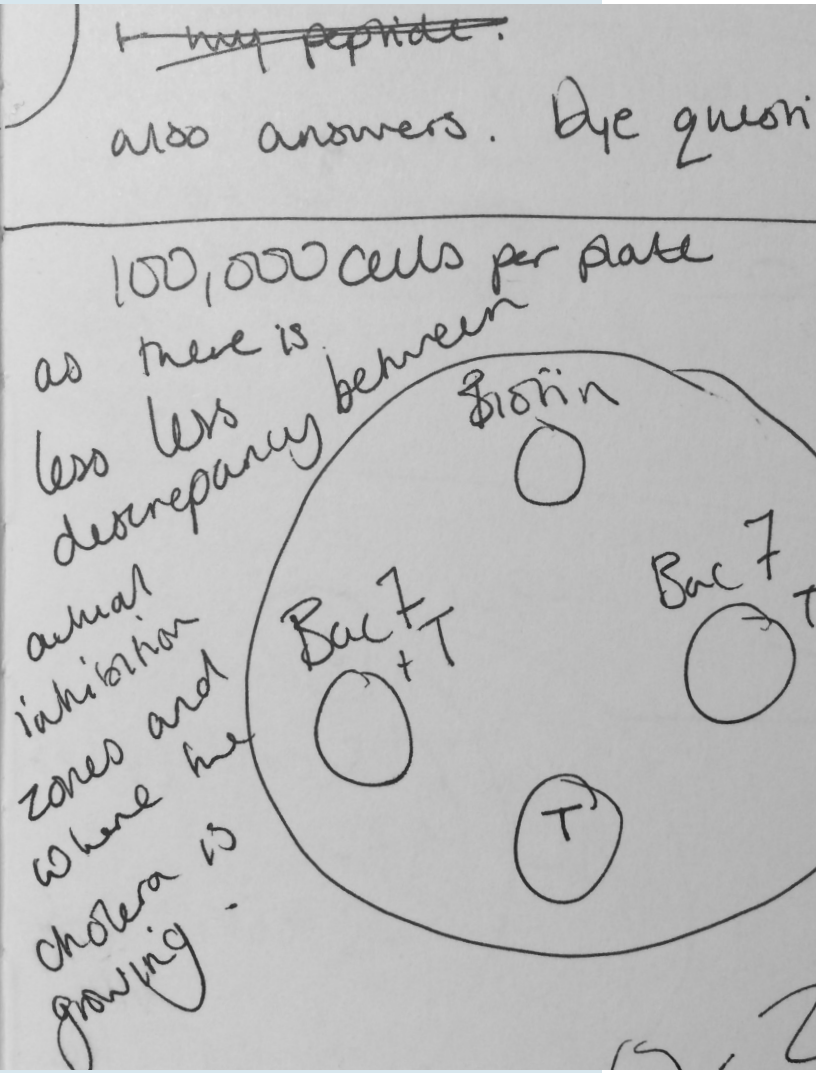
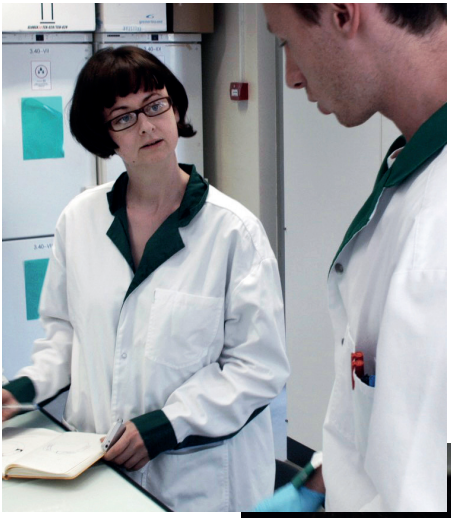
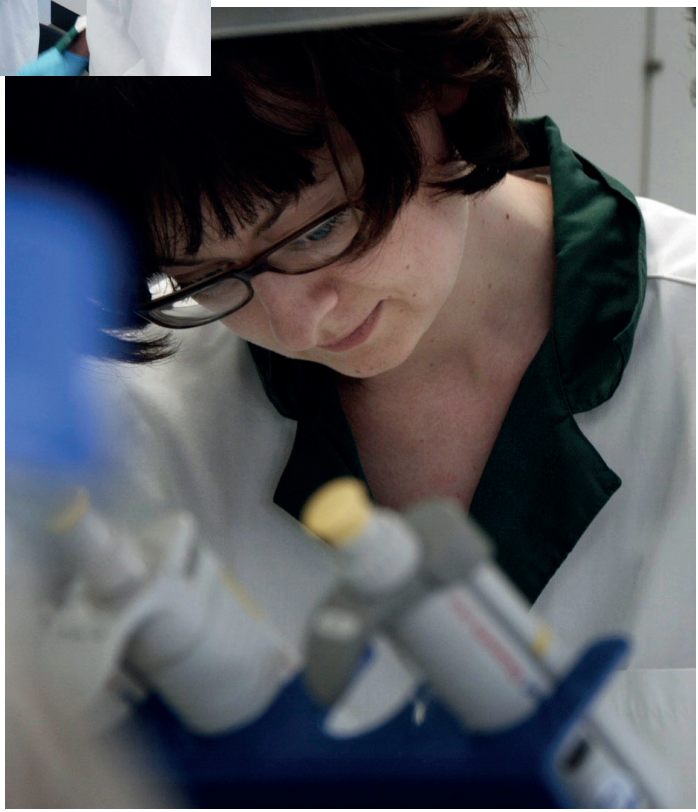
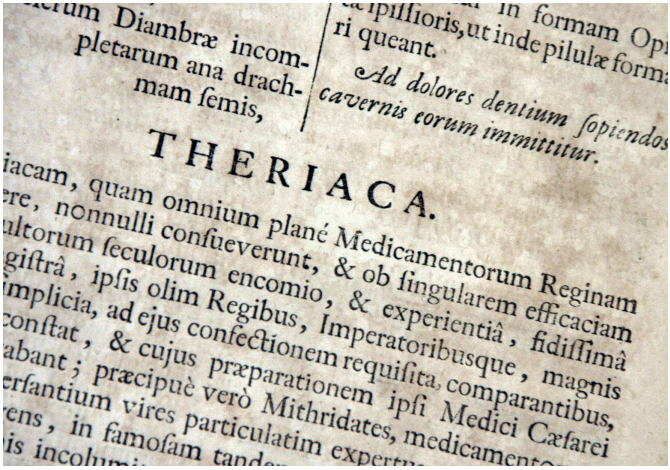


Image: Sarah Craske







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THERIACA.

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abant; præcipuè verò Mithridates, medicamento
erſantium vires particulatim experti
ens, in famoſam tande
is incolumi

Images: Camillo Meinhart

Image: Camillo Meinhart

The sickly struggle of a man is death in life,
For the proper life means instead to float in health,
Then, you dead, seek such means here
To dare your enemies and release their hold…
Andromachus alone has conceived a help
And put every poison to shame and ridicule
Here will be readied the joy and calm of life
And yet so costly as it were made in Venice
Then say farewell to death, and believe this truly:
Here meet the fierce enemy, who will arm you well!

Theriak - A poem announcing its availability by a pharmacist in Konigsberg, 1683. (Swiderski 2010)

Residency Report

Sarah Craske

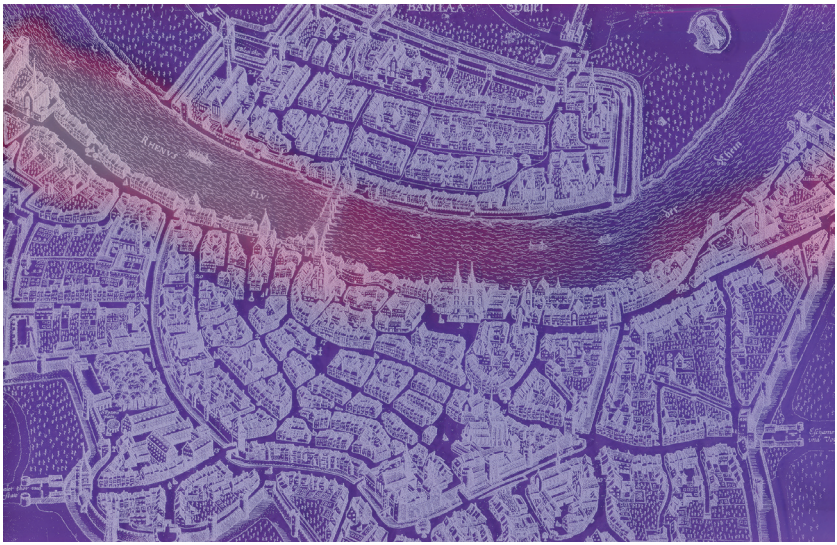

Figure 1. *A still from the film THERIAK*
(Source: Sarah Craske)

THERIAK

Asymmetry

From 2014 until 2016, I had been immersed in a transdisciplinary team in the UK. Through an Arts and Humanities Research Council Grant we explored innovative and collaborative interrelationships between the sciences, arts and humanities, and developed shared ways of working in new and emerging fields. We mapped languages and practices that united and divided artists and scientists, whilst enabling individual reflection on research approaches. We also produced exhibitions that presented our hybridised enquiry and furthermore yielded data for potential future research.

The transdisciplinary team specifically studied a 1735 edition of Ovid's Metamorphoses using both arts and science methodologies, and has achieved arts, humanities and biological readings of the original text. Our meta research method was reflexive, using frameworks from Science and Technologies Studies as a means of critical reflection upon our studio and laboratory activity.

One of the weaknesses in our research activity was that it was firmly rooted in the UK landscape. Furthermore, our team replicated an arts and science asymmetrical trope as observed by Martin Kemp in his article published in Nature 'Culture: Artists in the lab':

"Asymmetries abound in these collaborations. The projects matter in professional terms far more to the artists than the scientists. Little, if any, kudos is to be gained by the scientist in having a Sciart project on his or her CV. It would be good if scientists received more recognition for their participation. For the artist, the collaboration can be an important career move, opening up new venues and audiences. Participating scientists tend to be well enough established not to have to worry about 'wasting time' on an art project. They are often older, male and of high status. Large numbers of the artists are female, young and aspiring." (Kemp 2011)

An Attempt at Symmetry

Throughout 2017 I have been immersed in a synthetic biology lab (Bioprocess Laboratory (BPL)), at ETH Zürich in Basel, as part of the Biofaction Artist in Residence programme.

From the outset, what interested me about this opportunity at the point of application was the potential for me to test my current research beyond the UK border and within a larger scientific team of academics at various stages in their careers. Furthermore, there was an expectation that the artist achieved the following during the residency which initially was proposed to be between 4 and 6 weeks in length:

"to explore arts or alternative cultural practices' potential with regards to the visions, challenges, philosophical, aesthetic, and ethical aspects of synthetic biology;
to add a complementary outside-the-box perspective to synthetic biology, its societal ramifications and cultural aspects;
to help envision the potential long-term changes synthetic biology might bring to society." (Biofaction 2016)

The call out also requested that:

"You, as the artist in residence, will interact with scientists in the laboratory in Basel as well as with the team at Biofaction in Vienna, in order to ignite a cross-disciplinary exchange. You will learn and engage with the current research, connect it to your own practice, as well as to wider societal and cultural aspects, in order to create a body of work, to be presented at the end of the residency." (Biofaction 2016)

There were echoes of my own research frameworks within their aims, so I proposed both a meta reflexive and subjective research approach to the residency that would use my knowledge gained from my previous transdisciplinary research to date. I proposed that I would examine and develop existing common linguistic, philosophical, aesthetic and ethical ground between art and synthetic biology, with a focus on the societal and cultural relationships to synthetic biology and their pathways to public engagement. Furthermore,

and most importantly, I requested that Biofaction trust the creative process.

What was important to me was that I had time to familiarise myself with the scientist's research and laboratory environment before I developed any specific research questions and ideas. I also intended to develop research questions that were both of interest to me and the scientists involved, thus from the outset I had no specific plan proposed beyond my methodology.

Caution

Since 2014 I have been developing my own manifesto which is tentatively governing my own practice. Among many propositions, it currently establishes that I do not participate in purely scientific communication and public engagement programmes, and that I am remunerated for my contribution, as an artist, fairly. Consequently, before I apply for or take part in opportunities that intend to encourage an art and science collaboration, I review the landscape these opportunities reside in, in an attempt to understand my actual place within the broader context.

The residency invited an artist to join the SYNPEPTIDE research team in the Bioprocess Laboratory (BPL), at ETH Zürich in Basel. SYNPEPTIDE was a "FP7-sponsored project bringing together 5 academic groups and 3 SME's from across Europe to identify and use novel antibiotic molecules." (SYNPEPTIDE 2013). For four years, the academic groups from Switzerland, The Netherlands and Germany attempted to create new and active peptides using synthetic biology and high-throughput technologies.

It ran from the 1st September 2013 until 31st August 2017, and therefore I was being invited to join the team at the tail end of their research. With six months remaining, my experience suggested that the academic teams would be col-

lating and reporting on their work, rather than being in the midst of active research. I would also not have direct insight into their research pathway and essentially be reviewing their work to date. So why at this stage in the research process was an artist being invited into the laboratory?

The total cost of the research project was €7,170,757.60 over the four years (European Commission 2015). Biofaction, a research and science communication company was a partner in the research group and received €374,358 for public engagement. Science communication is usually in the service of science and a majority of the public engagement activity frequently occurs near the end of the research period to deliver the results of the research. The artist in residence programme was clearly part of this much larger public engagement programme and I was concerned that I would be expected to 'communicate results'. Biofaction however, was refreshing in its approach. I was reassured that this was not a public engagement exercise and that it was a much more exploratory activity that they hoped would lead to novel and exciting work.

Their proposed professional fee was comparatively reasonable. Many residencies in the current global financial landscape are offered to artists with the expectation that the artists will pay for the experience. Many others offer to cover expenses only, rather than acknowledging the artists time. This opportunity paid a transparent fee of €7000.00 to be spent by the artist accordingly, to cover the artists time and expenses over the four to six week period. Based on 4-6 full weeks of work however, that equates to between €166.67 to 250€/day. Depending on the final time needed, this is above or below the recommended fee suggested by Arts Council England and the Artists' Union (Artists' Union 2017) of €187.30/day (for newly graduated artists within 3 years of their BA only) and obviously this simple calculation does not take into consideration expenses associated with the activity like travel and accommodation. Ultimately however, it is up to the artist to accept these terms and manage the money accordingly.

Time was my final concern. There was a high expectation from four to six weeks of activity. It can take months to develop a body of work, from research, critical reflection to production. In conversation, Biofaction also intimated that they would like to see an exhibition resultant of the activity,

which of course requires further time, management and finance. Ultimately, and what is usually the case with research grants, they wanted a lot of return on their money. That said, the opportunity to test my current research beyond the UK border and within a larger scientific team of academics was timely, and to be supported and encouraged in the creation of new work is always exciting and appreciated.

Basel and Peptides

Week 1 & 2 – March 2017

Basel
Research is at the heart of my practice. Art college encouraged an acute awareness of the critical and historical relationship that my work has with predecessor artists and art history. Furthermore, I am extremely reflexive when considering the representational implications asserted by my choice of materials, media, methods, and context of display. I am familiar with my disciplinary landscape; intuition has developed from expertise.

This wider contextual gaze is quite different to the reductive detailed view that many scientists must adopt, as Professor Charlotte Sleigh asserts:

"Scientists have an awareness of the significance of their work in relation to recent history – that is, the work of researchers in closely-related fields. They know that a recent experiment, published in a research journal, leaves a particular question unanswered, and they will attempt to answer it through their own work (which, if successful, may be published in the very same journal – so the process continues). However, they have a relatively poor grasp of longue durée scientific history, and of the cultural implications (of gender, ethnicity, ableism and so forth) that are entrained by their choices in problem framing, research context, personnel, and funding."
(Sleigh and Craske 2017)

However, as much as I am comfortable practicing within my own disciplinary historical narrative, I experience feelings of uncertainty when practicing in a landscape of which I have no knowledge of its past. The history of synthetic biology is unfamiliar to me. Furthermore, before arriving at the laboratory I did not know the materials, media, methods and contexts of display available for use.

During my initial visit, I was driven to find out specifically why I was in Basel and to start to understand the disciplinary narrative that I was about to participate in. My time was spent both in the Bioprocess Laboratory as well as in cultural institutions that were History of Science repositories.

Figure 2. *A collection of remedies on display at the Basel Pharmacy Museum (Source: Sarah Craske)*

A quick survey of Basel's museums soon led me to the Pharmacy Museum, which is one of the world's largest collections of pharmaceutical history. It features complete pharmacy interiors, an alchemist's laboratory, medicines from across the globe from BC to the present day, and an extensive pharmaceutical manufacturing archive. It was also the home of the humanist Erasmus and the alchemist Paracelsus.

Through the museum's academic team, I soon understood that Basel has been actively fighting disease for centuries. One of the theories as to why Basel in particular has such a long tradition of having to fight disease is perhaps because of its bridge, the Mittlere Brücke. The Mittlere Brücke is not only one of the oldest bridges to cross the Rhine (1226), but it was also one of the only places to cross it. In the 14th century it became a recognised international trade route (Basel Culture Unlimited 2017) and perhaps not just in goods, culture and ideas, but one could also argue – in disease.

The Black Death swept across the city from 1349-1352 and has struck the city several times since. It was also brought to my attention that Basel had a famous skeleton wall mural, the Dance Macabre (Basler Totentanz), which is believed to have portrayed late medieval and early modern epidemics (coincidently, I was staying on that very square that used to be its location). The city also experienced an outbreak of syphilis around 1495 and in the 19th century, the city suffered several outbreaks of typhus and cholera which changed the architecture of the city dramatically through the introduction of sewers and the moving of waterways. Basel's fight against tuberculosis laid the foundation for the creation of Sirolin, the first commercial success of the pharmaceutical company Hoffmann-La Roche, which was founded in Basel, in 1896.

As early as the late medieval and early Renaissance periods, Basel has been the home to some remarkable thinkers who have responded to disease. Basel physician and humanist scholar Theodor Zwinger, among other things, extensively studied remedies. Another Basel physician, Felix Plater on returning to Basel in 1557, established himself as a professor of practical medicine at the university. Remarkably, he has been cited as one of the first people to advocate germ theory, understanding that microorganisms were the cause of disease (Wootton 2007).

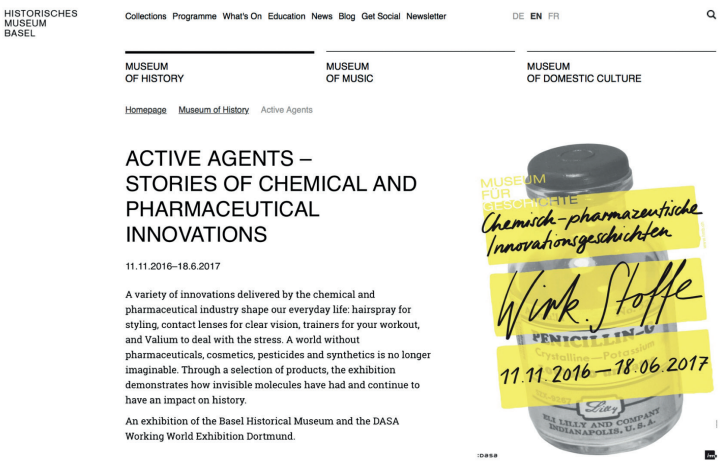

Figure 3. *Active Agents webpage*
(Source: Basel 2016)

Basel's history with the chemical industry happened to be reinforced by an exhibition called 'Active Agents' at the Basel Historical Museum, which ran from November 2016 until June 2017. Chemical and pharmaceutical innovations were on display including hairspray, contact lenses, trainers and Valium. Presenting a world of "pharmaceuticals, cosmetics, pesticides and synthetics… Through a selection of products, the exhibition demonstrates how invisible molecules have had and continue to have an impact on history" (Basel 2016).

Basel's relationship with the chemical and pharmaceutical industries developed from the 16th century silk trade and the manufacture of man-made pigments. Johann Rudolf Geigy-Gemuseus began trading in 1758 in "materials, chemicals, dyes and drugs of all kinds". Global companies like Novartis, who are still based in Basel, can trace their corporate routes back to these original companies through historic mergers and acquisitions (Lesney 2004).

What became abundantly clear, was that the synthetic biology laboratories I had been invited into were very much a part of over 300 years of pharmaceutical history.

Peptides

As a disciplinary stranger in a lab, the artist's role is unclear to both the artist and to those that have invited you, beyond the fact that there is an expectation that you will 'make work' in some form, inspired by the artist in residence experience.

The artist is a stranger and is strange. The immediate consequences of this social experiment are varied and include both practical and philosophical complications that reinforce the feeling of 'working in the margins' - an uncomfortable site that is frequently inhabited by artists.

I didn't quite fit the institutional structures. This meant that despite completing various administrative tasks to enable my presence within the building, I was physically unable to get into the building and had to come up with creative ways of bypassing security. As is usually the case when artists work in laboratories, there was no obvious institutional mechanism that accounted for an 'artist in residence' to 'conduct science' which meant that there was a lot of support from the SYNPEPTIDE team to try and make it work within the structures in place whilst coming up with creative solutions, if required. There was a lack of clarity as to what I could and couldn't do when in the laboratory itself as I didn't fit a model to then check against the protocols i.e. I wasn't a student, or a visitor. I was administratively a temporary member of staff; or was I?

Beyond these very basic practical challenges, when you adopt the role as outside observer within the lab (or any different landscape other than your immediate one), the artist becomes a confidante. By being present in a professional environment but not being an actual part of it, a space is created for candid discussion beyond internal professional relationships. From Imposter Syndrome, to gender and financial issues, private conversations were sought in my newfound liminal space between the laboratories. One of the challenges that became apparent was the conflicting relationship between essential collegiate behaviour and professional competitiveness. It is essential that team members work together, however, this is countered by the desire to keep

their jobs and extend their contracts, which also means that they are in direct competition with each other. The short termism of the research grants, institutional strategy of short term contracts and value placed on 'hungry researchers', means that research pathways are usually cut short as 'new blood' is sought.

During these first two weeks, I worked closely with Dr Irene Wüthrich, learning about her research and observing her scientific practice. Irene is specifically studying a peptide called 'Bac7' which can be found in the immune system of bovines. It is a string of 60 amino acids in the following specific order:

RRIRPRPPRLPRPRPRPLPFPRPGPRPIPRPLPFPRPGPRPIPRPLPFPRPGPRPIPRPL

R = Arginine | I = Isoleucine | P = Proline | F = Phenylalanine | G = Glycine | L = Leucine

In nature, it successfully finds its way into a bacterial cell's ribosome and inhibits translation, which means that it stops the ribosome's ability to function and the cell subsequently dies (a ribosome is an important cellular molecular machine that translates genetic information into peptides and enzymes). Her research includes examining the peptide's effectiveness if its length is shortened at different intervals and whether she can engineer a more effective Bac7, which could then potentially be used in the creation of a novel antibiotic.

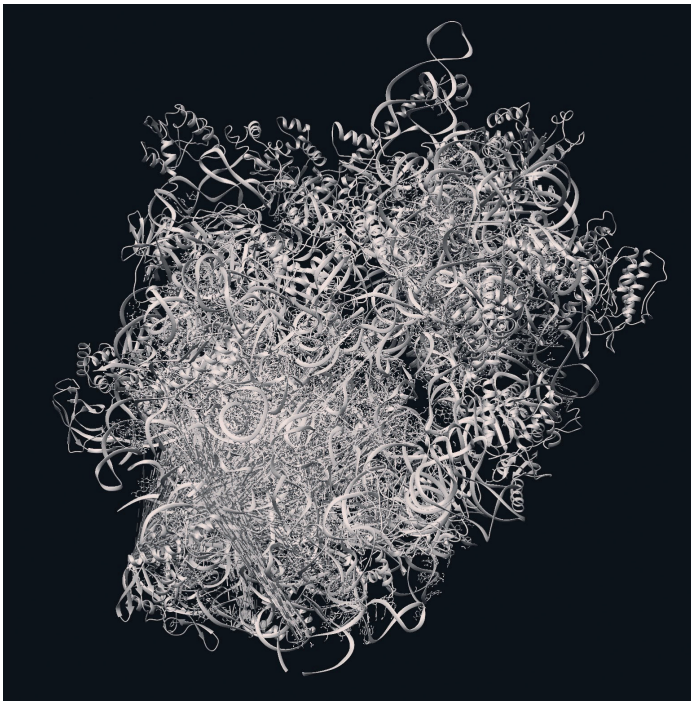

Figure 4. *A 3D visualisation of a ribosome (Source: Sarah Craske)*

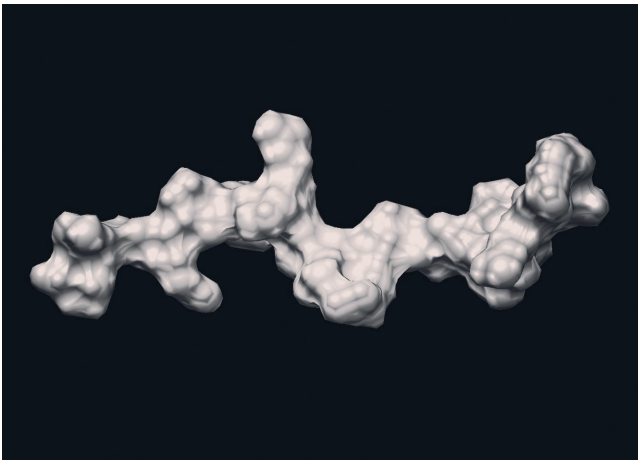

Figure 5. *A 3D visualisation of a Bac7 peptide (Source: Sarah Craske)*

During this process I was reminded of the language differences between the two disciplines. There were initially many moments where Irene and I were struggling to find commonality and understanding, before we began to adapt both our languages accordingly to somehow 'meet in the middle'. Because of this difficulty, I sought for visual clarification so that we could be both presented with an idea in front of us and discuss it accordingly, rather than each of us imagining that subject within our own semiotic frameworks and trying to discuss it from there. This led to a much more 'building block' approach when discussing Irene's subject and thus, 3D models were generated of the ribosomes and the Bac7 to help me understand what exactly I could be working with. This was followed rather conveniently with a couple of days observing Irene with Dr Vincent Lebrun in the University of Basel's chemistry laboratories, chemically synthesising Bac7.

Chemical synthesis was much more practical in approach than the experiments I had been observing at ETH Zurich. Irene and Vincent were quite literally sticking amino acids together and talking about things in a material sense. Furthermore, it became clear that some of the methodologies used in this process, were like the ones I would use in my studio, but at a much smaller scale.

An example of a protocol that I had to follow reads as such:

Protocol For Solid-Phase Peptide Synthesis by Dr Vincent Le Brun

With resin 2-Cl-Trt (add DIPEA in DCM to cancel acidity), grafting of first amino acids:

- Swell in DCM, 30 min, then rinse.
- Grafting 1st aa : in DCM, 1.2 eq Fmoc-AA-OH, 6 eq DIPEA, 30 min.
- DCM/DIPEA/meoh 7:2:1, 1 min.
- Wash: DCM 4 times, DMF 2 times

Cycle for peptide growth:

- Fmoc deprotection : DMF/Piperidine 4:1, 3 min, 3 times
- Wash: DMF 4 times, DCM, DMF
- Coupling: in DMF, 2 eq Fmoc-AA-OH, 2 eq pybop, 6 eq DIPEA, 30 min.
- Capping: DMF/DIPEA/Ac2O 7:2:1, 1 min.
- Wash: DMF 4 times, DCM, DMF

(peptide growth: repeat cycles in grey)

- Fmoc deprotection
- Wash: DMF 4 times, DCM 4 times.
- Cleavage of the peptide + side chain deprotection: 18 ml TFA, 600 µl TIS, 600µl H2O
- Precipitation in cold ether, then 3 washes of precipitate with cold ether.

Past in the Present

Week 3 & 4 – May 2017

With the disciplinary language barrier and the sheer amount of information presented during the first two weeks of my residency, my time was mostly spent recording information and ensuring that I understood what was being presented to me. Having time between visits to the lab was essential for critical reflection.

I am interested in patterns of behaviours across time, and the possibility that we are guilty of unquestioned belief systems that govern our self-determined frameworks. Within those frameworks however, we sincerely believe that we are changing and progressing as evidenced through advancements in technology and our perceived increased understanding of the world. The historian's lens, however, often will evidence the former being true.

When reflecting on the approaches to fighting disease through the centuries, it struck me that, philosophically, not much has changed. We have been in an endless struggle against diseases that sometimes defeat us, and evolve and advance accordingly so that they continue to do so. This pattern of evolution and defeat is unlikely to stop, and it is only through our unhealthy relationship with our own mortality that we continue to fight this inevitable cycle. Of course, there are huge successes in the reduction of human suffering across the world, however nature still prevails in presenting new microorganisms or evolved ones that specifically the SYNPEPTIDE team were responding to. However, I did wonder whether the existential question is ever asked – why bother? Isn't our position as 'disease fighters' one that is reactive to evolutionary activity that is in advance of ourselves, and is this an inevitable status quo?

The SYNPEPTIDE team were exploiting their high-throughput technologies to see if they could create a novel antibiotic through essentially, probability. A peptide can be up to 150 amino acids in length and there are 21 amino acids. Therefore, in theory you could, through synthetic biology, create approximately 2.152.300.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.0 00.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.

000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000.000 different peptides, each having different amino acid sequences and some of which would not occur in nature. The fundamental question was, can the synthetic biologists create something that nature hasn't, and will it be more effective than naturally occurring antimicrobial peptides?

Given the rise of antibiotic resistance and its existential threat to the human population across the world, this approach seems necessary and essential. The 'How many combinations can we come up with and test against disease, with the hope that something works?' question, however, is an approach that we have adopted over centuries.

I revisited the Basel Pharmacy museum and was struck by a remedy called Theriak. Theriac (English spelling) was considered a panacea and evidence of its existence can be found as far back as the first century AD. At the museum, they have a Theriak apothecary jar with a beautifully illuminated list of ingredients. It had a revival during the 17th century in Venice and contained over 64 ingredients, with the belief that all the ingredients and its possible combinations would be able to cure all diseases. This all-encompassing approach to remedy had reported successes, but it is assumed that it is mostly down to the opium present.

The sickly struggle of a man is death in life,
For the proper life means instead to float in health,
Then, you dead, seek such means here
To dare your enemies and release their hold…
Andromachus alone has conceived a help
And put every poison to shame and ridicule
Here will be readied the joy and calm of life
And yet so costly as it were made in Venice
Then say farewell to death, and believe this truly:
Here meet the fierce enemy, who will arm you well!

Theriak - A poem announcing its availability by a pharmacist in Konigsberg, 1683 (Swiderski 2010)

Materials, Methods, Experiments and Artworks

The purpose of my second visit as agreed with the SYNPEPTIDE team, was to present my initial ideas and through collaborative discussion design experiments with an understanding of what was feasible and achievable in the time frame proposed. Ultimately, I wanted the resulting body of work to achieve the following:

- To link synthetic biology, specifically the designing of molecules to kill bacteria, to a broader cultural, historical context
- To consider the history of synthetic biology and its impact
- To be of research interest to the SYNPEPTIDE team, perhaps responding to their research pathways
- To demonstrate viable experiments that are both interesting from an art and scientific perspective
- To present a final artwork that plays on the cultural and aesthetic heritage used within science, disease and fighting bacterial infections

Before I planned the schedule of work, however, I wanted to consider the materials to be used and ultimately presented within the artwork, rather than accept the materials initially presented in the laboratories. The team regularly use E.coli which has been developed into a model organism for lab work. However, when researching the cultural context of this bacteria, I didn't think it would achieve my aims.

WHO Priority Pathogens List for R&D of New Antibiotics

Priority 1: CRITICAL
- Acinetobacter baumannii, carbapenem-resistant
- Pseudomonas aeruginosa, carbapenem-resistant
- Enterobacteriaceae, carbapenem-resistant, ESBL-producing

Priority 2: HIGH
- Enterococcus faecium, vancomycin-resistant
- Staphylococcus aureus, methicillin-resistant, vancomycin-intermediate and resistant
- Helicobacter pylori, clarithromycin-resistant
- Campylobacter spp., fluoroquinolone-resistant
- Salmonellae, fluoroquinolone-resistant
- Neisseria gonorrhoeae, cephalosporin-resistant, fluoroquinolone-resistant

Priority 3: MEDIUM
- Streptococcus pneumoniae, penicillin-non-susceptible
- Haemophilus influenzae, ampicillin-resistant
- Shigella spp., fluoroquinolone-resistant

(WHO 2017)

The fight against antibiotic resistance is governed in part by the World Health Organisation. They publish a list of priority pathogens for research and development of new antibiotics, however, again, when cross referencing their cultural narratives, none of them seemed appropriate. They were politically driven, and appeared to be considered from a Western perspective.

I noticed for example that, colloquially, A. baumannii is referred to as 'Iraqibacter' due to its seemingly sudden emergence in military treatment facilities during the Iraq War. I didn't necessarily want to talk about war in my own artwork. Furthermore, as I had expected, the SYNPEPTIDE team's own re-

search had moved on since the original proposal. The global research focus is now on gram-negative bacteria. These are bacteria that have two cell walls for an antibiotic to pass through, as opposed to one, and have since been identified as the research priority.

I revisited my research on Basel's history and looked at its major epidemics. The five significant bacterial diseases were cholera, the plague, syphilis, typhus and tuberculosis. Irene looked at them in terms of their viability for laboratory work. Only cholera was potentially a low enough biosafety level classification to work with, at a biosafety level 2, but even that potential caused institutional complications.

DISEASE	ORGANISM	GRAM STAIN	BIOSAFETY LEVEL (BSL)	BSL-1 STRAIN ALTERNATIVE	GROWTH CONDITIONS	GROWTH MEDIA	BETA-GALACTOSIDASE
Cholera	*Vibrio cholerae*	negative	2	lots of options; e.g, *V. natriergens; V. orientalis*	26°C, aerobic; 30°C	ATCC® Medium 105: Nutrient agar with 1.5% NaCl; ATCC® Medium 731: Luminous medium, etc	yes
Plague	*Yersina pestis*	negative	3	*Y. bercovieri, Y. ruckeri, Y. rohdei; Y. aldovae*; etc	26°C, aerobic	ATCC® Medium 3: Nutrient agar or nutrient broth; ATCC® Medium 18: Trypticase Soy Agar/Broth; ATCC® Medium 260: Trypticase soy agar/broth with defibrinated sheep blood	yes
Syphilis	*Treponema pallidum*	negative	3	*T. phagedemis, T. vicentii*	37°C, aerobic	ATCC® Medium 2131: OMIZ - P4	yes
Typhus	*Rickettsia prowazekii*	negative	3	no	intracellular	Vero cells	unclear
Tuberculosis	*Mycobacterium tuberculosis*	impervious	3 or 2	*M. smegmatis*	37°C, aerobic	Middlebrook 7H11 or 7H10, egg-based solid media such as Lowenstein-Jensen	yes

Table 1. *Summary of the relevant infectious diseases to consider for use within the laboratory*

Cholera, however, became of increasing conceptual interest as a material to work with. It had contributed to the architectural restructuring of Basel and it played an important part in the history of our understanding of disease. It was during cholera epidemics where the world realised that disease was microbial and could be carried in water. Furthermore, there is currently a horrendous

cholera epidemic in Yemen which

"has become the largest and fastest-spreading outbreak of the disease in modern history, with a million cases expected by the end of the year and at least 600,000 children likely to be affected. The World Health Organization has reported more than 815,000 suspected cases of the disease in Yemen and 2,156 deaths." (Lyons 2017)

Despite it being easily treated in the West with good hygiene practice, vaccines and antibiotics, it is already demonstrating antibiotic resistance. Furthermore, the epidemics in Yemen have highlighted the huge wealth gap that occurs across the globe and how that plays out across politics, scientific research and frontline medicine.

It was established by the laboratory that cholera could be a viable way forward, and I then had to consider how I wanted to incorporate it into experimental activity. I asked Irene what her current research questions were, to see if I could frame the experiments in a manner that would be of research interest, even if in a small way. They included the following:

- Why is Bac7 the way it is?
- Why is it mainly composed of arginines and prolines?
- Why is it not exclusively made up of arginines and prolines?
- How important is the specific nature of a given amino acid at a precise position within the molecule, and what is the associated function?
- How flexible is Bac7 with regards to incorporation of other amino acids?
- What is the minimal functional unit of Bac7 with regards to translation inhibition?
- Why are there several short fragments of Bac7 that retain activity *in vivo*?
- Is Bac7 fragmented when it reaches the bacterial cytoplasm, and do the fragments retain activity? Does that result in intracellular potentiation of Bac7 toxicity?
- What is the most effective version of Bac7?
- Can we engineer more effective versions of Bac7?
- How can we do that in high-throughput?
- Why do short fragments of Bac7 inhibit translation when expressed *in vivo* from a plasmid, but do not inhibit translation in an *in vitro* transcription/translation assay?

The question that interested me the most was whether you could add amino acids to the Bac7 that had no relation to its original sequence, and whether this had any effect, positively or negatively. I started to wonder if I could add my own string of amino acids to the Bac7 that brought all the elements of my research pathway together.

Peptides as Art

Taking into consideration Irene's current research questions, I began to design my peptides in a manner that continued to engage the scientific research team. Working with Dr Steven Schimitt, we created some basic rules for me to follow to give my ideas at least some possibility of success. The Bac7 successfully travels into and blocks the ribosomal tunnnel, therefore it was considered a good idea to perhaps attach my amino acid sequence to the most effective section of the Bac7, so that it still had a good chance of blocking the tunnel accordingly.

I was also advised to use arginines and prolines, as the Bac7 is rich in both and to only use amino acids that are small in structure so there was less chance of it being inhibited in its journey to the ribosome tunnel and inhibiting its own entrance into the tunnel.

I started to enter the suitable amino acids into a word generator to see what would be created. 19 488 words were apparently possible which seemed too large a number to explore. There was also the added complication of what language the word should actually be in, given I was working in Switzerland and wanted the work to reflect a global and historic viewpoint.

I revisited cholera's historic remedies, and reflected on the teams research and designed the following peptides with the hope of then being able to test them against the disease.

	AMINO ACID CHAIN	LENGTH	CONCEPT	AMOUNT	
				mg	ug
PEPTIDE 1	RRIRPRPPRLPRPRPRTHERIAKDDFLCAGGCL	33	Bac7 + Theriak + Garlic	9.9	9900
PEPTIDE 2	RRIRPRPPRLPRPRPRTHERIAK	23	Bac7 + Theriak	9.4	9400
PEPTIDE 3	THERIAK	7	Theriak	2.7	2700
PEPTIDE 4	DDFLCAGGCL	10	Garlic	2	2000

Table 2. *Summary of the designed peptides to be used within the artwork*

My designs included 3 components. The most efficient part of the Bac7 as demonstrated through Irene's research, THERIAK spelt through the amino acids themselves and the garlic antimicrobial peptide. This was because through my research I had learnt that historically, if you couldn't have afforded Theriak, garlic was recommended as part of the fight against many diseases. The longest peptide included all three elements. The BioProcess Laboratory then very generously ordered the peptides to be synthesised and we awaited their delivery.

The Disease Map

Before the end of my fourth week I was still working out how I was going to interpret our activity artistically.

I revisited Irene's initial presentation and it was only when I looked at the following slide that I realised I had a visual tool that I could somehow exploit. Initially, I had absolutely no idea what this slide presented, which was further complicated by the use of words equally owned within the arts, like 'expression', 'culture', 'media' and 'control'. Somehow over the 4 weeks I was now able to understand what I was looking at. I had moved from ascribing my own meaning to the words presented whilst realising their dissonance, to reading the slide through the lens of science.

To illustrate this point, see Irene's slide below:

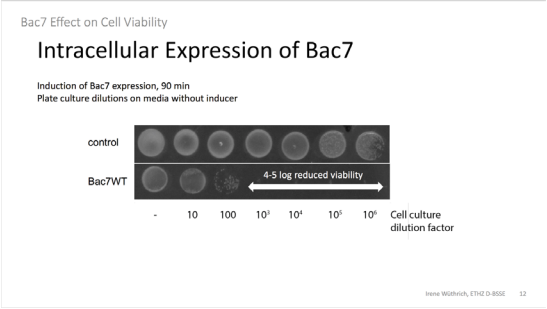

Figure 6. *PowerPoint slide*
(Source: Dr Irene Wüthrich)

Using the plate culture methodologies, I could reveal my invisible peptide through the absence of disease. In this instance, disease was represented by the presence of grey, and the peptide was represented by the presence of black.

The presentation of disease bacteria in block colours on petri dishes are now a common sight in our visual communications, most recently demonstrated in the London's Science Museum's exhibition "Superbugs – The fight of our lives" (The Science Museum 2017).

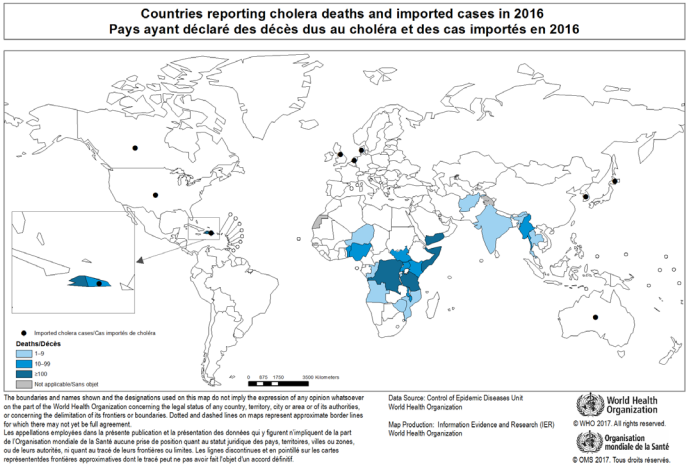

Figure 7. Countries reporting cholera deaths and imported cases in 2016
(Source: WHO 2017)

However, another method of visually representing disease on a macroscale that has developed over the centuries is the 'disease map'. It is still as relevant today, being used by The World Health Organisation, as it was over 100 years ago. The World Health Organisation publishes it's 'Map Gallery' online, and within a few clicks you are visually presented concise information on major health topics, including the recent spread of cholera prior to the major outbreak this year (see Figure 7).

"Maps make arguments about disease, their pattern of incidence, and their method of diffusion. They are workbenches on which we craft our theories about the things that cause health to fail, imaging data collected in this or that disease outbreak."
(Koch 2011)

The cholera disease map has a history, involving Dr John Snow in London (UK), who argued through his maps that the patterns of infection related to local water sources.

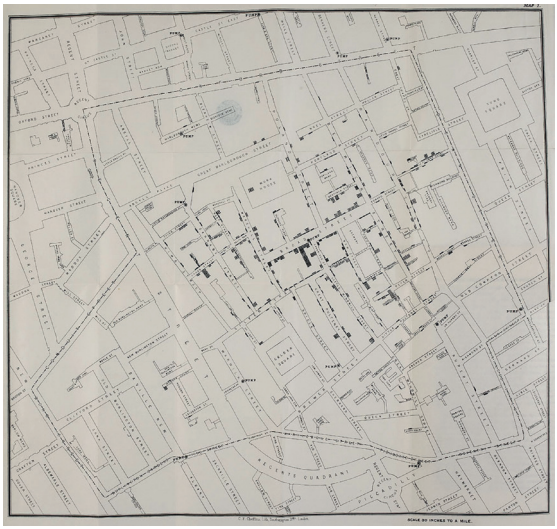

Figure 8. *On the Mode of Communication of Cholera, John Snow, 1855*
(Source: Sarah Craske)

However, I was drawn to Richard Grainger's 1849 'Cholera Map of the Metropolis' and presented this to the SYNPEPTIDE team as it looked more replicable when proposing the use of live cultures.

Figure 9. *Cholera Map of the Metropolis, Richard Grainger, 1849 (Source: Sarah Craske)*

My final idea was to recreate the disease map, using a historic map of Basel, perhaps from the early period of its pharmaceutical history. I proposed the application of cholera, across the city and the application of my peptides. The traditional use of the disease map would thus be inverted. Rather than demonstrating the spread of disease, I would demonstrate through the use of synthetic biology our fight against the disease.

Troubleshooting & the First Steps Towards Collaboration

There were many concerns about the various experiments required to realise my proposed artwork and I was assured most days that we were unlikely to be successful. In fact, it became a joke between the 'artist' and the 'scientists'. The 'artist', clearly in the honeymoon period of science, was full of naive optimism. The scientists, with years of experience, had learnt to emotionally protect themselves by forbidding the feeling of 'hope'.

From the outset there were many uncertainties, and not many certainties. The first problem raised was that cholera had developed a resistance to antimicrobial peptides and was particularly known for not allowing any to pass through its two cell walls. The main question therefore was how we could design the experiment to enable my peptides to pass through those cell walls using experimental 'tricks', to enable the artwork to 'work'. These tricks were especially needed, given it was statistically likely that my own peptides were going to have no antimicrobial function.

The SYNPEPTIDE team, through our various discussions, knew how important it was to uphold the concepts of the artwork through the materials used, and knew that cholera was important within the internal narrative. That said, this didn't stop them humorously trying to persuade me that using E. coli, their model organism, would be a truly excellent idea, and differing narratives followed in an attempt to persuade me that was the case.

Whilst we waited for my peptides to be synthesised, I returned to the UK, whilst Dr Steven Schmitt did extensive trouble shooting to start to understand the parameters of the experiment, so that he could suggest viable ways forward for me, on my return.

His notes written in a manner so that I could understand what he had done, included the following:

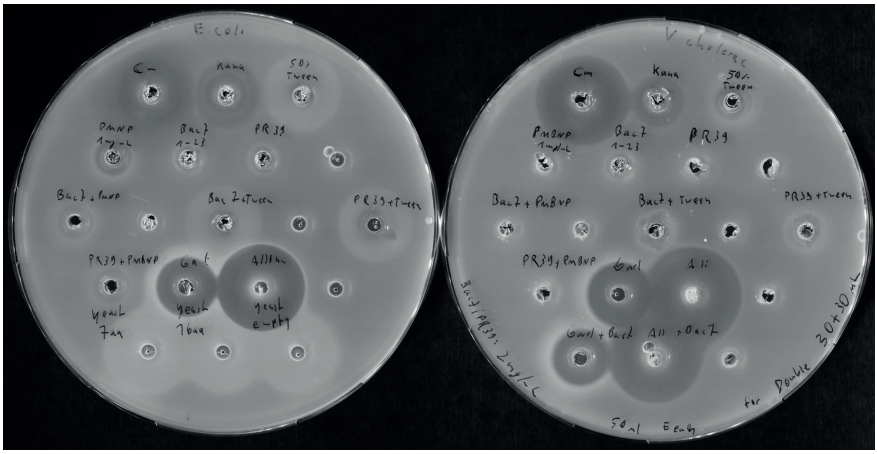

Figure 10. *Susceptibility of Vibrio cholerae and Escherichia coli to different Antibiotics in a diffusion-assay (Source: Dr Steven Schmitt)*

What has been done?

- Vibrio cholerae or Escherichia coli have been embedded into agar-plates (MHB-medium).
- Holes have been made into the agar (19 in total).
- In certain holes, 50 ul of an antibiotic solution was filled.
- The plates were incubated at 37°C and imaged after 18 h.

The following compounds have been tested

- Chloramphenicol and Kanamycin (standard antibiotics), each at 500 ug/ml.
- Bac7 and PR39 (another proline-rich antimicrobial peptide).
- Garlic extracts (one aqueous extract ("AQ") and one chloroform extract ("TCM") which Steven prepared from fresh garlic).

Notes: Ignore the other wells where he tried to find out whether he could improve Bac7 activity against the strains by adding a second compound.

What have you seen?

- During incubation *Vibrio cholerae* and *Escherichia coli* grow within the agar-plate.
- The antibiotics added into the holes diffuse within the agar plate.
- In an area around the holes where the concentration of antibiotics is high enough no growth of the bacteria is observed.
- The biomass turns the agar slightly more turbid – which is just enough to image it with a scanner.

Result

- We see good activity (and therefore big "halos" formed around the holes) for Chloramphenicol, Kanamycin and the garlic extracts.
- Unfortunately no or only low activity is observed for Bac7 or PR39.
- No enhancing activities for the second compounds were observed.

	E. coli MG1655	E. coli CLSI QC	V. cholerae
Chloramphenicol	3.9 ug/mL	2.0 ug/mL	0.5 ug/mL
Kanamycin	2.0 ug/mL	3.9 ug/mL	15.6 ug/mL
Bac7 1-23	3.4 ug/mL	1.7 ug/mL	108.0 ug/mL
PR39	2.9 ug/mL	1.4 ug/mL	>92 ug/mL
Garlic AQ	0.6 %	0.6 %	0.6 %
Garlic TCM	0.2 %	0.2 %	0.1 %

Table 3. *Susceptibility of Vibrio cholerae and Escherichia coli to different antibiotics dilution-assay*

What has been done?

- To see whether the bad activity of Bac7 and PR30 comes from the assay-type or is related to the sensitivity of the strains used, a test with a dilution assay was done.
- A dilution of the antibiotic (10-steps) was made in culture tubes (see graph).
- To each tube *Vibrio cholerae* or *Escherichia coli* (two different strains) were added.
- The tubes were incubated at 37°C.
- The concentration that is just enough to inhibit growth of the bacterium is called "minimum inhibitory concentration" (MIC).

The following compounds have been tested

- Chloramphenicol and Kanamycin (standard antibiotics)
- Bac7 and PR39 (another proline-rich antimicrobial peptide)
- Garlic extracts (one aqueous extract ("AQ") and one chloroform extract ("TCM") which he prepared from fresh garlic

Result

- Bac7 and PR39 are (almost) not active against *Vibrio cholerae* but show activity against *Escherichia coli*.
- As we did not see this activity against *Escherichia* coli in the diffusion-assay, this seems to be an artefact of the diffusion assay when Bac7 and PR39 are used.

Facing the Bad News

Week 5 – July 2017

I returned to Basel to discover that the initial results did not look hopeful. Firstly, the Bac7 peptide showed no effect against the cholera in both the diffusion assay (petri dish experiment) and the dilution assay (liquid culture experiment with no agar). Initially it was presupposed that having no effect on the cholera was a particular artefact of the diffusion assay itself, however when this result was replicated in the liquid culture and within the same experiment E. coli demonstrated success, the suggestion of switching to E. coli was raised again. This was reasonable, given some of my peptides included the most effective part of the Bac7.

There were also other areas that were yet to be addressed aside from the practical issue of getting my potentially non-antimicrobial peptides into cholera, and them then killing it, including:

- What dyes could I use to symbolise the life and death of the disease and at what concentrations so that it worked visually?
- The containment of the experiment which needed consideration, given I needed to incorporate a map and create a time-lapse film, all within the protocols ascribed to Biosafety Level 2 laboratories.

This was my most challenging visit. It involved a lot of trouble shooting and experiment design to ensure success, which equated to 14 hour days (or more), working to the rhythms presented by the experiments undertaken. A MIC Assay for example takes 16 hours to develop, so days had to be planned accordingly to achieve optimum working time in and around these considerations.

What interested me most about Steven's initial research, was the fact that the Garlic itself demonstrated clear inhibition. Given that it was a historic cholera remedy (it is unclear whether it had any effect at all), I was keen to include

Figure 11. *The Biosafety Level 2 Lab at ETH Zurich (Source: Sarah Craske)*

it in the assay design and Steven suggested that we could use it as a tool to weaken the cholera's cell wall to then allow the peptides through. Testing other detergents and garlic in both an aqueous solution and chloroform solution against Cholera in a MIC assay, we discovered the garlic's 'minimum inhibition concentration', which means the concentration at which it starts to have an effect against cholera but doesn't kill it outright. Steven suggested then adding this to the assay in the agar component, before the cholera and peptides were added, to thus weaken the cholera, making it easier for my synthetic peptide to take hold.

Figure 12. *Observing Dr Steven Schmitt at ETH Zurich (Source: Sarah Craske)*

Further experiment modifications included adjusting the diffusion assay to surface application of the cholera to see whether this had a greater chance of success, due to the hypothesis that the peptide might be inhibited in some way within the agar substrate. We also continued to test the Bac7 peptide in combination with the detergents against E. coli and cholera and began to see cholera inhibition in the dilution assays. During this visit, I observed the experiments being conducted by Steven, as time was of the essence and it was important to get the artwork to a stage where success looked possible. Whilst waiting for the experiment results, I would be in the laboratory establishing the visual techniques required for the final film. This included the exploration

of different dyes and their concentrations required to achieve the right visual contrast and scanning techniques to acquire a seamless time-lapse.

By the end of this visit, it looked possible that we might be able to create an assay that demonstrated a synergistic antimicrobial effect against cholera, when combining a garlic agar and my peptide. I had learnt very quickly though that experiments and results just lead to more and more unanswered questions, and I was very mindful of the fact that none of us had the time, or the money to take this research beyond what was required to create the intended artwork, despite our various interests.

Preparing the Petri Dish

Figure 13. *Civitates Orbis Terrarum, Basilaea, Georg Braun & Franz Hogenberg, 1640 (Source: Sarah Craske)*

Before my next visit, I needed to create a petri dish through which I could scan the growth and death of the cholera, whilst including a map of Basel. It needed to be a shallow, optically clear tray that fitted onto the flatbed scanner and I thought that I could engrave a map on its surface, which would then be incorporated into the scanned image.

I chose a map of Basel from around the initial development of its chemical industries and started to experiment back in my studio. Some unexpected results ensued, including the inability to engrave bioassay dishes as they are made of polystyrene, which in turn meant that they melted when in contact with a laser. However, with several samples ready and some back up ideas, in case my petri dish didn't work I returned to Basel in September.

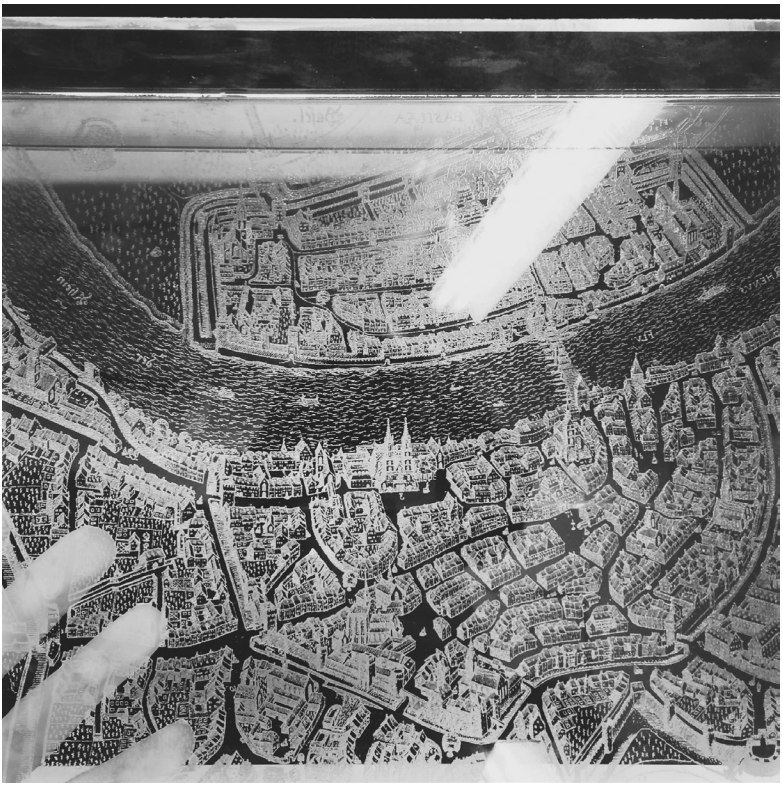

Figure 14. *Basilaea petri dish*
(Source: Sarah Craske)

The Scientific Poster & Peptide Successes

Week 6 & 7 – September 2017

The Poster

I arrived at ETH Zurich in the middle of an academic inspection. This involved deep cleaning, tidying organising, but most curiously, frenetic poster design. Initially, I hadn't fully comprehended how important these 'posters' were within the scientific community until I was asked to attempt one myself. This was suggested a useful exercise so that the department could prove its engagement with the outside world.

A 'Poster' in the fine art world rarely is an artwork in its own right. A close relation would be a fine art print, which frequently is a method of the commercialisation of ideas; a multiple that relates to original and unique artworks, that can be sold in the art market at a lower price and can be a lucrative way for an artist to make money. However, as I started to ask further questions I realised what a big part 'Posters' played in communicating research. At conferences across the world, space is given for rooms of posters for those who don't have the opportunity to present their research in the conference itself. Scientists will stand by their posters for hours with the hope to attract attention and be given the opportunity to demonstrate their work and ideas in hope that they will get recognised and invited into teams, to publish or to present themselves. It transpired that Poster design was competitive, so avoiding competition at all costs (and the template provided) I decided to deliver a more artistic response to the brief.

The Pathway to Peptide Success

My return to the lab bench was to find that once again the experiments I had left behind had not worked. Though we had established that the peptide Bac7 when applied in combination with garlic, could indeed inhibit the growth of cholera in

dilution assays, when I had set the experiments up as diffusion assays, nothing had happened. It was theorised that perhaps it was the sheer volume of cells present in the assay that might be the problem, so it was suggested that I set up some experiments exploring different cell concentrations to see if that made any difference.

For 2 weeks under the watchful eye of Irene, I was pretty much left to culture my own cholera cells, plate them in diffusion assays and experiment with cell concentration, dyes, garlic and the Bac7 peptide. As we had a limited amount of my own synthesised peptides it was agreed not to use them until we were as sure as we could be that the experiment would 'work'. One of my biggest difficulties was exponentiation. I couldn't think of numbers in this way so once it was understood that I simply didn't have these skills and subsequently the team had given up trying to teach me, a spreadsheet for 'exponentiation dummies' was created. Once I had measured the optical density of my cultures, by simply adding this to the sheet, I could then see how to dilute my culture to achieve a standardised number of cells per plate.

My breakthrough moment was, when I visited my plates mid scanning to find that the Bac7 peptide was indeed now visibly demonstrating cholera inhibition. It was now time to test my peptides.

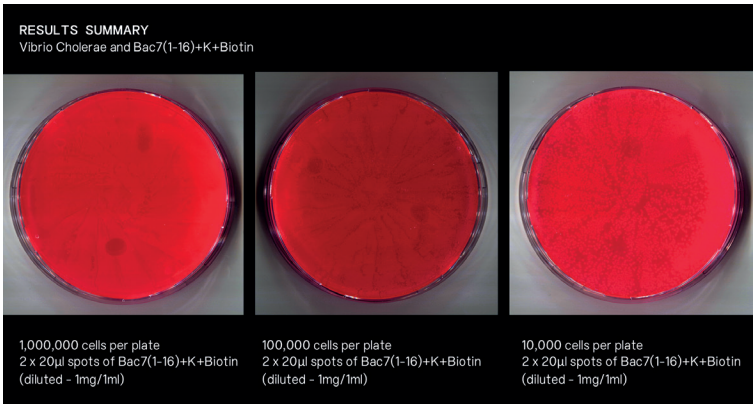

Figure 15. *PowerPoint slide*
(Source: Sarah Craske)

Through a MIC assay we proved that both my peptides that comprised of the Bac7 component, with the THERIAK and the garlic antimicrobial peptide, demonstrated cholera inhibition and also worked against E. coli. It was clear that unfortunately my synthetic peptide THERIAK on its own, had no antimicrobial effect as predicted – not dissimilar to the original historic cure-all.

[mg/mL]	1000	500	250	125	62.5	31.25	15.63	7.81	3.91	1.95	0	
<>	1	2	3	4	5	6	7	8	9	10	11	
A	-0.01852	-0.00962	-0.00972	-0.01522	-0.01192	-0.01132	0.39338	0.37038	0.51178	0.64158	0.46048	Bac7biotin
B	0.30348	0.25058	0.24048	0.30598	0.37208	0.44778	0.44638	0.53298	0.50328	0.42398	0.50978	Bac7THERIAKGarlic
C	-0.01372	-0.01142	-0.01212	0.15058	0.29148	0.30648	0.50328	0.49998	0.54338	0.47098	0.55818	Bac7THERIAK
D	0.71268	0.67538	0.56438	0.63688	0.57258	0.64448	0.57128	0.56738	0.49998	0.46278	0.47028	THERIAK
G	0.02338	0.00908	-0.01002	0.00078	0.02488	0.08718	0.23098	0.64438	0.73308	0.61948	0.68168	Bac7THERIAKGarlic
H	-0.00352	0.01278	0.02288	0.00538	0.01848	0.00768	0.01998	0.02308	0.61818	0.57938	0.59638	Bac7THERIAK

Table 4. *MIC Assay Results*

I could now develop the techniques required to apply cholera across the map of Basel in a manner that replicated a disease map and demonstrated the effectiveness of my antimicrobial peptide. This would represent both Past and Present methodologies in our approach to fighting disease through the centuries.

This involved testing application amounts of both components, application methods and further time-lapse techniques.

Next Steps

By the end of the visit I had managed to create the time-lapse film of cholera infecting Basel and being inhibited by my peptides. This was my first attempt and once again improvements can be made, so I will be returning in December to refine my techniques so that I am completely happy with the visual outcome. As expected the process took longer than the initial 4 weeks allocated, and will have totalled 8 weeks of lab time, with considerable time spent in the studio on research, construction and editing.

The work will be exhibited in Basel Pharmacy Museum next year, running from the 16th October for 3 months. It will include my original synthesised THERIAK peptide displayed alongside the original panacea within their cabinets, a projection of the disease map time-lapse within one of their dioramas and hopefully the BioProcess laboratory live streamed into the museum, again overlaying historic scientific spaces in an attempt to join both the past and present.

My residency experience has been published in Interalia - https://www.interaliamag.org/articles/sarah-craske/. Furthermore, Irene and I have had considerable discussion on language and research across the two disciplines and will be publishing an interdisciplinary response to a recent article written by myself and my collaborator Dr Charlotte Sleigh - https://www.interaliamag.org/articles/sarah-craske-charlotte-sleigh-nine-tenths-iceberg-research-unseen-component-artists-work/. This will be published by the University of Kent on the Centre of the History of Science's blog - https://blogs.kent.ac.uk/sciencecomma/.

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Lab Interviews

Bioprocess Laboratory ETH Zürich, Basel

Interview / Sven Panke

Biofaction: What was your first reaction when asked about hosting an artist in your laboratory?

Sven Panke: Curiosity! I was curious to see how an artist would see the work we are doing and what kind of artwork would come out of his or her work in the lab!

Why did you agree to host the artist in your lab?

Curiosity, to get to know a different perspective. Also a regret that in many artworks I have seen around SynBio and Genetic Engineering I felt there was a strong disconnect between what I care about and what I could see in the artworks. Maybe there was an explanation for that – or a way to do it differently.

How did your peer scientists/scientific staff react to the artist in their lab?

They were curious and interested in it as well.

Do you have any artistic background yourself? If yes, which one?

No.

What was the most suprising/exciting/interesting moment in the collaboration with the artist?

Seeing the process from a blank paper to the final idea to the final artwork.

Did you experience any negative impact on your work due to the presence of the artist?

Sure – the artist needed a lot of time for supervision by the scientists, to have their work properly supervised (working with microbes, introducing them to benchwork, etc.). Some researchers volunteered to devote more time than expected to discuss, prepare and run the experiments with/for the artist.

(The artist has learned a lot about antibiotics research from you and your colleagues in the past months...) Was there anything you learned from the artist?

I learned about British literature and the artistic process - and about the "sublime moment" that art is supposed to provoke.

How would you evaluate the art-science interaction as a whole?

Overall, very enjoyable and informative. I indeed had a good chance to get a more detailed impression of how an artist thinks and work and, I think, in general a better appreciation for the finer parts of an artwork. I also think that the specific artwork that was conceived here is very nice and without the disconnect I mentioned above. I am very much looking forward to finding out how it will be received by others.

Interview / Steven Schmitt

BF: How did your peer scientists/scientific staff react to the artist in their lab?

Steven Schmitt: (High) interest in what the artist is doing. Enthusiasm to suggest ideas. Doubts whether the goals can be reached within the timeframe. (Small) debates whether the resources are spent wisely.

Do you have any artistic background yourself? If yes, which one?

No.

What was the most suprising/exciting/interesting moment in the collaboration with the artist?

No special situation/moment.

Did you experience any negative impact on your work due to the presence of the artist?

Working with a person not trained in microbiological lab work, and in an ambitious project, consumes a large amount of time. So, the impact on my own time was negative – however, the only negative thing.

(The artist has learned a lot about antibiotics research from you and your colleagues in the past months...) Was there anything you learned from the artist?

As researchers, we are focused on plain results and data, however what I have learned in the collaboration is that (I) the way of how to obtain those results can have interesting aspects as well and (II) the plain data might not be sufficient to impress people outside the lab – e.g. in antibiotic activity assays, simple things like the color of an assay-result can have a larger impact than e.g. a better activity of a given compound determined in the assay.

How would you evaluate the art-science interaction as a whole?

Really positive – and a really good possibility to present our work to the outside in a visually attractive way.

Any other question I should have asked you? Anything else you would like to say?

Time is really limited – especially for a highly motivated but rather unexperienced artist.
A large part of the work, therefore, has to be done by the researchers. This is suboptimal, not only because of the resources but also because we are not trained and not experienced in delivering those results in a way that is attractive to the artist, which makes the process quite inefficient.

Interview / Irene Wüthrich

Biofaction: How did your peer scientists/scientific staff react to the artist in their lab?

Irene Wüthrich: Our lab does not have a long-standing tradition of collaboration with artists, therefore Sarah's residence was quite a novelty. My impression was that my peer scientists were at the beginning both curious about what was going to happen and a little bit skeptical as well. As the project progressed, reactions from different people were diverse. Sarah became a part of the antibiotic peptides team, where she was fully embraced as a temporary new member with a different mission. Generally, people liked interacting with her. Some were enthusiastic to help out on the periphery, while others felt no desire to involve themselves.

Do you have any artistic background yourself? If yes, which one?

I don't have any artistic background myself.

What was the most suprising/exciting/interesting moment in the collaboration with the artist?

I really enjoyed the conversations with Sarah. It was a joy to explain my work, because she assimilated new and fairly complex knowledge in a short time. It surprised me how logical she was in parsing in-

formation, which says all about my preconceived notions regarding "artists". I learned a lot about what it means to be an artist, it was great to discover a world so different from lab life. We also had great discussions comparing personal experiences, and about life in general. The most exciting and enjoyable part was "brainstorming" ideas with Sarah pertaining to her project with us. It felt like a very creative process to me, very associative, encompassing random "out there" ideas, historical facts, artistic vision, scientific reality checks, etc. It was a lively exchange, and we had great synergy. In fact, I wish that this fashion of conceiving projects played a greater role in my daily work. Usually, the ideas stage gets all too soon swapped for putting your nose to the grindstone on the bench.
It was also very interesting to ponder where it is admissible or even advisable to put the scientific method on the back burner (one could always run more preliminary experiments, and spend more time to methodically test a hypothesis), and let art take precedence (letting artistic vision guide experimental design). I suspect that the perfect meshing of art and science has to be calibrated anew with each project.

Did you experience any negative impact on your work due to the presence of the artist?

It did take away from the time I could have spent on my work. This was of course mostly my choice, and while my work suffered a bit, I gained a lot personally, so it was worth it. Coming from a different background and lacking experience, it is very hard for a non-scientist

to plan the time required for doing actual lab work, it tends to get underestimated. I'm very much looking forward to Sarah returning to the lab to complete the project, while also hoping that she will be able to do most of the bench work herself or with limited assistance, as I also need to get stuff done.

(The artist has learned a lot about antibiotics research from you and your colleagues in the past months...) Was there anything you learned from the artist?

I learned a lot about translation and not getting lost in it, when completely different fields conceive a project together.

How would you evaluate the art-science interaction as a whole?

It was a very refreshing and enriching experience, and I would love to do it again.

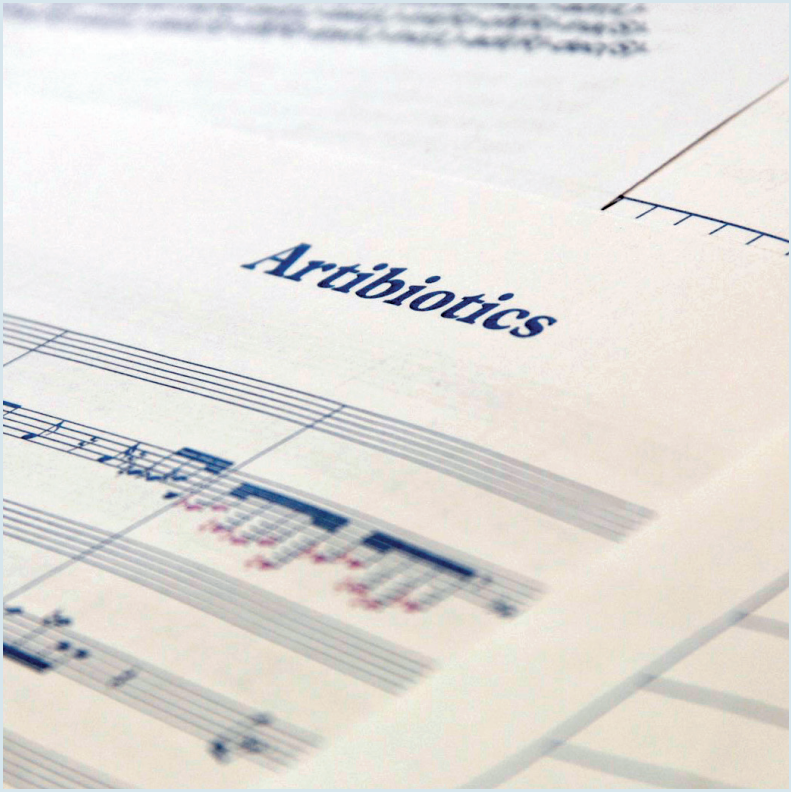
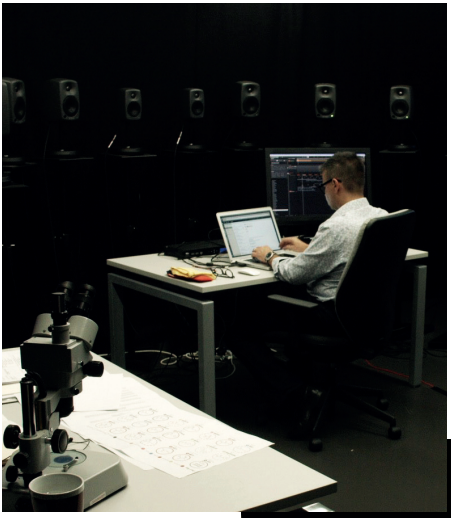


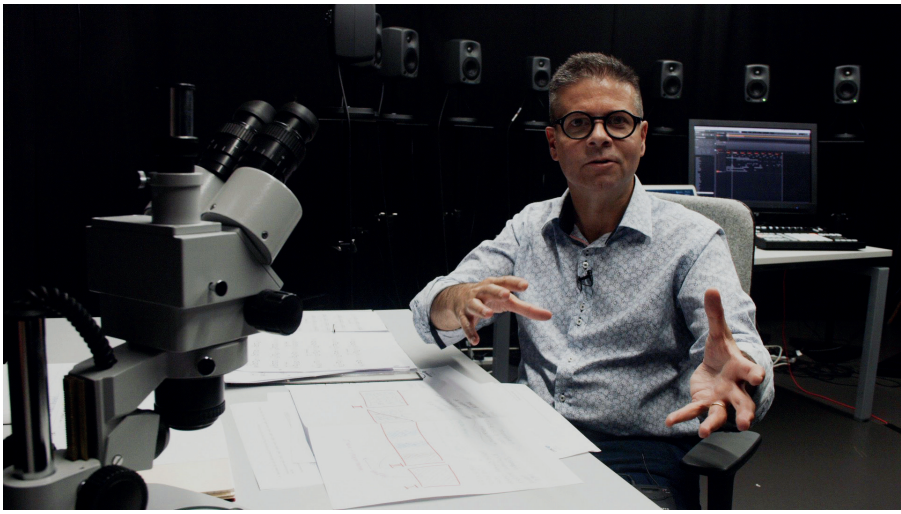
Image: Camillo Meinhart

Eduardo Miranda's Residency

Wagner Lab

Image: Camillo Meinhart





Images: Camillo Meinhart

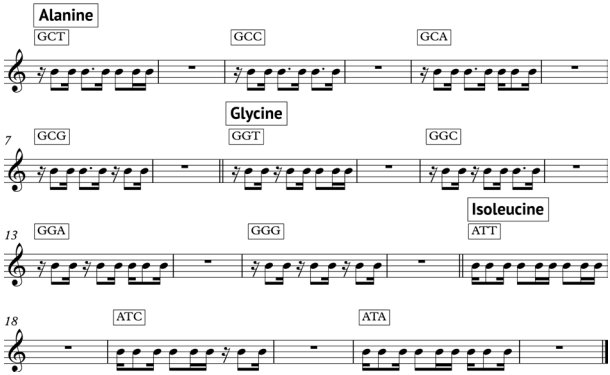


Image: Eduardo Miranda

Artibiotics: An Artificial Biology Musical Experiment

Eduardo Miranda

Introduction

Artibiotics is an experimental musical composition for percussion ensemble and electronics. It articulates the development of Artificial Biology, which is a new concept conceived during my residency at Wagner Lab in Regensburg in 2017.

The residency was supported by Biofaction in connection with the European Commission-funded SYNPEPTIDE project, aimed at the design of new antibiotics.

Artibiotics will be premiered at the Gala Concert of the Peninsula Arts Contemporary Music Festival, Plymouth, on 03 March 2018, by Ensemble Bash.

Background

Easy access to and misuse of antibiotics are prompting various types of harmful bacteria to develop resistance to existing antimicrobial substances. This is a problem of serious concern. The World Health Organisation has recently announced that the increasing difficulty of curing diseases caused by new drug-resistant bacteria is a threat worldwide. To address this problem, the SYNPEPTIDE project is looking into developing new types of lantibiotics, which is a class of antimicrobial molecules that have not been widely explored in antibiotics research yet.

Essentially, Wagner Lab is developing Synthetic Biology work. The team is unravelling the structure and function of naturally occurring lantibiotics with a view to engineering new kinds of lantibiotics. In a nutshell, the research involves shuffling the DNA code of known lantibiotics, synthesising the new molecules and testing them *in vivo* against specific kinds of bacteria. This is a laborious and time-demanding process, as the number of new possible recombinations is immense. Wagner Lab developed strategies to optimise this. For instance, given that lantitiotics' codes follow a modular structure, where each module contributes a distinct characteristic of the molecule, the recombinations are accomplished at the level of those modules. For example, sections marked as A, B, C, D and E in the structure shown in Figure 2 are different modules of a lantibiotic known as Nisin.

At its most fundamental level a lantibiotic is coded as a strand of the DNA bases: adenine (A), guanine (G), cytosine (C) and thymine (T), where A and G are referred to as purines and C and T are referred to as pyrimidines. The Nisin molecule is encoded with 102 DNA bases. However, the DNA representation does not fully represent the actual molecule per se. It needs to be rendered into a chain of amino acids, which forms a small protein, referred to as a peptide. In fact, this process involves 3 stages: transcription, translation and post-translational modifications.

Each triplet of DNA – referred to as a codon – encodes 1 amino acid of the chain. In simplistic terms, firstly DNA is transcribed into RNA, which is subsequently translated into amino acids. For instance, Nisin is formed by a chain of 34 amino acids; represented by 34 codons. After translation, chemical reactions take place (e.g. dehydration), resulting in the final peptide.

Although there are over 500 different amino acids in nature, only 20 of them are encoded by means of DNA directly, see the chart in Figure 1.

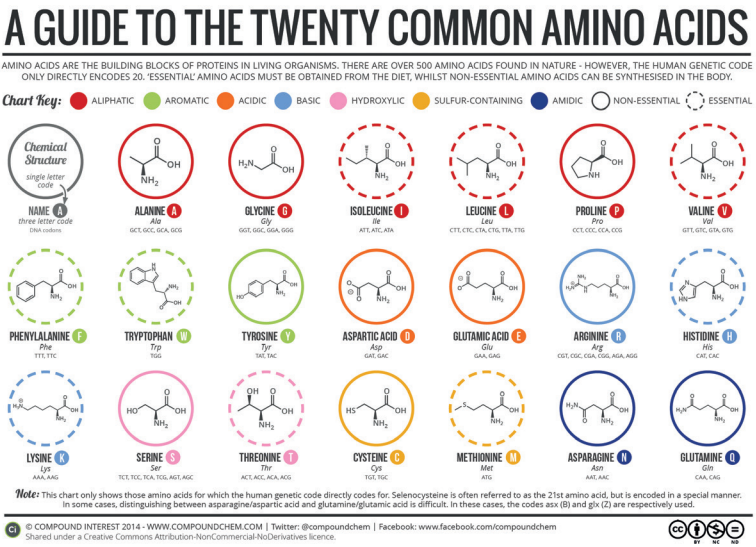


Figure 1. *Chart of amino acids, accessed 30th August, 2017 at http://www.compoundchem.com/2014/09/16/aminoacids (Source: Compound Interest 2014)*

What is important to understand here is that there are 64 possible DNA codons to encode these 20 basic amino acids, which means that most of them can be encoded by more than 1 codon. For instance, whereas Glutamine is encoded by CAA or CAG, Lysine is encoded by AAA and AAG (Figure 1).

Figure 2 shows a schematic rendering of Nisin from its DNA code. The first animo acid is Isoleucine (Ile), which corresponds to ATT (of the codon of the DNA strand). The last amino acid is Lysine (Lys), corresponding to the last codon: AAA. Note that Dhb and Dha, do not have an associated DNA codon in Figure 1. These two amino acids resulted from post-translational modifications.

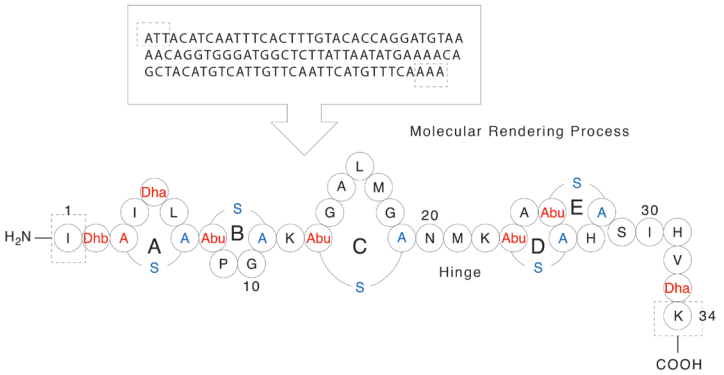


Figure 2. *Rendering of Nisin from its DNA code (Adapted from SYNPEPTIDE)*

A-Biology

The more I learned about the Synthetic Biology work developed at Wagner Lab during the first days of my residency in Regensburg, the more fascinated I became by the idea of synthesising new chimeric proteins. I wondered, if I could take the notion of Synthetic Biology even further, to the point where the very biochemistry of Biology could become chimeric, blending musical and biological processes.

In many ways, the scientific modus operandi that I witnessed in the laboratories in Regensburg reminded me of my own creative modus operandi. I felt that the process of synthesising new proteins is not so different from the process of creating new pieces of music. This led to the invention of a new concept: Artificial Biology, or A-Biology, which is the surreal biology of a parallel universe of musical molecules.

The A-Biology framework consists of a number of pieces of software that processes strands of DNA, including:

a. Miranda machine
b. Rhythmator
c. Pitch-folding
d. Post-translational musifications

a. Miranda Machine

At the core of A-Biology is the Miranda machine, which is an abstract Turing machine-like processor. Inspired by the Turing machine, which is an abstract machine that manipulates a sequence of symbols according to a set of rules, the Miranda machine was designed to manipulate sequences of DNA strands: it transcribes a DNA strand into a sequence of commands, or a DNA program.

Given a DNA strand, the Miranda machine produces a chain of data processing commands. In standard Biology this process would have produced a chain of amino acids, which would form an enzyme. In A-Biology, however, this chain of commands forms a program that processes the originating DNA strand itself. In other words, the Miranda machine transcribes a DNA code into a program to modify its own code.

In standard Biology, the resulting enzymes would operate on DNA strands. Similarly, the A-Biology each of the 20 basic amino acids is associated with a command of Miranda machine's programming language, as shown in Table 1. Each command has an orientation, S, L or R, the meaning of which will be explained later.

The machine parses a DNA strand in groups of three consecutively occurring bases, or codons. For instance, consider the following DNA strand consisting of 15 codons:

ATGAACGCGGAGAGGATTTGTCGCTGGCCTTAGTATCATTC-CAAA

The derived DNA program for the strand above is as follows:

cop - rpy - ina - lpu - swi - ing - cut - swi - rev - adl - off - ivl - deb - mvr - dec

For example ATG is transcribed as cop, AAC as rpy, GCG as ina, and so forth.

If a strand finishes with an incomplete codon (i.e., with 1 or 2 bases) than the parser will ignore them.

The application of the DNA program to process the originating DNA strand results in the following set of five new DNA strands:

CATATTGTCGCTGGCCTTAAGTATCATTCCAAA
TATG
GAGAGGCGGTA
C
CCT

See the Appendix for a step-by-step run of the example above. Effectively, the Miranda machine is normally set to chain reaction mode. In this case it will continue processing the newly generated DNA strands, which will subsequently generate new sets of strands and will carry on processing the new sets, and so on, until a given halting criterion is met. The end result will be a pool of DNA strands, consisting of the original strand and the groups of strands derived from each cycle.

Amino acid	Command	Codons	Action
Serine	mvr[S]	TCT, TCC, TCA, TCG, AGT, AGC	Move right by one unit
Threonine	mvl[S]	ACT, ACC, ACA, ACG	Move left by one unit
Alanine	ina[S]	GCT, GCC, GCA, GCG	Insert base A to the right
Glycine	inc[L]	GGT, GGC, GGA, GGG	Insert base C to the right
Isoleucine	ing[L]	ATT, ATC, ATA	Insert base G to the right
Leucine	int[R]	CTT, CTC, CTA, CTG, TTA, TTG	Insert base T to the right
Proline	adl[R]	CCT, CCC, CCA, CCG	Insert random base to the left
Valine	adr[L]	GTT, GTC, GTA, GTG	Insert random base to the right
Methionine	cop[L]	ATG	Enable copy mode
Cysteine	cut[S]	TGT, TGC	Cut strand
Arginine	swi[L]	CGT, CGC, CGA, CGG, AGA, AGG	Switch enzyme to another strand
Histidine	deb[S]	CAT, CAC	Delete base
Lysine	dec[S]	AAA, AAG	Delete codon
Asparagine	rpy[L]	AAT, AAC	Search for pyrimidine to the right
Aspartic acid	rpu[R]	GAT, GAC	Search for purine to the right
Glutamine	lpy[R]	CAA, CAG	Search for pyrimidine to the left
Glutamic acid	lpu[R]	GAA, GAG	Search for purine to the left
Phenilalanine	ivr[R]	TTT, TTC	Invert base to the right
Tyrosine	ivl[L]	TAT, TAC	Invert base to the left
Tryptophan	rev[S]	TGG	Perform lateral inversion on strand
	off[R]	TAA, TAG, TGA	Disable copy mode

Table 1. *The Miranda machine's commands associated to amino acids, their respective codons and action*

b. Rhythmator

The Rhythmator translates a given DNA strand into a rhythmic sequence. A-Biology includes a scheme to represent amino acids by means of distinct vocabularies of four rhythmic figures, referred to as nucleo-rhythms, each associated with the bases A, T, G and C. This enables the Rhythmator to parse a DNA strand and translate its codons into rhythmic codons.

For instance, Figure 3 shows a vocabulary of nucleo-rhythms and Figure 4 shows the respective rhythmic codons for the amino acids Cysteine (TGT and TGC) and Methionine (ATG).

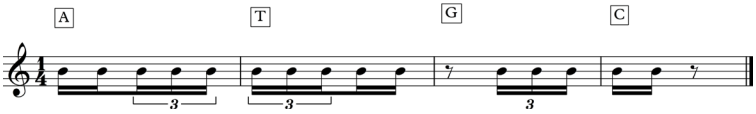


Figure 3. *An example of a vocabulary of nucleo-rhythms. (Source: Eduardo Miranda)*

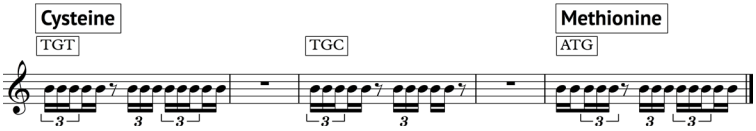


Figure 4. *Rhythmic codons for Cysteine and Methionine (Source: Eduardo Miranda)*

In standard Biology, amino acids are classified according to their chemical structure: aliphatic, aromatic, acidic, basic, and so on. In A-Biology, each of these classes is represented by a different vocabulary of nucleo-rhythms. For instance, the vocabulary in Figure 3 is used for Sulfur-containing amino acids.

Nucleo-rhythms vocabularies are built either manually or automatically. The one shown in Figure 3 was built manually; that is, I composed these nucleo-rhythms myself. However, I also generated vocabularies automatically for Artibiotics. In order to do this, I devised a piece of software that extracts basic

rhythmic figures from given musical scores.

I generated a number of vocabularies from Brazilian samba for Artibiotics. An example of a samba vocabulary is shown in Figure 5 and samba rhythmic codons for 3 aliphatic amino acids are shown in Figure 6.

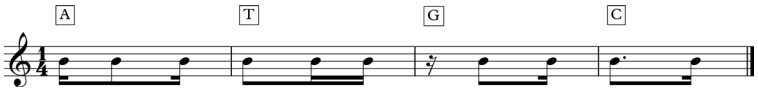


Figure 5. *An example of a vocabulary of nucleo-rhythms extracted from samba music (Source: Eduardo Miranda)*

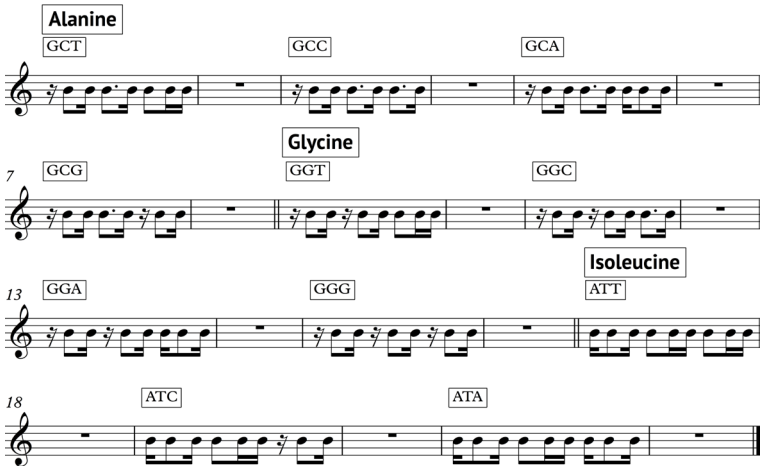


Figure 6. *Samba rhythmic codons for 3 aliphatic amino acids (Source: Eduardo Miranda)*

c. Pitch-Folding

Pitch-folding is inspired by the phenomenon of protein folding. Whereas in standard Biology protein folding defines the shape of a molecule, in A-Biology pitch-folding defines pitches for a rhythmic sequence. The pitch-folding phase is optional, depending on wether one wishes to assign pitches to the sequences or not. Indeed, pitch-folding was not always used for the composition of Antibiotics because the piece is for pitched and non-pitched percussion instruments.

If the pitch-folding mechanism is activated, then the Miranda machine takes into account the orientation information of DNA commands (represented inside brackets in Table 1) to "fold" the derived program. In order to visualise this process, consider each DNA command in Table 1 as a block, with the command name and its orientation in the centre, and an arrow pointing in the direction corresponding to its orientation. A command can have one of three possible orientations: right, straight and left, represented as R, S and L, respectively; e.g., rpu[R], mvr[S] and swi[L] (Figure 7).
The system produces a domino-like chain of blocks, such that each block is

Figure 7. *Visualisation of a command as block and its orientations (Source: Eduardo Miranda)*

connected to the top of the next block (Figure 8).
As an example, let us consider the hypothetical strand TCTGGTGTACC-

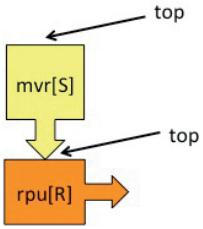


Figure 8. *Connection between 2 blocks*
(Source: Eduardo Miranda)

CCAG. This strand gives us the following sequence of commands and orientations: mvr[S] - inc[L] - adr[L] - adl[R] - lpy[R]. The resulting folded block sequence is depicted in Figure 9.
Once the command sequence is folded, the system establishes the cardinal

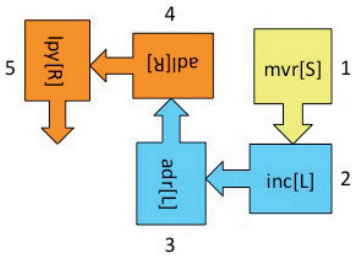


Figure 9. *Visual representation of a folded block sequence of DNA programming commands*
(Source: Eduardo Miranda)

direction of the command: north (NO), south (SO), east (EA) and west (WE), respectively. In the case of the above example, the sequence mvr[S] - inc[L] - adr[L] - adl[R] - lpy[R] becomes mvr[SO] - inc[WE] - adr[NO] - adl[WE] - lpy[SO].

Every DNA programming command is associated with 4 distinct algorithms for generating pitches, one for each cardinal direction. An example is given in Table 2.

Command	Generative Pitch Algorithm
swi[WE]	*s* = *r* – 7 ;transpose one major 5th down *x* = 1 for each note, do while there are notes to process { make_note(*s*) *u* = *s* + *x* make_note(*u*) *d* = *s* – *x* make_note(*d*) *x* = *x* + 1 }
swi[EA]	*s* = *r* – 7 ; transpose one major 5th down *x* = 1 for each note, do while there are notes to process { make_note(*s*) *d* = *s* – *x* make_note(*d*) *u* = *s* + *x* make_note(*u*) *x* = *x* + *1* }
swi[NO]	*s* = *r* – 7 ; transpose one major 5th down *x* = *1* for each note, do while there are notes to process { make_note(*s*) *u* = *s* + *x* make_note(*u*) *x* = *x* + 1 }
swi[SO]	*s* = *r* – 7 ; transpose one major 5th down *x* = *1* for each note, do while there are notes to process { make_note(*s*) *d* = *s* – *x* make_note(*d*) *x* = *x* + 1 }

Table 2. *Generative pitch algorithms for command swi. The variable r is for a pre-established reference pitch; that is, a MIDI note number (e.g. 60 corresponds to Middle C)*

As an example of the A-Biology generative process, let us consider the DNA strand for a lantibiotic referred to as Columbicin A:

GCTGGACGTGGATGGATTAAAACACTTACAAAAGATTGTC-
CAAATGTTATTTCATCAATTTGTGGAACAATTATTACAGCTTG-
TAAAAATTGTGCT

The first cycle of the Miranda machine applied to Columbicin A produced the following set of strands:

1.TCGTGTTAAAAATGTTCGACATTATCGCTACAAGGTGTT-
TAACTACTTTATTGTAAACCTGTTAGAAAACATCGATGGGAA

2. AAATTAGGTAGGTGCAGGTCG

3. GC

Let us focus on strand number 2. The outcome from applying the rhythmator to strand number 2 is shown in Figure 10.

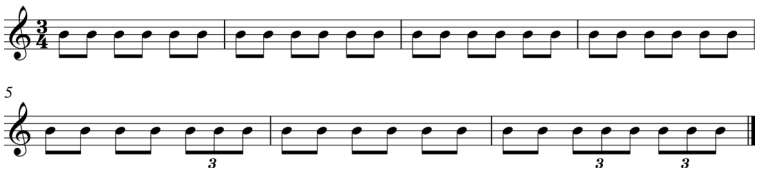


Figure 10. *The rhythmic sequence yielded by DNA strand number 2 (Source: Eduardo Miranda)*

If we apply pitch-folding to strand number two, then the resulting programming sequence with cardinal orientation information would be as follows:

dec(SO) - int(EA) - inc(SO) - swi(WE) - cut(WE) - swi(NO) - mvr(NO)

Figure 11 shows the rhythmic sequence with the respective pitch information; in this case the reference pitch is Middle C, or MIDI note 60.

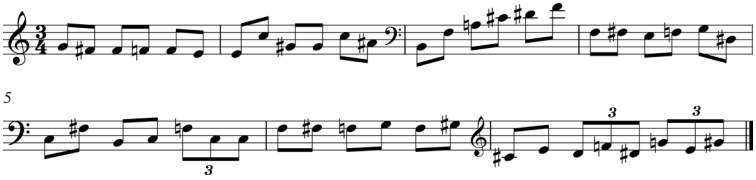


Figure 11. *The rhythmic sequence yielded by DNA strand number two with pitch-folding (Source: Eduardo Miranda)*

d. Post-translational Musifications

Post-translational musifications are modifications made on the resulting musical sequences generated by the processes described above. The results from these modifications are referred to as musical molecules.

Post-translational musifications involve processes that might be applied to the sequences automatically (e.g. the A-Biology equivalent of dehydration in standard Biology) and manually. For the composition of Artibiotics post-translational musifications were kept to a minimum and were applied mostly to those sequences that were scored for the percussionists to perform; for example, I transposed pitches that would not have been possible to play by a certain instrument. Those sequences played electronically were rarely modified; that is, they did not need post-translational musifications to become musical molecules.

Post-translational musifications gave me the opportunity to exercise my aesthetic judgement and adapt the sequences to produce musical molecules for specific musical contexts as I put these materials together to compose the piece.

4. The Composition Process

The composition process involved two stages: generation of musical molecules with the A-Biology system introduced above and assemblage of the piece. The latter occasionally required further editing of the musical molecules to fit practical requirements such as playing techniques, dynamics, and so on.

Artibiotics has three movements: Pathostuff, Trials and Musicin. The piece begins by exposing a pathogen that needs to be eliminated. Then, the second movement portrays a battle to kill the pathogen. Various lantibiotics are tried until one of them prevails. The third movement celebrates the successful lantibiotic.

For the first movement I ran the A-Biology system on the DNA strand of a hypothetical pathogen to generate a relatively large set of musical molecules, referred to as pathostuff, hence the name of the movement.

For the second movement I ran the system on the DNA of lantibiotics routinely used for research at Wagner Lab (e.g. Nisin, Pep5, Lactosin S, Columbicin A, etc.) and on the DNA strands of articins. Articins are chimeric lantibiotics of my own design using DNA information from Wagner Lab's library of lantibiotics. For instance the following is Articin 5, consisting of 114 DNA bases, which I designed by combining DNA modules from Lactosin S and Nisin:

TCAACACCAGTTTTAGCTTCAGTTGCTGTTTCAATG-
GAACTTCTTCCAACAGCTTCAGTTCTTTATACAGGTGCTCT-
TATGGGATGTTTTAAATATTCAGCTAAACATCATTGT

Musically, while pathostuff materials are developed throughout the second movement, 20 contrasting lantibiotic musical molecules emerge, one after another, as if they were attempting to eradicate pathostuff musical molecules. Towards the end of the movement, one of the lantibiotics prevails and pathostuff music finally fades out.

The third movement presents a scherzo with musical molecules associated with the winning lantibiotic.

Appendix:
A Detailed Step-by-Step Run of the Miranda Machine

Input strand:
ATGAACGCGGAGAGGATTTGTCGCTGGCCTTAGTATCATTCCAAA

Derived DNA programming code: cop – rpy – ina - lpu - swi - ing - cut - swi - rev - adl - off - ivl - deb - mvr - dec

By default, the Miranda machine starts on a randomly selected adenine.

Initial position:

A	T	G	A	A	C	G	C	G	G	A	G	A	G	G	A	T	T	T	G	T	C	G	C	T	G	G	C	C	T	T	A	G	T	A	T	C	A	T	T	C	C	A	A	A

1. cop

											T																																		
A	T	G	A	A	C	G	C	G	G	A	G	A	G	G	A	T	T	T	G	T	C	G	C	T	G	G	C	C	T	T	A	G	T	A	T	C	A	T	T	C	C	A	A	A

2. rpy

											T	C	C	T	A																														
A	T	G	A	A	C	G	C	G	G	A	G	A	G	G	A	T	T	T	G	T	C	G	C	T	G	G	C	C	T	T	A	G	T	A	T	C	A	T	T	C	C	A	A	A

3. ina

												T	C	C	T	A	T																												
A	T	G	A	A	C	G	C	G	G	A	G	A	G	G	A	T	A	T	G	T	C	G	C	T	G	G	C	C	T	T	A	G	T	A	T	C	A	T	T	C	C	A	A	A

4. lpu

												T	C	C	T	A	T																												
A	T	G	A	A	C	G	C	G	G	A	G	A	G	G	A	T	A	T	T	G	T	C	G	C	T	G	G	C	C	T	T	A	G	T	A	T	C	A	T	T	C	C	A	A	A

5. swi

												T	C	C	T	A	T																												
A	T	G	A	A	C	G	C	G	G	A	G	A	G	G	A	T	A	T	T	G	T	C	G	C	T	G	G	C	C	T	T	A	G	T	A	T	C	A	T	T	C	C	A	A	A

6.ing

												T	C	C	G	T	A	T																												
A	T	G	A	A	C	G	C	G	G	A	G	A	G	C	A	T	A	T	T	G	T	C	G	C	T	G	G	C	C	T	T	A	G	T	A	T	C	A	T	T	C	C	A	A	A

7. cut

											T	C	C	
A	T	G	A	A	C	G	C	G	G	A	G	A	G	

G	T	A	T																											
C	A	T	A	T	T	G	T	C	G	C	T	G	G	C	C	T	T	A	G	T	A	T	C	A	T	T	C	C	A	A	A

8. swi

											T	C	C	
A	T	G	A	A	C	G	C	G	G	A	G	A	G	

G	T	A	T																											
C	A	T	A	T	T	G	T	C	G	C	T	G	G	C	C	T	T	A	G	T	A	T	C	A	T	T	C	C	A	A	A

9. rev

T	C	C												
G	A	G	A	G	G	C	G	C	A	A	G	T	A	

G	T	A	T																											
C	A	T	A	T	T	G	T	C	G	C	T	G	G	C	C	T	T	A	G	T	A	T	C	A	T	T	C	C	A	A	A

10. adl

T	C	C							C					
G	A	G	A	G	G	C	G	C	G	A	A	G	T	A

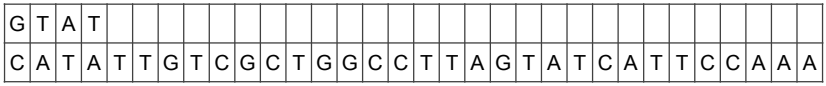
G	T	A	T																											
C	A	T	A	T	T	G	T	C	G	C	T	G	G	C	C	T	T	A	G	T	A	T	C	A	T	T	C	C	A	A	A

11. off

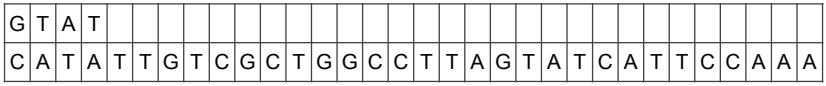
T	C	C							C					
G	A	G	A	G	G	C	G	C	G	A	A	G	T	A

G	T	A	T																											
C	A	T	A	T	T	G	T	C	G	C	T	G	G	C	C	T	T	A	G	T	A	T	C	A	T	T	C	C	A	A	A

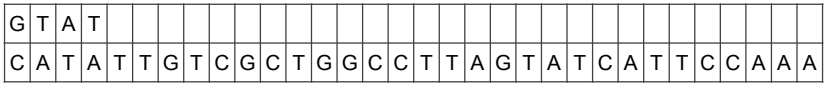
12. ivl



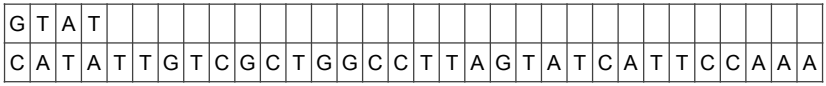
13. deb



13. mvr



14. dec



The resulting DNA strands are:

1. CATATTGTCGCTGGCCTTAAGTATCATTCCAAA
2. TATG
3. GAGAGGCGGTA
4. C
5. CCT

Lab Interview

Wagner Lab
University Regensburg

Interview / David Peterhoff

Biofaction: How did your peer scientists/scientific staff react to the artist in their lab?

David Peterhoff: Initially they were a bit uncertain how to understand the project. Then we had a presentation on other projects by Eduardo Miranda and some explanations by us and himself. That broke the ice.

Do you have any artistic background yourself? If yes, which one?

Yes, I'm a semiprofessional musician.

What was the most suprising/exciting/interesting moment in the collaboration with the artist?

Some discussions we had, where we shaped the project. We involved also the PhD students working in the SYNPEPTIDE project and they got increasingly enthusiastic during these discussions.

Did you experience any negative impact on your work due to the presence of the artist?

No. I was aware of the fact that this would consume some of my resources, so again – no.

(The artist has learned a lot about antibiotics research from you and your colleagues in the past months...) Was there anything you learned from the artist?

It is really possible to carve out a creative intersection between biological sciences and music!

How would you evaluate the art-science interaction as a whole?

Since we had many discussions on the details of the project I feel that the impact of both sides was very well balanced. Everyone liked the friendly atmosphere of the interaction. Besides and more generally speaking, an unbiased look and critical reflection on what we synthetical biologists do in the labs can be very helpful to realize what hopes and fears exist in the general public. Having an artist in the lab can help to perceive such an atmosphere in advance, thereby helping to avoid misunderstandings and arising prejudices on both sides.

About

List of Contributors

Sarah Craske
is a British artist, without category, working at the intersection of art, science and technology, specifically interested in exploring how the concept of knowledge & data, practice & space, language & method, equipment & materials transform through transdisciplinary working. She lives and works between London, Canterbury & Ramsgate.

Eduardo R. Miranda
is a Brazilian composer and AI scientist working at the crossroads of biology. programming and music, who has equally delved into music neurotechnology and composed for orchestras. He also continues to guide his students at Plymouth University (UK).

Sven Panke
has stood at the forefront of the implementation of synthetic biology in Europe and published landmark papers in the fields of synthetic biology, systems biology, and process engineering. He is also Director of Studies at ETH Zurich Basel's Department of Biosystems Science and Engineering.

Lei Pei
has a background in clinical bacteriology, which has led her from China to Sweden, to the USA and Belgium, and, finally, to Austria. Focusing on synthetic biology, at Biofaction she is in charge of regulatory, IP and biosafety issues.

Markus Schmidt

has an interdisciplinary background in biomedical engineering, biology and technology assessment, which led him to found Biofaction. His work centers around projects dealing with societal ramifications of research and innovation, bringing together stakeholders from science, regulation, industry, civil society and art.

Ralf Wagner

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SYNPEPTIDE

was a pan-European project bringing together 5 academic groups and 3 SMEs across Europe to identify and produce novel antibiotic molecules. It was a four year project funded by the European Commision FP7 framework (project number 613981).
www.synpeptide.eu

Biofaction

is a research and science communication company, established in 2010, and based in Vienna, Austria, with expertise in science communication, film production, science games, technology assessment, art and science, and the study of ethical, legal and social issues in a number of emerging sciences and technology.
www.biofaction.com