In Dialogue with Dr. Hilde Stenuit

iGEM CONCORDIA

ASTROYEAST 2020

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Ice Cubes Application Services
July 2020 with iGEM Concordia

SUMMARY KEYWORDS

space, projects, microgravity, Ice Cubes, inclusivity, Earth, people, companies, effects, astronauts, moon, research, hurdle, Cube, discipline

Part 1

Hilde Stenuit 0:00

Space Exploration for future exploration missions, maybe even what people would refer to as space colonization. So we need to make sure that we know how biology works on their space shuttle missions and how we can optimize the use of biology and how biology works, so that it can help us set up a sustainable way of living in space. I think that's one route. The other route is that actually when you bring biology in space, including a human body, you see very interesting effects, as you probably know, because your project is around microgravity. But there's a multitude of effects that you can actually turn in your advantage if you're smart about it. For example, you can easily create three dimensional cell culture structures. Which is something that is hard to do on Earth. If you use space in a smart way, can actually go and study, for example organoids, little small organs in their space conditions and use that to develop or to test new drugs. Which brings you in a situation that you cannot do it on Earth. And that is very valuable. I see a lot of biological or biotechnological applications of using space for Earth benefit. So for me, that's two big roots. We want to do biology because we want to understand biology in space for future space missions. And we want to understand and practically use the assets of space for Earth applications and that can be fun.

iGEM Concordia

And you mentioned that you want to look at different organelles in space. Do you know, in terms of the research that is being conducted right now, has there been any... I know that we know that microgravity is good in terms of the fact that cells can grow 3D, instead of just 2D here on Earth... but I'm wondering, do you know if the researchers are actually encountering any microgravity specific challenges? Because in our research, we're finding that, for example, yeast over the long term, they will have the stress responses to microgravity, and there's changes to the cell wall, the heat shock pathway, the osmoregularity, so, do you know anything about that?

Hilde Stenuit 2:55

First of all, I'm not a biologist as I mentioned, so on the specific Biology aspects, I would not be able to answer in much detail. What I can say is that microgravity or space in

general, because there's also the radiation aspect. You can use it to your advantage as I mentioned, but it does not only have to have the effect, of course, that you want to obtain. It has other effects as well.

For example, when you talk about radiation, it can lead to genetic modifications or mutations, which may not be what you want, because you want to investigate something specific. If it then starts to mutate, well you may be looking at something different that you didn't want to look at. So yeah, there is for sure these dual aspects that okay, on the one end, you can use microgravity in your advantage, but there are effects that you need to consider that might not be the effects that you are after.That sometimes means that you need to do some of the research in a couple of steps because you need to understand first, what is the impact on whatever you want to investigate? And understand, what are the effects that we didn't think of or that we didn't target before you can really sort out the effects that you wanted to obtain. Also when I was working with ESA, we see that okay, there's experiments and as well as you can prepare for them over the years. Sometimes you do realize during the flight experiment like, oh, here's something happening for which it would be good if we could now do a second experiment to sort out the effects of the specific factors.

iGEM Concordia 5:04
We're going on to more of a personal question. What was it like when you first started working in the space industry?

Hilde Stenuit 5:12
Haha that's already a while ago. What was it like? Well, I was doing research at university and in fact I loved research but for me one of the downsides of research was that I found I was knowing about these square millimeters subjects. I was knowing it inside out, and then I would meet once a year for example, in very nice sunny locations for a conference with the other people of the world that would know about the square millimeter topic. And then I would go back into my office to dig further on the square millimeter So I was actually interested in finding something that is very interactive and very dynamic. And that's actually I think what I found in the space environment, not only space industry, but in general, I think in this space ecosystem, by its nature, it touches on a lot of innovative aspects. It's very interactive, because you need so many different disciplines. You need to be able to talk to multiple, completely different types of disciplines, but also different nationalities and so on. And it's very dynamic. It changes so quickly, and especially, I think over the last couple of years, even more so than before.

I think there's so much changing in the space ecosystem. You know about SpaceX and they're bringing crew, based on commercial concepts. I mean, there's companies like Axiom that you may have heard of that are bringing complete commercial space stations. I mean, we're bringing projects for private companies that are interested

in using space. There's so many things that are changing. That's, I think, also really exciting. And then it touches on, as I said, on different disciplines. Like you guys, I think you're in a discipline that if I was starting studying this might be very high on my wish list. I consider myself so lucky because I'm in space, therefore I get to talk to you guys. We're doing a topic that at this moment I'm not studying, but I can see, how does it interact with what we are doing? And so that, for me, is also something very typical of space. We need to interact with all of these cool disciplines. And of course, it's very inspirational. I mean, it touches on so many different aspects. We might not be staying on this Earth. And we might want to explore, not just once, it's human kind's nature to explore. So being part of that is for sure very, very exciting.

iGEM Concordia 8:26
One of the ideas behind our projects in the beginning was, we recognize that there was a need to biomanufacture in space versus doing it here on Earth and then to ship it, because of the huge costs and time commitment that that is required. And I believe this is one thing that we have in common with Ice Cubes Services. We did go over the website, can you tell us a little bit more about Ice Cubes Services?

Hilde Stenuit 9:02
In general, what we are doing is providing access for research or for technology testing, or for educational or inspirational projects. One of the first projects that we supported was an artistic, inspirational project. We own our own facility onboard the International Space Station that we provide access to. We're a private company, so it's a commercial service. But we're very interested to look for doors that allow for anybody who needs, who can use access to space to help them. We also have been helping writing grant requests or if there's, for example, a university that wants access but doesn't immediately have the budget in their drawer. [shares Ice Cubes slides]

Hilde Stenuit 10:37
We actually have some interactions with a number of companies and research institutes that are doing things related to biofabrication in general. I think our dream is that one day we have all of these little bioreactors or drawers with all different types of things. And you have little tabs. I mean, just virtually thinking, where you can basically take all of the raw biological material that you need, that you put it together for whatever you need to biomanufacturer, biofabricate wherever you are. On this slide, I put a number of topics that we have been discussing with either companies or research institutes that we could support with our Ice Cubes Service, bringing some of these projects onto the space station. I mean, that ranges from 3D bioprinting I'm sure you guys are aware, we're having a project where I mentioned these organoids, we want to bring organoids on board of the space station to test for drugs or but there's also other things like the next generation wearables for us. Astronauts or biodesign for

astronauts like microbially active t-shirts or radiation-resistant clothing. I mean, there's also a lot of topics related to in situ resource utilization. More on the biological side, related to bio mining and how you can use, for example, bacteria to produce methane. So I think there's a lot of topics that have to do with biofabrication that are very relevant in space and for space, but also where again, space can be used for the benefit of Earth goals as well. I don't know if I answered if I answered your question.

iGEM Concordia 12:49
It did. I'm just wondering what is 3D food printing? I haven't heard about that one before.

Hilde Stenuit 12:55
Well, there's a number of topics ongoing where you have a 3D model printer bought where you apply that on food. In fact, I can maybe not go into much detail because we're all under NDA. But there's one specific project where they actually would print a specific type of food for the astronauts. Bringing back again, let's say raw material, raw ingredients that you put in the food printer, and you actually print the foods onboard. Also, here in the Netherlands, there's quite some activities. There's a Research Institute called TNO. So it's a Dutch national institute, and they're also very active on topics related to 3D food printing. I think it's interesting to see if, and how, that is relevant for space.

iGEM Concordia 13:53
That's very interesting. We'll definitely look into the slides more closely. And my next question, we were wondering, does Ice Cubes have specific challenges in terms of microgravity? Let's say, because when you're in space, cells aren't stuck on a dish, they are kind of free floating. How do you mitigate that in terms of the Ice Cubes setup that you have?

Hilde Stenuit 14:22
In very general terms, I go back to this very high-level overview of what the service provides. So, we have this facility on board of a space station. And what we try to do when we talk to people that have not done many activities in space is actually do what we call spacialization, Translating of what they would be typically doing on Earth to a space environment. And that touches on a lot of what you are referring to. Microgravity has effects at the level of biology but also at the level of fluids or mean for example, if you want to create a bioreactor, making a bioreactor for Earth is very different than making a bioreactor that needs to work in space. Because I mean, you need to take into account how gas will be produced , what filters you need, and so on. That's a lot of what we actually do. We set the level of systems like, how would the system work on the microgravity conditions, but then also at the level of biology? This is the slide I was referring to before. As I said before, these are, let's say, how you can use microgravity

effects in your benefit. But yeah, as we were saying, it can also work against you. I mean, gene expression changes can also work against you, for example, I mean, to take one of them, there might be a different expression of genes that you're not after. So, yeah, it works in both directions. The glue is to make it work in such a way, both at the level of system or at the level of your science, that it creates the effect that you desire, and you block the effects that you don't desire.

iGEM Concordia 16:18
In terms of all these researchers who approached you to send their experiments to the International Space Station, what are the barriers and accessibility issues that they face? I'm assuming costs would be a major one. And how does Ice Cubes address them?

Hilde Stenuit 16:43
I think in the past, there were a good list of hurdles. And I think services like ours actually, definitely the purpose of setting up services like ours is to actually reduce, or remove these hurdles. That's even more true now that we're doing more applied research. There's more companies that I mean, for example, pharmaceutical companies that want to access space for reasons which you cannot say to a pharmaceutical company, you will fly in 10 years. I mean, obviously they will want to see how it can happen and how quick it can happen. One thing that has completely changed and that was a hurdle in the past, you mentioned cost that was for sure a hurdle. You could still say it is a hurdle because I mean, if we talk, I mean, one cube, I mean, for example, a kilo. Okay, that starts from 40 K. dollar, Okay, not everybody has 40 k dollar in their drawer as much as we like. What we try to do is, as I said before, is either helping grant writing or set up collaborations with consortiums that may include funding sources that can be either investors or that can be companies that are interested in the IP resulting from some of these projects.

And what we also do is try also to set up projects that can be shared, for example, we do one collaboration that we have with a Japanese company related to protein crystallization. That's one new cube, so 10 by 10 by 10 centimeters, but it can contain 96 different types and different cubes that all have different proteins or different large molecules that they want to crystallize. That means that one such tube costs of the order of 4K, so that becomes much more accessible.

We also have our own cube. We call it an educational cube because it can also allow for some projects, for example, in plants or in fluids. Again, that's where one school or one university can basically do one, two, and so there's, for example, six tubes in that one unit. So that breaks down the cost. And so that makes it accessible basically, even for students or even for high schools. So that's the way we approach that. In general, I think prices

have come down a lot because there's different collaborations. I mean, we work on the European side, we work through partnership with the European Space Agency, but we also work in the US with what is called the ISS National Lab. I don't know if you heard about that. No. So it's a - organization that has been set up in the US to make the International Space Station accessible for anybody else and NASA basically. They support in several ways also by providing resources they fund or support different projects from companies from research institutes. We work with them on the American side.

Let's see. That was a long answer. So yeah, cost and schedule. And I think the third one, I would say, that is a hurdle is in general awareness. We realize that in fact, the awareness of people that they can access space and how space is relevant to them, is also still very low. I think awareness is also still an issue. I realized that actually in a lot of universities, there is not much thought on Space Science and specifically for microgravity. Yeah, so cost and schedule, awareness. And maybe the last one is processes. People think, okay, space, it's such a specialized niche thing where you need to understand the inside out.

That's also where we try to, with our service, we try to set up a service where we take care of the space processes so that people can actually, I mean, if you guys would want to fly your project, you don't need to learn about what it means to manage first on the launcher, so that we can tell you about it because it's cool and exciting. But you don't need to know this. The difficult parts, let's say, of the space processes, so that you can do, what you want to do, which is your synthetic biology or your bio fabrication project.

iGEM Concordia 23:22
I've seen that there's projects to set up a space station near the moon. And so is that in the plans for Ice Cubes as well?

Hilde Stenuit 23:34
Where we want to get with Ice Cubes is that we think our users or our customers don't need to think about space platforms. Because I mean, we would space whatever we'd like to show this type of pictures that you see on the right bottom, very complicated, very nice looking, but in fact, it's not very interesting for most of the people, it looks like a very technological endeavor for sure. But what we would like is that people think, okay, I can get through space, but what is it on the side of space that that is relevant for me? Is it indeed microgravity? Is it radiation? Or is it the fact that I can observe the Earth, that I can get to the moon, as you mentioned, around the moon? So there's this, I think you were referring to maybe this orbital platform that will go around the moon so the Deep Space Gateway, or do you want to get on the moon because you want to investigate something on the moon surface.

We want to understand our users, what they are after from space, and then we can define for, or with them, which platform or which space location is more suitable for them. In fact, with the company- there's this very little picture here- it's a lunar rover. We developed such a rover under a project with the European Commission. We will fly this rover to the moon, we hope in 2024/25. And it will actually carry the same type of cubes. If you say, I'm interested in the moon. We can bring you also to the surface of the moon. A Deep Space gateway source that's been thought of or designed right now. We intend that we have a similar type of facility or access so that if you're interested in the deep space radiation you would find around the moon, that we can bring you there as well. It's absolutely the viewpoint of Ice Cubes that we can basically provide you with access to space in general, wherever it is, and whatever it is you want from space you need.

iGEM Concordia 25:56
One of the things that we are addressing as part of our iGEM project This issue of inclusivity, as you probably aware, it's all over the news and social media. And we're just wondering, can you tell us how does your industry address inclusivity in general?

Hilde Stenuit 26:21
This is my personal opinion.I think the space industry in general, I don't think it is as good as I think it should be, given its innovative nature and given the fact that we should be at the forefront of a lot of technology and a lot of disciplines. I don't think we are where we should be in terms of inclusivity of all types that one can consider.I'm actually happy with the team that we are here. At least we are two ladies, but I can assure you that these are the only two in our team. I think percentage wise, we're not good. And especially I think, for me, that was a big surprise when I started working. For a while, I worked a lot also with Russian colleagues. And in fact, I was surprised to see that on the European site at that point, were by far not reaching, for example, gender inclusion, or the different type of inclusivity that I saw actually on, for example, on the Russian side at that point. That's my personal opinion. I wouldn't quote me on that one. Well, you can include it in my personal name, I don't mind doing it. It's just that I don't want to make statements for the company. I personally feel very close to a lot of what is going on at the moment. And I don't think our industry is at the forefront of these fights and I wish it was.

iGEM Concordia 28:21
Out of these researchers that are working with Ice Cubes and looking at microgravity induced effects, what do you see are the common approaches or methods?

Hilde Stenuit 28:54
Common approaches or methods, that's a tough one. That's a very tough one, because I will show you how very different types of projects are… so I mean, I mentioned this

artistic project, which was a kaleidoscope that people could interact with from the ground. We have research going on that relates to plants. We have technologies, for example, related to cyber security. In terms of common technologies are common approaches.

They all fit in our Ice Cubes platform. I think that's basically the commonality. We made it in such a way that it's very modular, and it can accommodate very different types of projects. Andre was also in line. He's following a lot of, for example, the projects that relate to artificial intelligence in space, which is yet another completely different universe of possibilities. Also the person you are referring to Timothy, is actually touching more on the human side. We have these little boxes in our, as you see here on the right, these little modules or units or cubes. Obviously, you don't fit the human in there. But we can actually have some equipment or some artificial intelligence, for example, that can work with astronauts. It's yet another universe. In terms of commonalities, well, I think the commonalities is really the models that you see here and the interfaces that we use, which are power and data, but for us, I would not say that there's a lot of commonalities but that's exactly what makes it so, so cool and so varied in terms of everything that can be accommodated.

iGEM Concordia 2:24
One of the things we were really passionate about creating is a control strain because we know as you mentioned before, genes are up and downregulated in microgravity and researchers are interested in these effects, they send their experiments to space. But as far as we know, there is no control strain to which they can compare their results to be able to say, Oh, these effects are really microgravity specific and we are developing such strain. Maybe this is a question more for biologists. But we also wanted to have your opinion. How do you think such a strain could contribute to the research field? And more researchers would be seeking out experiments onboard the ISS.

Hilde Stenuit 3:20
You mean specifically to have such a control strain?

i**GEM Concordia** Yes.

Hilde Stenuit 3:25
I think, fully understanding the control of such a strain would be helpful for others, then to build on that, to apply other effects and to be able to determine what comes from what, what effects are in that sense. I think it could definitely contribute. I think in general, looking into, 'what are the stressors and how do they play?' I mean, which effect do they have? I think it's very important. I mean, and again, not only for space, but also for Earth. I'm gonna ask something actually in return. I understood that you guys would get access to

simulated microgravity. Is that right for your project? iGEM ConcordiaYes, that's what I was going to talk about next, we are going to be using a 3D clinostat, I mean, the dream for us would be to send our experiments to the ISS. But my next question was going to be, what is the approximate cost to send our project to space?

Hilde Stenuit 4:33
I think first of all, it's good to do things on simulated gravity also to test both your technical setup, but also your science in a way, I say in a way because it's been shown another level of biology that simulated microgravity is not always fully representative of real microgravity in terms of the biology. So it would still be interesting also to get to real microgravity. I think in terms of cost, I would say like a reference price, it depends on a number of factors. But if you would consider a one unit, I would say it starts from 40 K. We typically do a reduction for educational projects, we typically refer to education for primary and secondary school. I think if it comes to that, then if that's really your dream, as I said already, we are happy to help you look at how you can fund it.

For example, we have links to the Canadian Space Agency. I talked to some of them on Friday. Or two companies that might be interested in some of the applications that relate to your research, or we might see if we can find collaborations with other institutes or, for example, with the ISS national lab that I referred to before. There's a couple of people that you may have met or that are doing research related to what you guys are doing that might be interesting to see. To link on and to see if there's possibilities for collaborations that might allow you to accommodate also your research question, maybe as part of a bigger project. I can also send you something complex, but I think you guys are very good in your networking so you might know them already.If it comes to that, we will be more than happy to help you look and see how we can find a way so that you can actually fund your access to space.

iGEM Concordia 7:05
I feel like the team in general is very interested in that. I do have to mention our project is a two-year project. This year, we don't have access to the lab because of COVID-19. So we're doing a lot of software work, we're creating a database that is going to have as many published publications that are related to gene regulation in microgravity. We're going to just compile everything and put it in one into one big database or all the researchers that are interested in microgravity. It's open source and free to access. Then next year we get to go into the lab and start working on our strains- our resistance strains and control strain- then we'll start to test so we do have some time to look for funding to send our experiment.

Hilde Stenuit
And you guys started designing your setup, what it would look like, not the biological side, of the technical side?

iGEM Concordia 8:11
Not yet, we're doing a lot of biological work right now. Just we want to make sure that conceptually and theoretically everything is sound. Right now we're working on gene selection. How are we going to select our reporter? How we're going to tag our genes, which ones, etc. And then we're going to start talking about the technicalities. And one of the things that is interesting about our control strain is that we want to look at changes in real time. You had mentioned previously how it would be interesting to know what role the stressors have. We're looking at doing some kind of luminescent monitoring that would be able to work. We have a spectrophotometer that one of our teammates is working on. And we were hoping that by recording in real time, that we would garner more information. What the stressors are like when the genes are being activated in order to help determine what exactly is happening in the cell?

Hilde Stenuit 9:32
I love seeing experiments where you actually, real time see biology happening. You don't have that so often, in fact, we had one experiment when I was working with ESA that was also using luminescence to see certain effects and I it would be really, yeah, it would be really nice. One of the very nice features of our facility and our services is that you can actually have real time interactions in the sense that you can send commands up from wherever you like and get the data down within less than a second. So, I mean, the type of experiments where you see the biology luminescence changing in real time, that would be really nice.

iGEM Concordia 11:24
We were looking into YURI Gravity before and we're just wondering how your program compares to them?

Hilde Stenuit 11:40
We actually work together with them. They're based in Germany and where their strength lies is that they have access to hardware that has flown in the past. Mostly for ESA experiments. For example, for biology, and so we have a partnership agreement with them because they don't have a facility onboard. But they have hardware so that they can be easily made compatible with our facility or are already, for some aspects. We had, for example, one experiment that somehow relates to what you guys. It was also a bio mining experiment that

involved NASA Ames as well, where we use their hardware in our facility. They also provide access to microgravity, about their strength or their unique added value, let's say that they have hardware that they can refurbish that has been certified, where we have a facility where we can use the type of hardware.

[End]