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Commemoration

# *Anno Domini* two, zero, zero, three: still orbiting around Uppsala . . .

*''In the beginning God . . . ''*
*The Genesis 1,1*

This is the verse of the Bible that a number of philatelists will remember vividly, as it was printed in a very unique stamp, which appeared in 1968. In the foreground one could see a greyish, rough surface, which might have been mistaken for one of the deserts occupying so much land on spaceship earth. On top of it not a blue sky, but as black as a ''black hole''. Well above the horizon, a blue planet. But it was not the ''blue moon'', our most celebrated satellite sung in innumerable songs. It was mother earth, spied for the first time by a handful of courageous astronauts (Borman, Lovell Jr. and Anders), orbiting around it. No wonder the sky appeared pitch black! So, ''Space-Ship Earth'' was seen for the first time from the surface (well, very close to it, they were seven months away from the landing!) of our silvery satellite, a desolate desert deprived of life. That was mission Apollo 8. Had the astronauts being trained too in separation science, they would have learned that, much to their dismay, one year before they went orbiting around the moon, one obscure Ph.D. from Sweden, a chap called Stellan Hjertén (*nomen omen*, his first name was surely coming from parents very fond of astronomy!) had been sending proteins, nucleic acids, all kinds of analytes, orbiting around in a quartz tube, desperately scuttling towards the opposite electrode, and trying to avoid a disastrous free fall at the bottom of said tube, on their ''mission impossible''. Yes, this is because the tube was not filled with the anti-gravitons, the famous belts invented in the Buck Rogers strips for keeping humans afloat. In the electrophoretic counterpart, such antigravity devices would be any nano-capillary system, such as a polyacrylamide, starch, or agarose gel, acting as a parachute for preventing sedimentation to occur. Stellan had decided he would send his macromolecules running in a free liquid system, thus defying all gravity laws, which up to that time demanded that any object denser than the surrounding liquid would simply have to sink to the bottom. As Stellan, before joining Maestro Tiselius, had been trained as an astronomer, his was a Copernican revolution in separation science: how to defy gravity laws and get away with it!

Those were the electrophoretic days, my friends, under the iron fist of Dom Tiselius! There was no escape from it. His first pupil, Harry Svensson, had two Nobel laureates (almost, the second one came in 1948!) communicating his thesis on 28 November 1945 (just at the end of World War II), The Svedberg (not just any ordinary Svedberg, but **THE Svedberg**, that was the way they had to address him!) and Arne Tiselius, although, curiously, the inaugural dissertation took place in the lecture room of the Chemical Institute, on 9th March 1946, at 10 am (by due permission of the Philosophical Faculty of the University of Uppsala). His thesis, just guess, was a theoretical and experimental study on moving boundary electrophoresis [1]. From then on, it was electrophoresis for breakfast, lunch and dinner, although with a heavy accent, now, on zonal methods, i.e. in anticonvective support media. In 1955, Inger Brattsten discussed a thesis on preparative, continuous-flow electrophoresis by adopting, of all possible supports, powdered glass [2]. Even Jerker Porath, when presenting his thesis, in 1957, as monogamous

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as he was for the rest of his scientific career in his marriage with chromatography, had to work on zone electrophoresis in columns filled with ethanolized cellulose powder [3]. So, when Stellan entered the stage, what else could he do but electrophoresis? With a proviso, though. His predecessor had been working on a mammoth scale, building huge instruments for separating gram amounts of proteins. Stellan, as skinny as he was, wanted to work with skinny instruments as well. He desired to be the Rudolph Nureyev of separation science, able to dance on his tips, so he needed a miniaturized instrument. It was a constant fight with Arne, who required him to follow the trodden path of his previous pupils. But stubborn Stellan had another vision in mind: he wanted to beat his Maestro in his own field, separating macromolecules in a free liquid phase. Arne had achieved that only by moving boundary electrophoresis (MBE); he could not let his method evolve into a zonal mode, because pure macromolecular zones, surrounded by plain buffer, would sediment in the gravitational field and the Space Shuttle had not been conceived as yet. Thus, his cell was rigorously designed as a U-tube, so that the protein distribution in the ascending and descending limbs of the apparatus would generate a density gradient in harmony with our gravity field. No follower of Tiselius had ever dared to straighten the U-tube, which kept hunting the epigons for decades. Even Alexander Kolin, a physicist who, on the other side of the Atlantic, devised the ingenious method of ''isoelectric line spectra'' (a whiff away for true isoelectric focusing, a matter of continuous quarrels between him and Svensson!), decennia after the MBE instrument, constructed his electrophoretic cell just in the shape, for a change, of a U-tube [4]! Svensson himself (who by that time had taken the pen name of Rilbe) replied to him that his ''isoelectric spectra'' were like ''Banquo's spectrum'', haunting poor scientists for generations to come; so he branded his method ''artificial pH gradients'', while baptizing his own with the Christian name of ''natural pH gradients'' [5]. Svensson-Rilbe was in fact the first one to defy Tiselius by straightening his U-tube; when reading the story of the evolution of that masterpiece of his invention, isoelectric focusing, one would notice that it was born as a preparative technique, run in vertical glass tubes, of 110 or 440 mL capacity [6]. So, how did Svensson-Rilbe get away with it? Well, these tubes were filled with a sucrose density gradient, a zonal support, albeit fully liquid, thus, in principle equivalent to the various gel media in vogue in those days in terms of providing the much wanted anti-gravity effects! But when Maestro Hjertén straightened Arne's U-tube ... well, that was a true revolution, some would call it a ''Copernican revolution'', since he kept rotating his quartz tube on its axis, at about 40 rpm, slow by modern standards, but fast enough to keep his macromolecules floating in this terrestrial space just as stars, planets and satellites are kept up in the celestial space by orbiting around [7]! Also his electrophoretic cell was just as tiny as one could devise in those days: a straight quartz tube 3 mm inner, 7.8 mm outer diameter. One could justly suspect that, with his Ph.D. thesis [7], true capillary zone electrophoresis was just around the corner! A triumph for science, a commercial defeat though! Hjertén-Nureyev could not dance on his tips and launch himself in the air like the true ballerino Rudolph: only the quartz tube was miniaturized, the rest of the machine around it was just as mammoth and hard to operate like the predecessors and it never sold a unit! The company producing it went bankrupt.

You might ask how did Stellan succeed in being so successful in his scientific career? There were a number of elements responsible for his glorious career, which I will try to analyze here. First of all, it is quite clear that he was nourished in an environment calling for heroic efforts in science. If you have a look at the Swedish Nobel spectrogram (or scattergram, even pherogram if you like it) of Fig. 1, you will notice some unique features in it. To start with, since the turning of 1900, there were peaks of laureates spaced at a regular periodicity of ca. 20–22 years, just one generation away from each other. Secondly, you will surely capture the explosion of two big supernovae, one in 1981, the second immediately the year after, in 1982. Moreover, in both cases, those were binary stars (although there seems to be no trace of black holes in between sucking their energies, as astronomers suggest). Thirdly, it will not escape your trained eye that the first three, in succession, were just and only in the field of chemistry. Surely such an environment must have

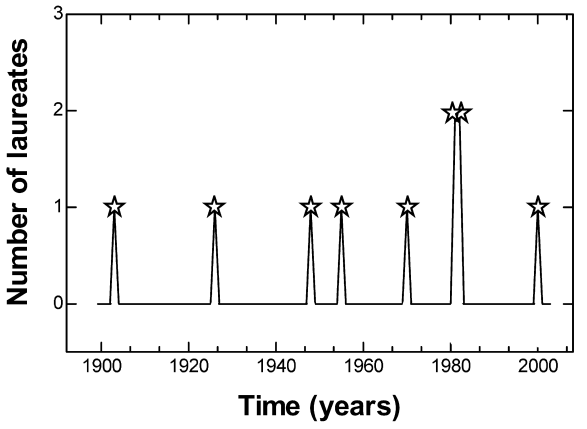


Fig. 1. The Nobel spectrogram in Sweden, years 1900 to 2000. The stars are: 1903, S.A. Arrhenius; 1926: T. Swedberg; 1948: A. Tiselius; 1955: A.H.T. Theorell; 1970: U. von Euler; 1981: K.M. Siegbhan and T.N. Wiesel; 1982: S. Bergstrom and B. Samuelsson; 2000: A. Carlsson (the drawing is by Dr. L. Castelletti).

spurred the souls working at the Uppsala University. Although you might argue that the spectrogram of Fig. 1 shows perhaps a paucity of such Nobel laureates, one should not be deceived by these data; they have to be related to the total population of this country, vast indeed, but scarcely inhabited. When normalizing these data, one can truly appreciate the unique contribution of Sweden to science. Stellan must have inhaled daily such a contagious atmosphere!

The other reason for Stellan's success could be the fact that he was the only true Swede working in those days in Uppsala. Most of the other fellow scientists there must have been half-bred, perhaps half Italian, half Swedish. It was customary that, in the summer days, those souls would vacate the building at around 3 p.m., in order to fully enjoy the sunshine, so scarce in the winter (had they been true Sicilians they would have abandoned their posts at noon time, or not even shown up for work). But not Stellan; he loved the summer because there was sunlight up to eleven o'clock at night, so he could stay much longer to work; like a good captain at the helm, he never abandoned ship. His drive for work was legendary: my friend Toshio Takagi (now professor emeritus at Osaka University) narrated to me this unique episode of his life, highly instructive. Stellan one day fell while working at the Institute and broke a leg. Fellow scientists were relieved, since they thought that finally this relentless chap would stay home and relax a bit. No way! The day after he appeared in the long corridor leading to his laboratory clutching a pair of crutches. Since he refused to ask anybody for help, and was not a centipede, he had solved the problem of his inseparable briefcase in a most ingenious way: it was dangling from his belt fastened by a rope! There are rumours that he risked lynching by his fellow co-workers.

Another good reason for his highly successful career in science could be the fact that he reasoned like a Roman emperor, like a Nero or a Caligola. Whereas most of us have enough difficulties just riding a single horse, Stellan choose the imperial way, he drove a biga, i.e. the chariot of Roman emperors pulled by two horses. In fact most of his work was split about equally between chromatography and electrophoresis, making fundamental contributions in both fields. Sometimes, in his heroic days, he even rode a quadriga, i.e. a chariot pulled by four horses, since he was also an outstanding theoretician and equally skilled in mathematics and physics. Common mortals like us have enough difficulties going at the speed of 1 HP (horse power); how can we possibly compete with somebody zooming in front of us at 4 HP?

I am tempted to stop here this modest contribution to my friend Stellan, but I would like to leave with a note of warning. When he first retired about a decade ago (it is a joke, he is still as active as ever) I was one of the authors who contributed a note of well wishes to him in the journal *Electrophoresis*. Now, almost ten years later, I still have to double my efforts. I now have a terrible suspicion: when he will be 100 years old, who will write another note of celebration for him? I know he will be there, and how do I know this? Well, my friends, remember he is a Swedish fellow. He told me that, when he was young, he was very fond of movies and he rarely missed the masterpieces of his epoch (I suspect he still does like cinema a lot, although maybe today the true epochal movies are rarer). His favoured movie director was the most famous Ingmar Bergman and I suspect he must have seen his movie ''Det sjunde inseglet'' (The seventh seal) innumerable times. As you will recall, the crusader embodied by Max von

Sydow engages a final battle (on a chess board) with a mysterious personage hidden under the hood of an ample burnus. He wins the game and chases away the obscure opponent, which turns out to be Death who had visited him to take his soul! I bet you that Stellan has learned the trick, which is the only one he will not reveal to this audience. This is why I know for sure that he will be here when he will be 100 year old, although I doubt I will have this privilege (even though I suspect I will from now on go less and less to scientific congresses and more and more to visit Ingmar Bergman; one never knows)! Thus, if anyone in the audience is ready for the next celebration, please move one step forward; I will be glad to pass along the baton.

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*(A.D. 2003, 18 January, 6.00 p.m., sharp)*

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