[Screen begins with **Professor Milos Popovic's** first slide – fades to **Professor Farid Najm** speaking]

Professor Farid Najm: Good evening, thank you for coming. My name is Farid Najm, I am a professor and department chair in the electrical and computer engineering department. It is great to see so many of you here today. This is an event that we hold on an annual basis, the idea being to invite alumni to come back to the department and listen to a great speaker about what's happening with the field and where it is going in the future. Also, we find that this is a great chance for alumni to network with each other, so that is almost a bigger benefit for the group I find. So today as I said, we have a great speaker; we have professor Milos Popovic who is going to talk about the connections between electrical engineering and the medicine or biomedical field. I don't have a long speech, big font [Audience Laughter]. So I just want to update you about one or two things that we are doing in the department. You've heard me talk before about the energy systems lab; this has been a continuing project for about three years now. We are done. We have made significant renovations to the lab. Overall cost has been about 2.5 million dollars, some of that from the department, some of it from the Dean. The result of this is that the lab is completely new, all the way back to the power supplies. We took out the old switch gear, the power supply; we put in brand new ones up to code. We changed 100s of metres of cabling, underground cabling, we have put fibre in and we have new equipment that is, whose purpose is to run experiments on the way you control the smart grid, in case of perturbations, the way you can integrate renewable energy sources, like solar and wind, into the grid without disturbances. We are running a DC microgrid in the lab and we changed the equipment at the stations, it's all custom designed by our professors for our needs and I would say it's better than any facility I've seen or heard of anywhere in North America. So if at some point you would like to take a tour of the lab, let us know. Let me know, let Jess know and we'll schedule something at a later date, not today, right. On another front, we are reaching out, as always, to other parts of the university to establish research collaborations and connections with facility members in other areas. And so this summer we had a research retreat that included many of our professors, as well as professors from other areas and one of those areas is the biomedical field. And so as a result of that we are now working to create an institute for neuromodulation that will be a link between ECE and IBBME and the medical sector in the university and the city. So we are very excited about that. This neuromodulation institute will work to develop, test, and implement systems to be used to control the brain, spinal cord, and peripheral nervous system. I have to read these things, not my field. It will really show the activity at the frontier between electrical engineering and the human body.

On that topic we are going to hear from Professor Milos Popovic today. Milos is the associate scientific director at the Toronto rehab institute and Toronto rehab chair and spinal cord injury research. He's done amazing work at the intersection of ECE and medicine. He is also a professor in the institute of biomaterials and biomedical engineering, that's IBBME, as well as a senior scientist at the neural engineering and therapeutic team leader at the Toronto Rehab institute. Professor Popovic received his PhD degree in mechanical engineering from UofT in 96 and his degree in electrical engineering from the University of Belgrade, in Serbia in 1990. His research interests include, let me see if I can say these words [Audience Laughter], functional electrical stimulation, neural prosthesis, neural rehabilitation, neuromodulation, that I'm use to by now, brain machine interfaces, physiological control systems, assistive technology, modeling and control of linear and non-linear dynamic systems, robotics and signal processing. Milos all yours. [Applause]

Milos Popovic: Thank you Farid. Thank you Farid very much for inviting me. This is a very distinct pleasure to have the opportunity to show you what we've been doing. So the topic, as you see, is neuroplasticity and neuroplasticity is a method in which you can re-program the circuits in a section of the system in the brain and make them behave differently or try to repair them after an injury and I'll show you one of the examples soon. So this particular neuromodulation methodology that I will show you today is used to help people who have severe paralysis recover ability to use their arms and legs and such. So conflicts of interest, I have conflicts all over, so one of the biggest conflicts I have is that I have created this company which is called MyndTec and some of the things you will see in the presentation ended up being commercialized as to the company but all of the results you will see have been done before the company actually existed. So the science was done before we start thinking about money. So the motivation is the following, so I'll let this go and then we will talk about it later.

[VIDEO – Narrator: **Unknown Female** in her car having trouble speaking]

Narrator: It is at 6:42 and the sensation is happening again [She lifts the left side of her mouth up and down 4 times]. It's a smile they said, a smile [She purses her lips together twice]. It's all tingally on the left side, on the left side. The doctor said to breathe in, breathe out, manage the stress and I'm trying. I don't know why this happening to me. It happened this morning again and when I left the hospital Monday night at like 12:30 in the morning. So now I am taking a picture for an example of what happens. It's 6:43. My hand is hard to lift up [She lifts her left arm up] and I should touch something, touch my nose [She touches her nose 3 times and lifts her left arm up and opens her hand twice, all with difficulty]. Ok.

[Video ends and returns to **Professor Milos Popovic speaking**]

Professor Milos Popovic: Do you know what you are looking at? This is a stroke. This is a gentile stroke, so it is not the one which immediately removes the power from the patient. So what she is going through is her vision starts blurring, she loses control over her left arm, she loses control of her speech and her face starts sagging. So fortunately that was a mild stroke, that's why she was able to take all the videos. If the stroke was profound, she will not be able to do that.

[VIDEO- One male with a covering on his arm and one female sitting, **Professor Milos Popovic** narrates over the video]

So here is an example of a patient who had a more severe stroke. So look at his arm, he is not able to move shoulder, elbow, fingers. This cover is just to protect the arm from injury and Jennifer will slowly take everything, none of these movements he is able to do himself. Ok. Very common thing, there is about 50 million strokes per year, worldwide. And in the US about a million, so with us about 100,000. So you can see she is asking him to extend the wrist, open the fingers, he is not able to do any of those things. Now what is interesting is that when a person has a stroke, if this is the condition he is 3 weeks after the stroke, the probability of that person getting better is less than 10 percent. So imagine the average age today to get a stroke is 50.

[Video ends –returns to **Professor Popovic** speaking]

So you can have 30 years or plus of life like that. And no technology out there is available - or until we came along, to deal with this type of issue. So here's some numbers right. In the US, Europe, Canada, 2 million people have strokes. 10 percent recover, 15% die, and then you have all this in between. So about a million or so have impaired upper limb function. Why is that a problem if we have impaired upper limb function? Try to get your credit card and pay something with one hand in your pocket. You can't do it. You can't take a shower if you don't have the arm available, you cannot even make the sandwich for yourself. So everything you take for granted you can't do it period. So what happens is you need an attendant to be with you and help you to deal with all this. Ok. So as a result of all that, the cost of caring for these people is ridiculous. And this is the cost you can kind of calculate, if you get an expert in expenses, medical expenses, you don't calculate how much medication you take for pain or whatever attendant care you need. But they will not tell you that the family gets a stroke, it's not that the patient got a stroke, it's the family who got a stroke. So if your family member got a stroke, you have to leave from work early or you have to attend to this person and all the members of the family run after that person to enable this person to dress up, undress, go to bed, eat and whatever. And because this person is going to live for 30 years with the stroke, this is a protracting experience for the whole family right. So these are the obvious costs and there is a lot of hidden costs that people can't even calculate properly.

So in the 60s or 70s some interesting people came up with an idea to use neuroprostheses, but not for stroke patients, for spinal cord injury patients to help them restore hand function. So what is this all about? They found that if you use very short current pulses and deliver them to the peripheral nervous system, you can generate muscle contraction. So you can fire different muscle groups in the arm and you can open the hand and close the hand and what not. So they came up with the following idea, you are going to put electrodes all over the muscles that are relevant for grasping and reaching for example, or locomotion, and they are going to fire them in a sequence to enable the movement of the hand or arm to grab an object and release the object. So in the 60s and 70s and until the late 90s we actually believed that these people would never improve their hand function. I'll give you an example. So this is a spinal cord injury patient. He cannot use both arms, he can move his shoulders and elbows but he cannot open his hand, he cannot pick up the object. And we have instrumented him with a neuroprostetic system in his left hand. So what he is going to do is he is going to try to pick up the toothpaste with his hand, he will fail doing that and then he will activate the neuroprostetic system by pushing a button here, he will pick up the object, and he is going to move it. So that's what you are looking at.

[VIDEO – Subject, male, attempting to pick up the toothpaste, **Professor Milos Popovic** narrates over the video]

Typically spinal cord injury patients they have both hands injured or paralyzed and they depend on others for everything… Ok. So the idea was that we're going to build these types of things, it's all electronics, so it's all what you do for a living - software, hardware. So you're essentially going to provide these low energy pulses to the muscles, in a co-ordinated way to get different grasping styles. And of course the vision is the following.

I am going to have a patient and I am going to instrument the patient with a system early in the morning or maybe I implant it in the patient, all the way. And then each time the patient wants to shave, he'll turn on the system, shave and use the electronic technology of this whole system to shave, bathe and what not. So the idea was that it was going to be orthosis and there was two different approaches to it. One is to have it implanted and you have all the wires come out of the skin to different muscles and you have a joystick on the opposite shoulder or voice control, whatever you want, and you turn it on, you open the hand, you issue a command, you close the hand and that is how the system would work. Or you can have a surface system, which looks like that [New picture appears], that was another way of dealing with this but this is only for hand opening, hand closing. This is what we have done for 40 years; we believe that this is the way to go. We are building implants, electrodes, systems, put them on patients and send them home to do this. So you know when you're in Rome, you do what the Romans do, so I did the same. So we built an electronic system, which designs that, does these upper things, gives you different grasping styles and you get the patient number 1, instrument the patient, that is the guy you have seen in the beginning, instrument the patient and we send him home to use it to brush his teeth, do whatever.

And about 3 months later the gentleman comes back, not the gentleman, it's another guy, and says 'I don't want this anymore'. So if you have ever worked in assistive technology, this is a normal thing right. You know all these walkers, wheelchairs, people are going to return them all the time, about 67 percent of assistive devices are returned back, people don't like them, they're useless, they're complicated, they're cumbersome, they don't like the colour, it affects their sexual life, you can't even imagine the slew of possibilities is ridiculous right. So we thought you know that's the same one of those. So we said 'Ok, is the problem with the colour?' 'No no no, I actually don't need it anymore'. So that was the funny thing right. I didn't know anything, you know I'm the guy that came from airspace, I was building airplanes before that, now I'm building this thing right. And the patient says 'I don't need this anymore'. So I rolled him up to the neurologist on the fourth floor, knock on the door, pull Dr. Kurt out because I was in Switzerland at the time, and say "How is this?" And he tells me this is a spontaneous recovery. When you hear something like that from a neurologist, it means they have no clue what the hell is going on [Audience Laughter] but he recovered so tough luck, right. So after the third spontaneous recovery I stopped talking to my friend Dr. Kurt and I said we have something here, so let's try something different with this. So this is what we proposed, use it as a short-term therapy.

So we applied this technology, which is quite sophisticated, we run the patients every day to grasp things and manipulate things and then after some time we pull it away and see how much they have recovered. So when they proposed this in 2000, people just point fingers at myself and [blows air], 'so stupid right'? Ok, we endured that ridiculing, ok. So this is what is interesting about this concept, which is they didn't think about it. You ask the patient to perform a task, for example open a hand, and this poor patient is going to struggle, he is going to strain, he is going to be upset with me because I ask him to open his hand and he hasn't opened his hand for the last 6 months, 'What the beep are you asking me to do, are you insane, I couldn't do that'. So I say no, try to open your hand, he's struggling to do it, and then you fire all the muscles and he opens the hand. So why is this important? Because as he is imaging the movement and trying to open the hand, he is firing all the motor, let's say resources, that he has in the brain and the brain stem and the lower levels. And then he gets feedback because the muscles start moving in exactly the physiological manner. And he gets all the feedback coming back through the system and looks through the paths to connect the planning and execution. Now the good news is that the brain is not a PC, so it's not like board for this, chip for that, it's a distributed system. So these paths start finding their own ways and over time you rewire the patient.

So this is a simplistic explanation of what is going on. So somebody has a stroke, that command from the motor cortex cannot go through the spinal cord and to the muscles, to generate the movement. So then you apply electrical stimulation, these are kinds of electrodes of an electrical stimulator. Then you do this, you ask the patient to imagine the movement and as he is straining to do that and he is not able to actually move the muscle, you fire the muscle, you move the muscle and he gets all the feedback to the spinal cord and back to the upper levels of the central nervous system. And if you do this repetitively, you create a new pathway and the patient is able to do it on his own. Now the critical thing is this, you actually need a therapist who actually knows what is going on, so she can pick the right movements for this patient based on what he is able to do, choose the right movements, and guide the therapy. Second is to have a patient who understands what is going on because if the patient doesn't understand or is cognitively not all there, this is not working right? If you are trying to get him to reach and he is looking at a nurse, it is not happening, it is not going to happen. So the patient has to be involved and then you have a device which actually activates all the muscles in a physiologically correct manner. Electrical stimulation exists for 40, 50 years now, but nobody has done it in a sophisticated manner as we have done. To fire different reaching and grasping tasks exactly the way how the brain does it.

So that's where some of the intellectual property laws. But this is important, all three elements you need to have for this to work. So this is for example the position of the electrodes, I'll just show you a few [electrodes appear on the arm, shoulder]. And they're all on the surface of the body and you can do very sophisticated like pinch grasps, you can do that with the system, no other electrical stimulation system does that. So you can do this, hand opening forward, open a hand; grab an object, retrieve an object. You can actually pick a pen and write with it. You can do lumbrical grasps like that. You can do a key grasp and you can do bimanual things, so I can pick an object with one hand, bring it to another hand, pick it up with other hand, release, release the object. So you can do collaborative, you can pick up a tray with both hands. Ok, this is how the device looks like. It has 30 different protocols for reaching and grasping. That is unique; when you buy a stimulator you get one or two. Or neuroprostheses you get two or if you are lucky you may get three. But this is like a whole slew of different reaching and grasping strategies that people have not thought of. This is how the interface looks like. So you can pick whichever one you want and it can drive the whole thing. And here is a reaching forward, opening a hand, picking up an object, retrieving an object, this is a stroke patient and that is after two years following her stroke. So everything that she has been doing is done by electrical stimulation. So we have this synergistic movement, firing of eight or nine channels, actually eight channels getting the hand forward to open object, grasp an object, and retrieve an object. So this is how the therapy looks like.

And you repeat it, you do it for five minutes and then you have another task. Touch the nose, extend the arm, touch the opposite knee or extend the arm, do that.

So, engineers love to build toys. You can build a toy; you can impress people with this. And then you can go to an MD and the MD is going to say 'Ehhhhhh'. The reason he is going to say 'Ehhhh' is because unless you have a clinically done trial, randomized control trial, properly done randomized control trial, you aren't going to impress anybody. So here is where the nightmare starts because any of these clinical trials the price tag is 2 million dollars and up. You have to have a team, you need to know what the hell you are doing, you cannot afford to make a mistake and you have to build this properly. So I'll show you one of those, it's a phase 2 randomized control trial, it is done at a single site, the price tag for that was about 700,000 dollars. So we did the following thing, we get patients as they come in a stroke group, stroke patients and we randomize them into two groups, intervention group and control group. The control groups gets the best occupational therapy that money can buy in this town - the Toronto Rehab, number one rehabilitation institution in the world, you bring them there. And the other group gets 1 hour of this therapy, which I showed you a minute ago. They get 40, 1 hour sessions, 40 days in a row. And we choose the most complicated cases, this is… less than 15. In engineering terms, these guys can't do anything. Period. They're toast and they're not going to improve, I am sorry for the language but that's what it is right.

So here are the results. The randomized trial we have 21 patients, it ended up 11 in control and 10 in the intervention group. And they were between 17-57 days post stroke, which means at this time you already know they are not going to improve. So that's how we choose them. So this is an interesting thing. You don't have to remember this one but it is called the Functional Independence Measure Self-Care Subscore, why am I showing you this? Because clinicians and actually insure companies could care less if you improve the range of motion, what is the angle of the finger. No, they want to know: can you feed yourself, can you bath yourself, and can you dress your upper body, your lower body, groom, and toilet yourself. And as you can see, the score goes from 6 to 42 points, obviously this is not done by an engineer [Audience laughter] because we would start with 0 but occupational therapists start at 6. It starts at 6 and goes to 42. The clinically important difference is 6 points, what does it mean? If you are below 6 point, they ignore you. If you are above 6 points, the physiotherapist goes [Kissing sound] great. Because she can pay for it, she can actually go to the insurance company and get the cash.

So, this is engineering 0, they can't do anything. So these are control patients 1-11, treatment 1-10 and you see how many of them are in that shape. Ok, you see how many of them, all of them are below 18/19, why is that? Why is this important? Nobody works with these patients. When the patient comes to the MD and they assess the patient and they are below this level. Ok let's do something else. So you can see the patients now and this is after the therapy. So here it changes 8 points, here the median change is 22 points. Ok so if you don't like statistics, which I passionately hate, there is a few options. Here they are arranged from 6-10, 11-20, 21-30, and 31-42 points on the Self Care FIM score. This is the control group, this is the treatment group, this is the control group where it ends, this is where the treatment group ends. You know where you want to be, do you want to be in this group, or do you want to be in the other group? The answer is obvious.

Here is another test which is called the Fugl-Meyer Assessment. It looks more precisely with what you can do with your shoulder, elbow, forearm, wrist, and hand. It goes from 0 to 66 points, 6 points is a clinically meaningful difference. If you have a prognosis at 6 points, you have done something useful for the patient. So here are our patients, they're all less than 15. Why are we stressing this line? Because these are the patients, we don't treat them today. So you're less than 15 and you go 'can you do something about my arm?' They say 'Ah, we'll work on balance today.' 'But what about my arm?' 'Ah tomorrow.' And then you come tomorrow: 'Ah let's look at sitting.' And they will talk about all these other things that you need to deal with but they will no talk about hand function, upper limb function because they know they can't do anything there. So this is where they start and you can see many of them have no, nothing. This is after. So this is that spontaneous recovery [**Professor Milos Popovic** and audience laugh], we have no idea what happened to these guys, by the way. But this spontaneous recovery happens in 10 percent of patients, that is exactly what we would expect. And this is our people. So you see the lowest change, is bigger than the clinical minimum difference, that's why these results are exciting.

So this is, you remember the guy before? This is him after.

[VIDEO-Male subject attempting to lift a cup, **Professor Milos Popovic** narrates over the video]

No electrical stimulation, nothing, just him and a cup. The cup has wax inside, so it simulates a load like it's full of tea or coffee. [Subject lifts mouth up to his mouth and down] And that's what he is able to do on his own after 40 hours. [Video changes to show the subject lifting up a bag of balls] So if I tell you that before that he had some dishabilitation, he is taking pain medication and that I could not even touch him with my hand because he would be very uncomfortable with that, you can imagine how much he progressed.

[Video ends and returns to a speaking **Professor Milos Popovic**]

Now this is nice, lovely, we published that yada yada yada. Then of course people say, you're doing some Serbian business, I'm not so sure, this is all strange, nobody else in the world has these results, can we validate this. I will be really quick. So we gave the technology to Sunnybrook, to what's the name of the lady, can't remember her name right now and she went, Sandra Black she was a prominent neurologist in the country. And she gets the patients and these are the results.

[VIDEO – Unknown Male Subject named Andrew begins speaking]

Andrew: This big 300 pound guy had the ball and came running like straight at me. It went horribly wrong, I immediately realized, well I have a broken face because my jaw was over here.

[Video text: While in hospital that night, Andrew suffered a massive stroke]

Andrew's Mother: It was so serious; they didn't know whether Andrew would survive the stroke.

[Video text: Andrew survived the night. The stroke left his right side paralyzed]

Andrew's Mother: Well we were fearful that we might never hear our son's voice again or that he might not ever be able to walk again or use his hand or arm.

Professor Popovic: If somebody has a high level stroke injury, the probability of improvement is less than 10 percent.

[Video Text: Stimulation Therapy: A Wake-Up Call for Muscles]

Naaz Kapadia Desai: So basically what functional electrical stimulation, we are re-training function. One component of the signal goes to the muscle but at the same time we are also sending a signal to the brain of the movement that is being executed.

Andrew: They were saying that it would train muscle and my brain would obviously connect that pathway.

Andrew's Mother: Within months we could see improvement.

Andrew's Father: It was very encouraging, like we saw hope.

Andrew: It did wonders for me; it improved me and gave me back my arm.

Andrew's Father: If it wasn't for the functional electrical stimulation, he wouldn't be what he is today.

Andrew's Mother: Oh it's definitely made a huge difference for him.

Andrew: During rehab, FES has been great for me; it's basically got me from dependent to independent.

[VIDEO ends and returns to a speaking **Professor Milos Popovic**]

Professor Popovic: So then we launched the product. We gave them half the dose of therapy. And we gave the device to the people that either haven't used electrical stimulation before or hated it passionately, physiotherapists. So we trained those people, we launched the project. 24 patients, this is where they started and this is where they ended up. These were not experts in using electrical stimulation, so they were learning on the job. 58 percent of patients had a clinically meaningful difference for half the dose of the therapy. And they were all chronic, the patients you saw before, they were all sub-acute and have a tendency of recovering better. This was 2 years after, these guys should never recover. So that was very exciting. So this is a guy who is 19 years post stroke. That's him 20 hours after therapy [man moves his arm up and down]. He is doing party tricks in the restaurant. That's Howard 60 hours later; he is moving his fingers, after 90 years. Now he is swimming in a pool. Ok. I will skip this one. While we were having fun, that's how many people were having a stroke [1050 people]. This is the take home message. This a non-invasive neuromodulation intervention. There is no side effects, there is nothing. If you take an aspirin to deal with your blood pressure, you have side effects. There is no side-effects, so that is number 1. Very easy, can be delivered at home, can be delivered in a clinic, as long as you have a physiotherapist. Patients have to be mentally engaged, that's the only restriction. The therapy has to be repetitive and you need at least 40 sessions to really have meaningful clinical improvements. And the therapy has to be done in combination, physiotherapy, occupational therapy. And this is the only therapy on the market right now that can truly recover voluntary upper limb function. And that's it. We are running a conference in Niagara, next year in November and if you want to find out what else we do that's the web page. [Audience Applause]

Professor Farid Najm: Thank you Milos. Very exciting work. Do you have questions for Professor Popovic. Yes, sorry.

Audience Member: Sorry I just want to talk as usual. Just one question related to the use of this technology. How widespread is the use of this technology in Toronto and Canada and the world?

Professor Milos Popovic: So right now we have 16 or 17, 16 clinics, 17 units are deployed and already over 100 patients have already received it. And we had done no marketing, zero marketing. I have not put a single ad yet. So I am getting some serious marketing people, of course I need money to do that, so any of you who is ready to put half a million dollars, please [Audience Laughter]. I was joking. [Audience comment] Yeah you can, it's available right now. So we are trying to launch, we had a beta launch just to see how it works in the field and we hope to launch in the first quarter of 2017, full force with advertising and everything, try to get revenue.

Audience Member: Can you also see if there is still room for improvement.

Professor Milos Popovic: Oh yeah, absolutely. Just to give you an example, the whole technology behind this, which I didn't really talk too much about it and Farid is going to be upset with me, but we have built a special language for writing neuroprostetic systems and those people who run this business they know that it takes at least 3 months to build neuroprostheses, for anything. I can do neuroprostheses for anything, for locomotion, for sitting, swallowing, and coughing in 15 minutes with that toy. It's like an app and it's all in a cloud and you can download as many apps as you want. So right now we have 30 apps just for hand function, we in the drawer have 10 for locomotion, we have apps for sitting, we have apps for depression of the face, we have apps for all kinds of things.

Audience Member: And do you think that this technology could be used at home by somebody who is healthy…

Professor Milos Popovic: Some aspects yes. So reaching is complicated, right. Sitting, yes. Hand opening you can do it at home, face depressing you can do it at home.

Audience Member: For someone who has something like cerebral palsy where you have nerve damage, does it work for them also?

Professor Milos Popovic: We actually, we have a very good friend who is the CEO of spinal cord injury Ontario. He has that right, full peripheral nerve damage for 60 years and we brought him in, we stimulated him, we got the hand to open, so it's the question if he wants to do it.

Audience Member: So but like when the nerves are damaged how does the brain create pathways if the nerves are damaged, once they're damaged, you don't have, you don't have wires helping you.

Professor Milos Popovic: You are asking an excellent question. So my logic was that if the peripheral nervous system is substantially damaged, you can't do anything with that. Period. And then a year ago, we got somebody who got a cervical myelopathy and all his peripheral nerves were damaged substantially, that when you tried to stimulate his muscles, you get zero. Nothing. And then I said 'Oh lets stimulate him, he wants to come, I have the therapist, he's a cute guy, so let's do it [Audience Laughter]. So we did it for 16 hours and after 16 hours he is doing that [**Professor Milos Popovic** moves his fingers] [Audience Laughter]. So if you ask me 'How the hell does this happen?' I don't know. Because according to physiology, according to books, according to whatever we know and others can confirm that should not happen. Period.

Professor Farid Najm: That tells you something about books.

Professor Milos Popovic: Exactly, don't read books. [Audience Laughter] Bad things.

Professor Farid Najm: Milos! There are students here [Audience Laughter]. Yes.

Audience Member: Does it require continuous stimulation for the patient to have this co-ordinated function. So does it stay for the whole…?

Professor Milos Popovic: So you saw the same gentleman who was the whole video, Ok. So what we did with him was, he was able to pick up objects very roughly, bring them in very slowly, ok. Off he goes home and 8 years later you… and you merge. Do we have anything intelligent to show and advertise for Toronto rehab. So my kind Mentor in the… said 'Why don't we get one of your patients?' I stopped doing clinical trials for some time on that because we were commercializing, so I don't have a patient. And my patients are older people so they tend to die. So you do a therapy on them, they live for the next 10 years and then they die. So I need a younger patient who probably didn't die so I said 'Ok why don't you, why don't you go to him'. So the crew went to the guy, filmed him, got the data. 'How's the video?' 'Good!' So I haven't seen the video, they blast it on CTVO or I don't know whatever news and the guy is doing chin ups, he's lifting his whole body. That was not in the manual, right. In the manual, you can touch your nose, you can maybe pick up a cup and bring it to your chest and maybe drink out of it. There is no lifting 75, 80 kilos in chin-ups. So what's happening is the patients who have gained some function, they keep it, and because they use their hands every day, they train and train and train and they get better and better and better. That's the good news. So they don't revert. The only time the patient reverts is if they don't improve enough function to have some functional movement out of it. If they don't have functional movement, it's gone.

Professor Farid Najm: Ok so there's a question here.

Audience member: In your studies have you assessed if different parts of the brain are firing, so for example if you have a stroke there's a shut down in certain parts of the brain. Have you studied whether it's those same shut down parts of the brain that are now functioning again or if it is other parts of the brain firing on their own.

Professor Milos Popovic: That's great. Can I, can I go back to the video to show you something, which you rightfully so didn't pay attention to because nobody does. [Audience Comment] No no no no, the question is great, I'm not trying to be disrespectful or silly. I want to show you something, ok. So when you look at this video [The video of the subject Howard replays]. What you are looking at is in this hand, right? That's exciting but look at this hand. He is actually lifting both arms simultaneously. So what does it tell you? It tells you that actually this is the part of the brain that's injured in his case, this part – that's why he cannot use his left hand. But each lateral side, which is controlling this arm, starts controlling this hand. That's why he activates both of them simultaneously

Audience Member: So that's what you meant by neuroplasticity?

Professor Milos Popovic: Exactly. Is that another part of the brain starts doing it. Exactly. Now what happens is that in the beginning what happens is that he cannot separate the two arms, he is moving them both simultaneously. It is only after a number of hours he starts functionally splitting neurons and says these are for this hand, those are for this hand.

Audience member: So you are keep some statistics of whatever is transpiring.

Professor Popovic: Of course, of course. But it is much more complicated, sorry. What is complicated is that really the hardware is distributed all over. So they have done a study very nicely, actually this year or last with mice, rats. They train the rats to like perform morse code type of thing, in order to get food. And they went and they literally took their motor cortex out with a spoon. And the rat was able to do that, showing that the control of the hand function or upper limb function or any function, you use the motor cortex to learn the task and then you download the protocol to the lower levels and then they could repeat it. However that rat would not be able to learn a new task.

Audience Member: So what is the longest period of time that anyone has used for your therapy?

Professor Milos Popovic: 37, no 27 years. It was traumatic brain injury patient, it was 27 years.

Audience Member: Sorry you mentioned that FES has existed for a long time, what kind of barriers do you think existed that prevented a technology like this from being created?

Professor Milos Popovic: That's a good one, so I had a problem because whenever I tried to pitch this to the investors, they would say 'Oh FES has been there forever, what is the difference between your technology and their technology?' And I could not answer that question for a very long time. Six month I woke up in the middle of the night [**Professor Popovic** makes a buzzer sound]. So here is the thing, you look at a didgeridoo and you look at the flute. They're both wind instruments. The didgeridoo you can just do bzzzz, whatever right. With the flute you can play Mozart. So what we have done is we have taken this technology and brought the flexibility and dexterity that other technologies don't have. So, what they do is open the hand, activate muscles, relax muscles, and that's it. We actually activate muscles antagonist and agonist simultaneously. We have like, we have what do you call it, extra extensions so you can fire this muscle and reduce the firing of the muscles to do that [Lowers arm up and down], which you and I normally do every day. Other stimulators don't do that. And they combine all this temporally such that it adds a complex movement that people have not done that. They have done this, done this and done that [opens and closes his hand, pinches fingers, and move thumb] but done [performs a reaching movement] type of things. And that's what makes this very attractive. But of course not everyone knows how you have done it because they will copy it, but that's another story. That's ok.

Audience Member: I have another question. So when you're putting electrodes on the patient are there optimum locations for these electrodes to achieve better results and I guess you have obviously researched this to some extent but do you find there may be a major difference depending how many electrodes were used and where on the body they could be?

Professor Milos Popovic: We know where to put it because the muscles and the innervation of the muscles is the more or less same in all of us, more or less, there are some exceptions — my son of all the people! But anyway there are some exceptions and then you have to go and look for the proper location to put the electrode to get that muscle and get it innervated. So anatomically we know where they should be coming from and the physiotherapist could train to find the muscle and know which muscle they are looking for, they know what the innervating path is, they know how to do this.

Audience member: It's not too sensitive?

Professor Milos Popovic: No, not that sensitive but there is, you need to know how to do it and we train them and those positions of the electrodes, actually help therapists understand where to put them. Some of our muscles are very small, so you need fidelity of finding the muscle but when the electrodes are big, it means it doesn't really matter

Professor Farid Najm: Ok, yes one more question

Audience Member: How do you measure the mental effort exerted, are you thinking of using EEG or other technologies to?

Professor Milos Popovic: So that is one of the most important things of this therapy, which we have neglected profoundly, right. Because it's complicated. How do you measure somebody's involvement? However, César Márquez who is one of my ex-graduate students, he is now a scientist in his own right, came up with an EEG technology to actually determine different reaching and grasping tasks or hand movements and be able to detect it with a high fidelity. So what we did very recently, the paper is actually submitted, we got one of the patients, ran them through this whole thing and he got no improvement whatsoever. His problem is that he was cognitively affected by the injury. So then we brought him to César, he put EEG electrodes on his scalp, he was able to detect intent to move and then he connected to the electrical stimulator to trigger the stimulator and told him that he has an intention to do this. 40 hours later, clinically meaningful difference, done. So we are going, we are in that direction of moving, moving in that direction, we are doing spinal cord injury patients, we are doing stroke patients but we had only patient number one so far and I recruited a second patient today. So we are slowly going there but it's more complicated, you need to do EEG, you have to train them how to do this, you have to figure out – so you increase the complexity of the system and complexity is always a bad thing when you got to clinics. In the clinic, there is a single red button ‘Go’, if its two buttons that’s a problem.

Professor Farid Najm: Ok well I think we’ll stop here. We still have lots of time for networking and discussion. And Milos will be here; we can ask him some more questions but please enjoy the drinks and the food that’s still going to come. And thank you again for coming and I look forward to talking to you the rest of this evening, bye.

[Audience Applause]