Issue III / June 2020

Newsletter

Swiss Engineering STV
Professional Group Life Science

Der Berufsverband der Ingenieure und Architekten in der Schweiz.

SWISS ENGINEERING
PROFESSIONAL GROUP LIFE SCIENCE

Content

President message

Dear Colleagues,

Welcome to the third edition of our group newsletter.

Who would have imagined six month ago, how the COVID-19 pandemic will impact our life. We had to learn new words like “Social Distancing” or “Lockdown” and to rethink the way we work. On the other hand, for those of us working in the pharmaceutical industry on the development or manufacturing of a vaccine, it’s a very motivating challenge.

Due to the pandemic, we had to cancel the visit of the Lonza Visp Campus. The next planned visit will take place on the 10th September at the *Swiss Integrative Center for Human Health SA (SICHH)* and at the *bioFactory Competence Center SA (BCC)* in Fribourg. We will have the unique opportunity to visit research lab facilities of those two companies, both located on the Blue Factory Campus (former Cardinal Brewery site) and learn more about ongoing research projects. A networking apéro will close the event.

I recommend also the reading (on page 6) of the article by Prof. Dr. Daniela S. Nosch and her team at the University of Applied Sciences and Arts Northwestern Switzerland (FHNW) on *corneal sensitivity measurements*. It gives a very detailed insight on the innovative R&D performed at the FHNW. Special thanks to Prof. Karl Schenk for making the link between the FHNW and Swiss Engineering.

Best regards,

Valentin Herbez

Board Information

In order to proceed to the consolidation and development of the group, we are currently looking for additional Board members. If you are active in the Pharma, Bio- or Medical-Technology area and want to contribute to the success of our professional association, we would be glad to welcome you in the Board.

After having greatly contributed to the start-up phase of our group, Prof. Dr. Volker Koch (Academic Liaison) and Marco Ribolla (Secretary) have decided not to run for a new mandate and will step out by the next General Assembly (November 2020). Thanks to both of them for having contributed to the creation of the group.

Activities schedule

You may find below a list of events organized by the professional group or by partnering associations. Details will be published on the group webpage and LinkedIn page.

SE Professional Group Life Science

Date	Event	Where
10th September 2020 **16:00 -18:00**	MEDTECH / PHARMA / BIOTECHNOLOGY **Projects presentation & visit of the the Swiss Integrative Center for Human Health and the bioFactory Competence Center** Agenda: 16:00 - Welcome 16:05 – Introduction SICHH 16:10 – Introduction BCC 16:15 – Project presentation – by BCC 16:30 – Project presentation – by SICHH 16:45 – 1st Lab Tour BCC & SICHH (2 groups) 17:15 – 2nd Lab Tour BCC & SICHH (2 groups) 17 :30 – Aperitif Registration & Details under https://www.swissengineering.ch/web/fachgruppe-life-science until 30th August 20	BLUEFACTORY FRIBOURG – FREIBURG SA, Passage du Cardinal 1, 1700 Fribourg https://www.bluefactory.ch/contact
11th November 2019 **19:00- 21:30**	**General Assembly** 19:00 - 19:30 Keynote Talk 19:30 - 20:15 General Assembly 20:15 - 21:30 Networking Apero	Sorell Hotel Ador, Laupenstrasse 15, 3001 Bern

Date	Event	Where
15th March 2021	**Day of the engineers** Basic idea of the Day of the Engineers: Promotion of junior engineers and visualization of the outstanding achievements of the engineers in public. https://www.tagderingenieure.ch/en/ TAG DER INGENIEURE 15. März	See dedicated website for more info

Partnering Associations

Date	Event	Where
August 27, 2020	**SSBE Annual Meeting (ONLINE)** https://www.artorg.unibe.ch/events/ssbe2020/index_eng.html	Bern

Review of past events

General assembly 2019

The General Assembly 2019 of the Professional Group Life Science of Swiss Engineering STV UTS ATS took place on the 27th November in Berne.

Thanks a lot to **Stéphane Gumy** (picture), General Manager at PMS Process Management System (Fribourg) for his Keynote on "QC-Test profile and release strategy for extemporaneous Advanced therapy medicinal products (ATMPs)".

Stéphane gave us a very good insight in the regulatory aspects, which applies to ATMPs.

The minutes of the meeting is available on demand via email to our secretary.

Project presentation

In that part, we intend to present innovative research or industrial projects in the Life Science field. As a member of the professional group, you have the opportunity to present a topic as well; do not hesitate to contact a board member if you are interested.

In the present edition, we are glad to present a project from the University of Applied Sciences and Arts Northwestern Switzerland (FHNW).

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The development of two prototypes for corneal sensitivity measurement – an interdisciplinary project

Authors: Prof. Dr. Daniela S. Nosch,[1] Prof. Dr. Markus Loepfe,[2] Prof. Dr. Roland Joos,[1] Matthias Oscity[2], Peter Steigmeier,[2] Emanuele Käser,[1] Jörg Breitenstein[3]

[1]Institute of Optometry, University of Applied Sciences and Arts Northwestern Switzerland (FHNW), Olten

[2]Institute of Sensors and Electronics, University of Applied Sciences and Arts Northwestern Switzerland (FHNW), Windisch

[3]Haag Streit AG, Köniz

The human cornea is innervated with a dense network of sensory nerves that respond to mechanical, chemical, and thermal stimulation. These sensory nerves serve four functions: detection of foreign bodies or noxious substances, detection of tear film thinning to promote tear production, detection of changes in the tear film to promote blinking, and a neurotrophic role in the maintenance of the corneal epithelium. An indication of an intact ocular nerve system is the ocular surface sensitivity.

The quantification of ocular surface sensitivity is hence an important indicator of corneal functioning and may be affected in situations and / or disease processes such as dry eye disease, before or after refractive surgery (surgical correction of refractive errors such as short-sightedness), after transplantation of the cornea, peripheral neuropathy (i.e. in diabetes), corneal infections, corneal dystrophies and contact lens wear.

Corneal sensitivity measurement would therefore be very useful for optometrists and ophthalmologists from both, a research and daily clinical perspective.

Only one instrument is commercially available for corneal sensitivity measurement (Cochet Bonnet aesthesiometer; Figure 1), but it has been criticised for its many shortfalls (risk of abrasion of the cornea, questionable reliability, alignment and precision difficulties, limited stimulus range, and the influence of ambient humidity) and is therefore very rarely used in clinical setups. This instrument looks like a pen and incorporates a fine nylon filament of 0.08 or 0.12 mm in diameter, and its end is applied to the cornea. The applied pressure is varied by adjusting the length of the nylon filament: the shorter the filament, the higher the resulting pressure onto the cornea will be.

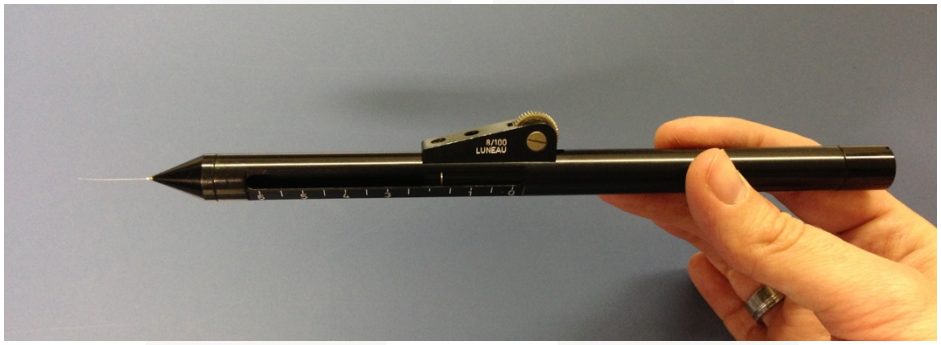

Figure 1: The Cochet-Bonnet aesthesiometer

Indeed, as the cornea represents the most densely innervated tissue in the human body (300 – 500 times more sensitive than the skin), the measurement of its sensitivity poses a considerable challenge, as this instrument must apply a force to the cornea that is as small as 50µN. The reaction of the nerve fibres can then not be tested directly, but instead psychophysically by the patient's feedback to an applied stimulus on the cornea, via activation of brain circuits.

For realisation of the engineering challenge to develop a new instrument for corneal sensitivity measurement, an interdisciplinary collaboration was founded between the Institute of Sensors and Electronics and the Institute of Optometry, which both belong to the School of Engineering of FHNW. The first feasibility study was financed by Innosuisse and completed in 2017. Two possible concepts emerged from this first project and a new collaboration with Haag Streit AG could be established that resulted in a larger project funded by Innosuisse (planned duration of 33 months, due to be completed by March 2021). Haag Streit AG is a Swiss company, that develops and distributes optical-medical instruments for optometric / ophthalmic use in worldwide 145 countries.

We are working on the following two concepts:

1) <u>Liquid Jet method (Figures 2 and 3):</u>
   A liquid jet (isotonic saline) of a temperature to match ocular surface temperature is applied to the ocular surface with low pressure and low volume, from a distance of 15mm.

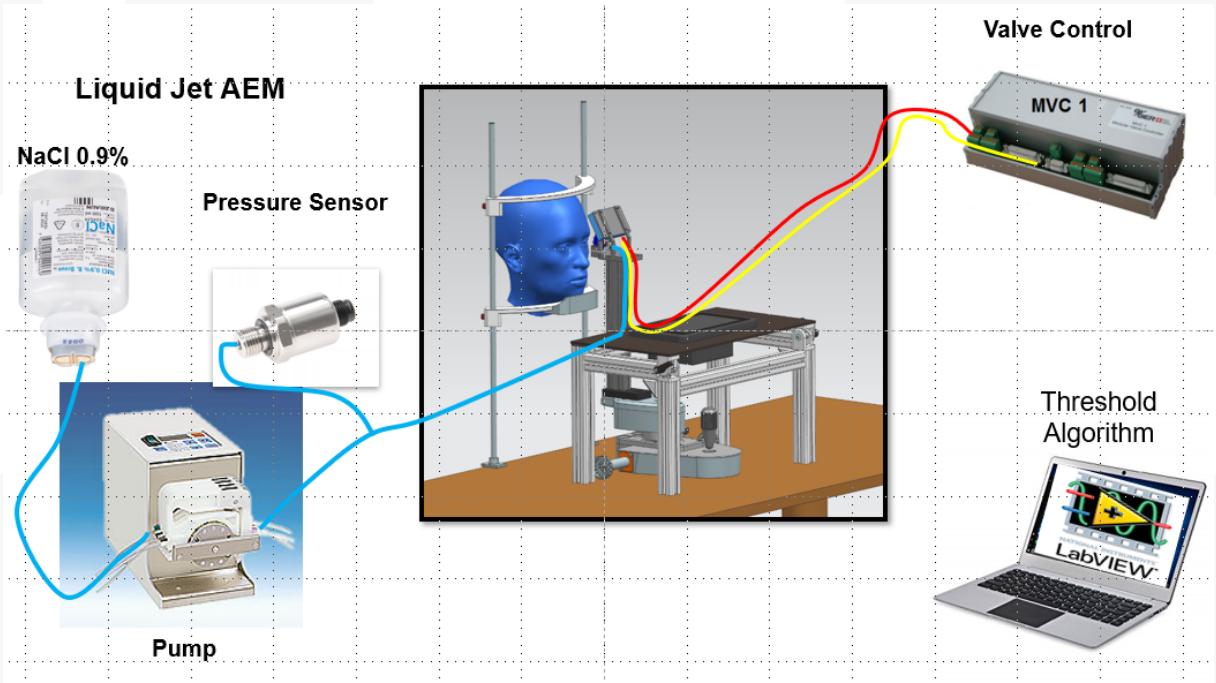

Figure 2: Liquid Jet Aesthesiometer Prototype

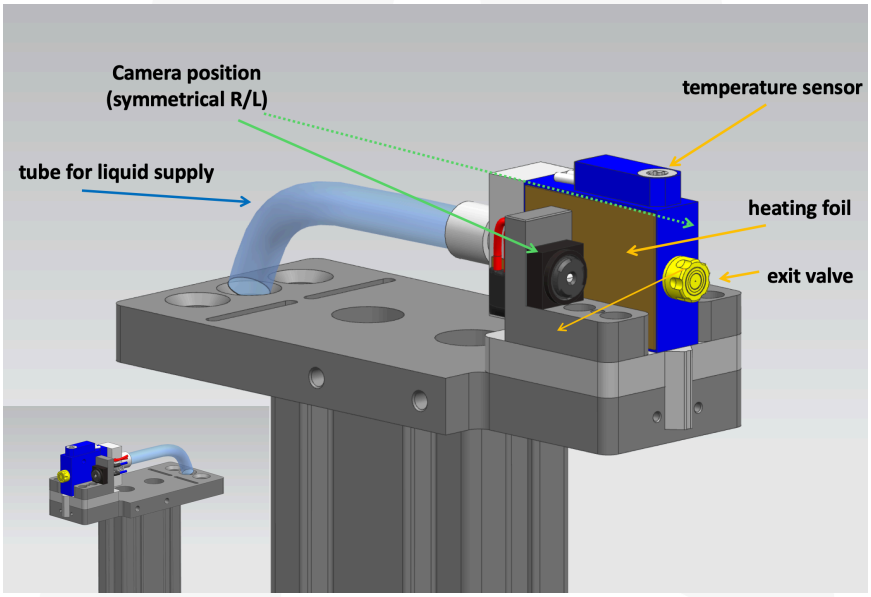

Figure 3: Liquid Jet Aesthesiometry (close-up view).

The subject's head is positioned on a chin rest. The exit valve for the liquid jet is positioned at 15mm in front of the corneal centre. Balanced salt solution (BSS; isotonic saline solution usually used for eye rinsing during intra- and extraocular surgery) with a pH value and osmolarity similar to the tear film is used as the liquid jet. This jet is sent through a silicone tube towards the ocular surface with a specific pressure, controlled in millibar by a peristaltic pump and a pressure sensor.

The force of this liquid jet is so low (typically approx. 300mbar, pressure range 0-2.1mbar), that it cannot be felt on the surface of a finger. The liquid jet is heated up to 37°C, in order to avoid cooling on the ocular surface, matching or slightly exceeding ocular surface temperature. A digital camera system controls the precise location of the liquid jet onto the corneal centre. The exit valve (diameter: 0.1mm) for the liquid jet is computer controlled. For corneal sensitivity threshold determination, an algorithm was developed, in order to avoid examiner bias.

2) <u>Tactile method (Figures 4 and 5):</u>
A round conducting 'tip' (1.8 mm diameter) is applied to the ocular surface with a defined, low force for a duration of 40ms.

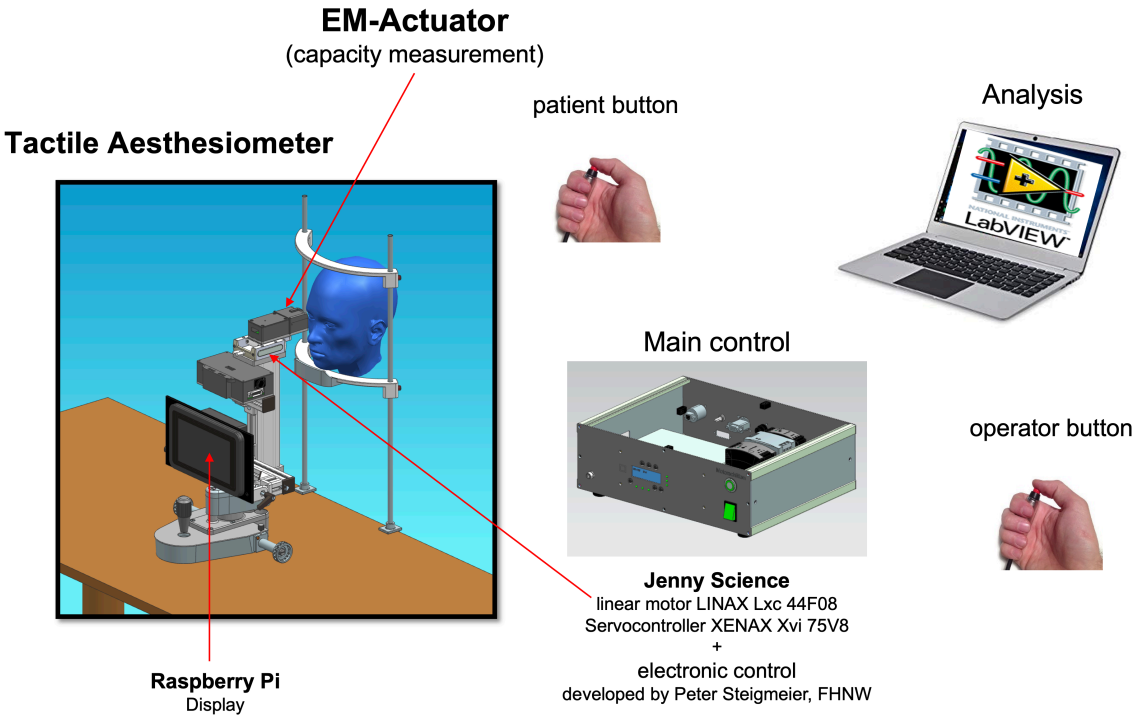

Figure 4: Tactile Aesthesiometer Prototype

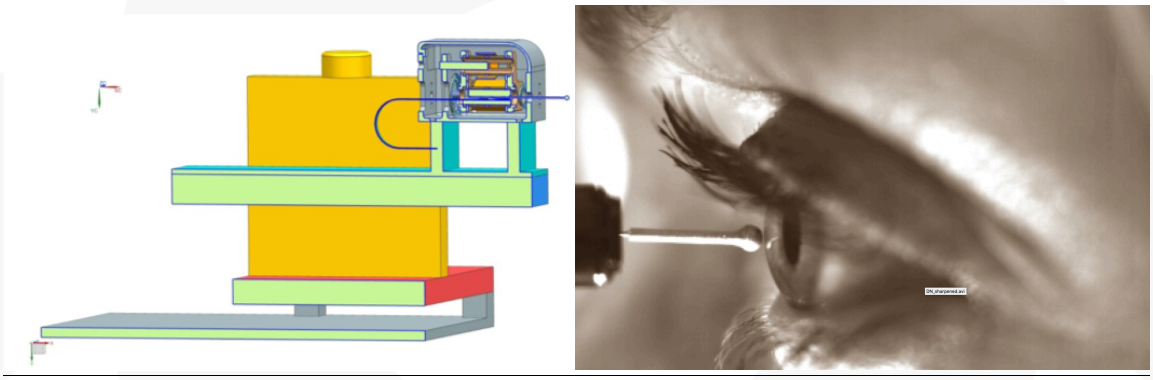

Figure 5: Tactile Aesthesiometer Prototype (clos up view)

The subject's head is positioned on a chin rest. A round conducting 'tip' (1.8mm diameter) is positioned at 15mm in front of the corneal centre and applies a defined force to the corneal centre (50-1000 μN). A digital camera system controls the precise location of the 'tip' onto the corneal centre. The 'tip' then approaches the cornea in two steps: into a position about 0.5mm in front of the cornea by means of a fast linear motor and – subsequently with a miniature electromagnetic motor until into contact with the tear film. Then the same mechanism can apply the 'force' for corneal sensitivity threshold measurement for a duration of 40ms. The distance between the 'tip' and the corneal surface is measured capacitively leading to a theoretical distance resolution of approx. 40nm and subsequent a force resolution of 16 μN.

The main concepts for both prototypes were developed during the feasibility study.

This current Innosuisse project consists of two main phases (Phase I and Phase II) which each contain one technical and one clinical phase. Phase I was completed in January this year, which involved the following technical developments:

- Algorithm for determination of sensitivity threshold for both methods (liquid jet and tactile) that randomly presents stimuli at intensities above and below the subject's threshold, which then calculates the threshold based on the subject's responses (i.e. if stimuli were felt / not felt).
- Compact instrument housing based on 3D printed parts.
- Camera system for precise centring of the stimulus presentation to the subject's cornea for both methods
- Pressure regulation and pressure sensor including a software for automatic control (PI-Loop), including a MVC valve regulation for the Liquid Jet prototype
- Push-buttons for stimulus presentation (operator) and for the subject feedback (for both methods)

During the second part of phase I, a prospective clinical study was carried out on 90 subjects, with the aim to find out more about how corneal sensory fibres react to different types of stimuli (liquid jet, tactile and Cochet Bonnet) and how this can be consciously perceived by the individual. Ethics approval was obtained from the Swiss ethics commission 'Northwest and Central Switzerland (project ID 2019-01252) and registered with clinical trials.gov (NCT04045509). The study group was divided into two age groups (group A: 18-30 years, group B: 50-70 years), as sensitivity changes are thought to occur in dependence of age. Variability was highest for the tactile aesthesiometer and some decrease in sensitivity could be observed for the study group B (Figure 6).

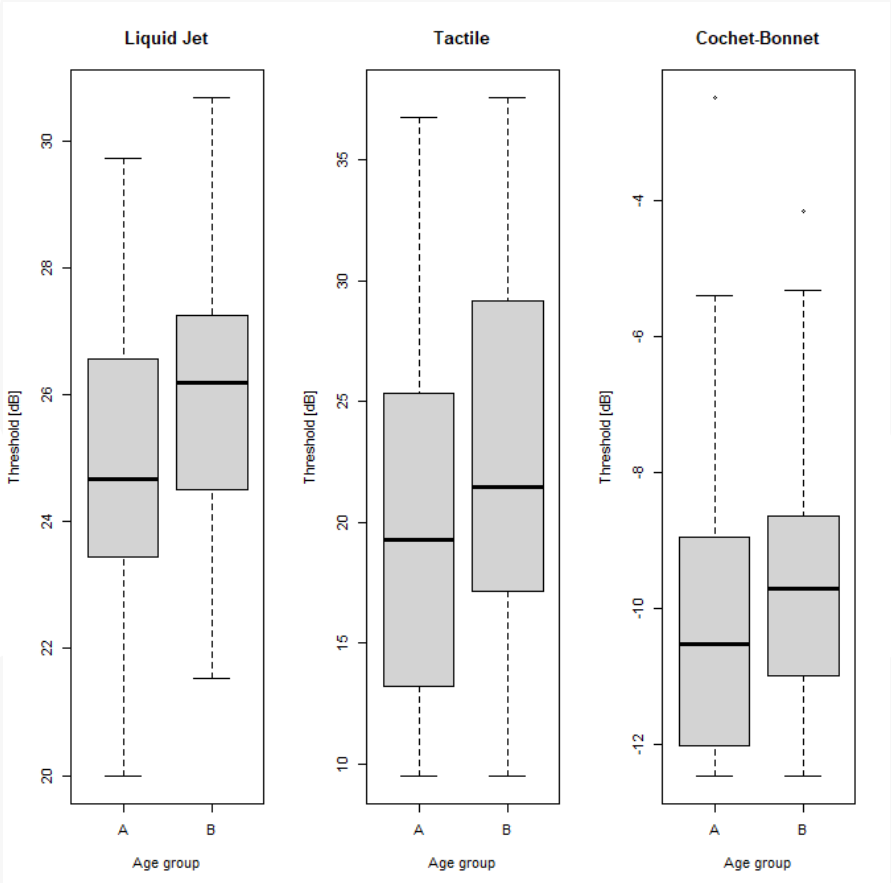

Figure 6: Boxplots for corneal sensitivity thresholds with liquid jet, tactile and Cochet-Bonnet aesthesiometer for two different age groups.

Currently, during Phase II, we are mostly concentrating our efforts on the improvement of technical aspects for the tactile aesthesiometer prototype, in preparation for one more clinical study during the second part of phase II of this project. As variability was considerably lower for the Liquid Jet Prototype, only minor technical issues will be improved upon at this stage. During the second clinical study, an additional group of patients with known compromised corneal sensitivity will be recruited, in order to have a better comparison for what would be considered 'normal' sensitivity range and to ascertain if and how well these instruments are able to pick up the differences.

This interdisciplinary project is particularly challenging, as we do not have a good gold standard for corneal sensitivity measurement that we can compare our prototype measurements against. In other words, we do not know what a normal, expected range of corneal sensitivity should be and what kind of variability would be acceptable. In addition, due to the high density of nerve fibers in the cornea and the resulting high sensitivity, we are dealing with extremely small stimulus intensities, that are difficult to generate and control.

We are optimistic that either of these prototypes has plenty of potential for future research in the field of corneal physiology in healthy and diseased corneas, providing advances in our understanding of disease processes and how to improve treatment. In everyday clinical optometry and ophthalmology, there is also great interest for the possibility to take into account knowledge about corneal sensitivity for diagnosis, choice of treatment and evaluation of treatment success. For commercialization, development and manufacturing costs, and especially marketing considerations are key and we certainly hope that at least one of the two concepts proposed will be a winner.

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Upcoming Conferences & Events

Date	Event	Where
September 15, 2020	**Swiss Biotech Day** https://swissbiotechday.ch/home/	Basel
September 21, 2020	**Swiss Medtech Day** https://www.swissmedtechday.ch	Bern
November 29 – December 3, 2020.	**EMBEC 2020** http://www.embec2020.org	Slovenia

Board Members

Valentin Herbez	Chair
Antoine Derriey	Vice-Chair
Frank Zeugin	Treasurer
Marco Ribolla	Secretary
Prof. Dr. Volker Koch	Academic Liaison
Oliver Röben	Industry Liaison

You may contact the board members per email via the group webpage:

https://www.swissengineering.ch/web/fachgruppe-life-science

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