

Welcome to the Ernst Strüngmann Forum podcasts—a series of discussions designed to explore how people collaborate under real-life settings. Joining us in the series are high-profile experts from diverse areas in society, whose experiences will lend insight to what collaboration is, what it requires, and why it might break down. This series is produced in collaboration with the Convergent Science Network.

P. Verschure This is Paul Verschure and today I am speaking with Sten Grillner from the Karolinska Institute in Stockholm. Before we dive into the issue of collaboration, could you give us a summary of the trajectory that brought you to where you are today in science and other activities?

S. Grillner My initial interest was in researching the intrinsic function of networks that coordinate locomotion, mostly in the spine; how they entrain the neuronal and synaptic properties of a network. Simulation was a very important aspect of this research. For more than 30 years, this involved a bottom-up approach, together with detailed analysis. And since work with mammals was very difficult and complex—you simply could not get the necessary information—I quickly changed over to the simplest vertebrate group available: the lamprey. There are several advantages of working with the lamprey, e.g., you can easily prepare the spinal cord *in vitro* and induce activity in the networks. This took some time, of course, but then we proceeded to look in the brain for the mechanism that underpins its spatial orientation, in particular, the tectum. Once we felt that we had analyzed the different networks that coordinate movement sufficiently, we needed to understand the forebrain mechanisms that determine when a given pattern of behavior or network is called into action. We analyzed the basal ganglia as one central part. We had thought, wrongly, that we would find a very simplified circuit, because the lamprey's basal ganglia diverged 60 million years ago from mammals. In actuality, both had similar properties: the same type of neurons, the same type of connectivity, the same type of transmission, the same type of organization. It turned out that basal ganglia emerged very early in evolution, some 500 million years ago, and the basic circuit was already there. Modules then developed to help control different patterns of behavior. Evolution retained the structure but multiplied the number of modules to control different patterns of behavior. Essentially, the development of complex meta-behavior from lamprey to humans rapidly multiplied the unit's control more and more.

P. Verschure All your work, Sten, has taken place while working at the Karolinska Institute.

S. Grillner Yes. I started in Gothenburg in 1975.

P. Verschure And we met in the 1990s in the context of the Economic Cooperation Development's Global Science Forum, discussing international collaboration and cooperation. As a faculty member at Karolinska, you have also been involved in the decision-making committees for the Nobel Prize recipients.

S. Grillner Yes. I started in 1986 and was a member of the Nobel Committee for about 14 years. I was also a member of the Nobel Assembly, which is a larger entity comprised of 50 professors from the Karolinska Institute. I had the privilege of being part of the Nobel Committee, which is smaller.

P. Verschure Is the work of that committee a form of collaboration?

S. Grillner Yes, indeed.

P. Verschure What makes it collaborative?

S. Grillner The Nobel Prize started in 1901. At the time, the Academy of Science and the Karolinska Institute were not particularly interested in the award. The king also thought it was a very bad idea to have an international prize. It took several years for the Academy of Science and the Karolinska Institute to reach agreement on what would be recognized, but when they did, they created a very interesting structure that is still in use today. It was very insightful,

e.g., to invite universities and academies around the world to nominate candidates. Then, at the end of the nomination period, the committee meets to review the various nominations. Some nominees may have been previously nominated and thus known to the committee. For others who are nominated for the first time, the review process is more extensive: experts in the field who are on the committee prepare short, written accounts (2-3 pp) to help the committee evaluate the nominee's contribution. Those found to be particularly interesting undergo further analysis. Once this barrier is crossed, several people are asked to submit an in-depth analysis (e.g., status of the field, unique contribution of the nominee), which takes several weeks to prepare. A crucial criterion for the Nobel Prize is that of discovery. It is not an award for lifetime achievement. It honors a distinct discovery. Sometimes, after several years, different specialists may come to light, and everybody agrees that this work seems to have the appropriate scientific value. If so, it becomes a possible candidate. Again, this selection process was conceived over a century ago. No other prize has the structure of a written account and a history. This means that when the committee considers a specific area, it can go back to review what was discussed ten years ago. Within the committee, deliberations are usually very collegial. Of course, different people have different interests and inclinations, but in general, people are very enthused about being able to select a discovery that represents a very good prize.

- P. Verschure What you're describing is a procedure, and this procedure sets up two forms of collaboration: one that plays out in real time, and another which spans time. Do you see different aspects in these forms of collaboration?
- S. Grillner I think what has led to the survival of the Nobel Prize, with comparatively few mistakes, is the historical record that can be accessed. It's not simply a meeting that you attend. You can review have different comments or positions. Gradually, over time, you can glean an understanding of what is a good or perhaps not so good contribution. Very important to the selection process of a prize is that you have the right combination of people on the panel.
- P. Verschure This means that panel members also feel a weight on their shoulders to make the proper decision. How would you define that sense of responsibility? Is it a responsibility to the prize as an abstract notion or to scientific standards? What is the common objective that exerts this moral pressure?
- S. Grillner I think it is the respect for science and the recognition that you should be able to select the very best in science. That is highlighted to the public and the recipient. The value of the scientific idea is the determinant.
- P. Verschure If there was not much appreciation for the idea of the award at the onset, those who proposed putting this framework in place had to convince a critical environment. Why were people so worried about doing it properly? Did they want to avoid serious criticism from the outside world?
- S. Grillner I'm not certain. This was the first major scientific prize, and it was a new conception of a prize. It was not to be awarded to the best Swedish or Scandinavian scientist. It was conceived as an international award, which a very was a foreign idea at the time. Gradually, it has taken on an important aspect; namely, to promote the best of science and often (not always, of course) discoveries in basic science, which highlights that fact that very basic discoveries often lead to new insights.
- P. Verschure Although this process has worked most of the time, it is also important to look at when it failed, as in the dramatic example from 2017 involving the literature prize. Perhaps the procedure that we just discussed, the shaping of the process through a sense of responsibility, was not enough. Was there a "bug" in the system that got exploited and, if so, what was it?

- S. Grillner There was a very severe problem involving the interactions of the committee within the Swedish Academy, as well as a lot of personnel problems to which I have no real insight. But the selection process itself was not severely criticized.
- P. Verschure One year was skipped for the Nobel Prize.
- S. Grillner It was skipped because the Academy got into a civil war and a lot of people left. The secretary left. The committee almost collapsed but was eventually refurbished through new membership and is now probably on track again. Literature, of course, is very difficult. It's so much simpler with science.
- P. Verschure Why the failure? This might tell us something about how collaboration works.
- S. Grillner Essentially the Swedish Academy failed because of interaction. They had to cancel the literature prize for one year, which was really terrible.
- P. Verschure Is there any way to change how the protocol is defined to converge on the decision, so that such catastrophic failures could be avoided in the future?
- S. Grillner I don't know. The Swedish Academy is a special case. The committee that meets to award prizes in science, physics and chemistry, and medicine have experienced very few problems. This could be because the members for these three different prizes rotate, whereas members of the Swedish Academy have a lifetime appointment and cannot resign. The Academy consists of only 18 people, and a couple of the members never attended, and so forth. The Academy had difficulties in obtaining an opinion on more than one occasion. It was actually quite impressive that work proceeded so well for so many years.
- P. Verschure You have also been involved in other international scientific initiatives, almost diplomacy, around science. I mentioned the Global Science Forum of the OECD (Organisation for Economic Co-operation and Development), but you also have been involved in the International Brain Research Organization (IBRO) and other organizations. Do you see patterns in international collaboration in the science community? Do you see commonalities with how you look at collaboration within the Nobel Prize election process? Or do you see them as very separate processes?
- S. Grillner The selection process for the Nobel Prize is rather unique. The boards of the Federation of European Neuroscience Societies (FENS) or IBRO, by contrast, are made up of people from different backgrounds, and there is a lot of rotation on the boards. Most of the time, the board works rather nicely together: there are a few clearly defined things to do, and occasionally new things might be implemented. Unfortunate fights can erupt, but more often people work together. In international organizations where people are appointed from very different parts of the world, it's sometimes difficult.
- P. Verschure There could be a potential contradiction between these two processes of collaboration. For the Nobel Prize, the focus is on a specific discovery. That's not something that a huge community will put their name to, at least not in the life sciences. Looking at these international organizations, the focus is different: it's all about drawing people into a large community and shared infrastructure. This is very different to the Nobel Prize, which seeks to identify an individual and their unique discovery. What does that tell us about scientific collaboration? Is it just an accident?
- S. Grillner The importance of the Nobel Prize is not so much on the individuals that are rewarded but on a given discovery, certain developments, and their potential benefits for humankind. At the Nobel Prize Museum in Stockholm, different prizes in the life sciences illustrate how science has evolved over time and the areas of primary importance. Sometimes these areas become old very fast, while others retain their importance to society. I think the importance is not the individual, but rather on an important part of science.
- P. Verschure Nonetheless, just as you emphasize the habit system in the dorsolateral striatum, value and incentives do shape behavior. A Nobel Prize, and other such prizes, do profile an individual

researcher. In parallel, we spend a lot of energy building large communities and infrastructure. Are we merely pursuing a dream about how science could be on an industrial scale, or is it just a small group of people, an individual, who pushes a certain issue to the limit for years?

- S. Grillner Take the example of the Human Genome Project, which was very important but not the major discovery. One didn't understand anything from it, but it served as a springboard and has benefited many researchers. You can apply the same sort of reasoning to the infrastructure for neuroscience. The Allen Brain Atlas is similar as is the development of simulation tools, neuroinformatics, etc. There are two types of development. It is very important to have platforms from which an individual researcher can choose what is interesting and see relationships that would have not been possible to reveal without the platform.
- P. Verschure The Human Genome Project is a good example because the result was not due to a large community working together, but rather an individual having the insight that doing it with automated screening would speed up the whole process tremendously.
- S. Grillner Absolutely. It is an infrastructure development that made it possible to ask questions you couldn't ask before.
- P. Verschure Isn't there a risk of putting the cart before the horse? Someone might say that we need a specific infrastructure to get the Nobel Prize.
- S. Grillner I'm not talking about Nobel Prizes in this context.
- P. Verschure But do you see what I'm saying? Maybe the infrastructure that an individual researcher requires to permit breakthroughs in the life sciences is at a much smaller scale.
- S. Grillner The Human Genome Project and all the other genomes has allowed the small guys to pose a lot of interesting questions, which they would nor have been able to do without it.
- P. Verschure Fair enough. So, it's like an enabler.
- S. Grillner It is an enabler. To develop infrastructure is very important, whether it's science or not, and if that is predictive, you benefit all the different researchers who like to ask questions.
- P. Verschure The infrastructure becomes a backbone for collaboration, even if the individual users don't directly collaborate.
- S. Grillner Yes.
- P. Verschure Is that the reality of science as you see it?
- S. Grillner Essentially, if you suddenly pose a question that you think is very interesting, and then realize that to pursue it, you need to look at things that people (who you may not know) have doubts about, then it's conducive to create collaboration. Such collaboration is motivated by the project. In science, it's always very important to have a specific question or set of questions that you can interpret.
- P. Verschure For individual scientists, in particular young scientists who are growing into their careers, do you see science as a collaborative process or a competitive process predicated on the shared infrastructure?
- S. Grillner For training people, I think it's very important to have the freedom to make mistakes as well as make discoveries within the framework for which they are funded. Sometimes you hear about labs that put two post-docs on the same project and make them compete. That's not exactly what I prefer.
- P. Verschure But does it work? After World War II, there was a famous report by Vannevar Bush: *Science, The Endless Frontier*. In it, a decisive argument was made that science won the war. These large-scale collaborative projects, which gave us the super fortress and the atomic bomb, helped guarantee prosperity for our society. Industrial-scale science, grounded in physics and

engineering, has almost become a standard. But should we strive toward such a model in the life sciences, particularly in neuroscience? Do we want large-scale, industrial-scale collaboration (as in the discovery of the Higgs boson), with teams of a 1000+ physicists working together to analyze the data? Is that the future for this domain? Or do we want individuals and small teams that share tools, because that is where the breakthroughs are made that this field needs?

S. Grillner Large-scale efforts are clearly useful, as in the Human Genome Project. But novel, unique contributions are very often small scale. It's individual brains, or a couple of individual brains that interact. They need, of course, infrastructure, they need the money, they need all this. So, the answer is not either-or.

P. Verschure If we take neuroscience as our example, do you believe that humans will be able to fully realize the potential of collaboration? Or will they always just come close and then stumble at the last moment? Like in the case of the Nobel Prize for literature. Do you see a real possibility to realize this?

S. Grillner It's only statistics; sometimes it's successful.

P. Verschure I want your prediction, not statistics.

S. Grillner Essentially, collaborations work well in a certain proportion of the cases. In other cases, due to personal issues, it may never work. Irritate yourself immensely on some little detail, and it's gone.

P. Verschure If you could change one thing in the average neuroscientist, what would it be so that they more effectively collaborate to target the understanding of the human brain.

S. Grillner Not to jump on the bandwagon each time.

P. Verschure But jumping on the bandwagon is also a form of collaboration.

S. Grillner Yes, a rather expensive type.

P. Verschure But it might be a way to get resources, because it represents the interests of the field.

S. Grillner It may be a way to get resources, but if the aim is to reveal and understand new important aspects, sometimes you have to look away.

P. Verschure That's a good point, especially coming from you, having worked on a vertebrate animal model that was not necessarily everyone's center of attention (the lamprey) and which, in the end, led to a lot of breakthroughs in understanding motor control and behavior. Looking back on our experience in the Global Science Forum, do you think it is wise to speak of it in this context? Maybe what is needed is also a variability of different approaches without trying to coordinate too much, because that creates the risks of building bandwagons.

S. Grillner The strength of the Global Science Forum was that representatives of different governments discussed science and agreed on certain types of collaborations. If you remember, setting up the International Neuroinformatics Coordinating Facility (INCF), which we were both part of the process, was a very laborious process with lots of disagreement. Ultimately, a written proposal was produced. Then the Global Science Forum played a role: after several revisions, it accepted the proposal. Thereafter, the various ministers, researchers, and research institutes in the different OECD countries all recommended to their governments that it was the way to go.

P. Verschure Which didn't happen the first time around. That was interesting. This only happened once the request became very concrete in terms of a building and infrastructure, as opposed to something more abstract, which was collaborative. A collaborative network was considered too abstract to gain political traction. It had to be concrete.

S. Grillner It was a business plan.

*Text Summary: Interview with Sten Grillner (June 18, 2021)*

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- P. Verschure Yes. But looking back on that process, which took over ten years to accomplish, could things have been done more efficiently?
- S. Grillner Absolutely.
- P. Verschure What was the biggest hindrance?
- S. Grillner Most certainly, different stakeholders had very different interests, and some of them had difficulty listening and remembering.
- P. Verschure That brings us back to the Nobel Prize procedure of remembering what was discussed. Sten Grillner, thank you very much for this conversation.
- S. Grillner Thank you.