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Perspective from a 2nd generation, woman neuroscientist

16:28:49:05
Q: So when did you first join the Society for Neuroscience?

A: I think it was when I came from Harvard Medical School to the Albert Einstein College of Medicine where I was doing a second post-doc in the lab of Dr. Stanley M. Crain. Stan has been a pioneer neurophysiologist on the development of network interactions, emphasizing opioid sensitivity in sensory ganglia attached to spinal cord explants (see his book Neurophysiologic Studies in Tissue Culture, 1976). And Stan told me "why don't you join the Society?" So we're talking now, 1983.

Q: Why did he think it was important for you to join?

16:29:36:21
A: Well, because we had new interesting data to present at the SFN meeting and he said "that's the minimum you should do, join the Society". Note that Stan was also one of the founding members of the Society.

Q: What was the first meeting that you attended?

A: I actually attended the first meeting of the Society in Washington D.C. in 1971. I did because I came from France as a foreign graduate student at the NIH. In those days there was a program at the NIH for foreign students only. And most of the people who were going to the NIH at the time were at least at the post-doc level. There were a lot of yellow berets (physicians who joined the Public Health Service in lieu of being drafted into the army) at the time such as Michael Shelanski, (the present Chair of the Dept. of Pathology and Cell Biology at Columbia where I now work) and Gerald Fischbach (among other honors, SfN President) with whom I have interacted over the years. We're talking early 70's and my official position was "student scientist". I had a French Master's degree in Physiology from the University of Aix-Marseille and I guess that was good enough to get me to the NIH.

[16:30:42:26] But for research work only, you had to be a foreigner to be accepted to this graduate research program at the NIH. They were not

accepting American graduate students then as they do now with John Hopkins or Georgetown for instance. I did my research work in the laboratory of Dr. Marshall Nirenberg, who was the first Nobel Prize awardee at the NIH (awarded in 1968, for deciphering the genetic code with Drs. Khorana and Holley) and as you can imagine, it was the best lab to be accepted in! Marshall said to me "I want to go from the genes to neurobiology, I think that's the exciting field now, and onto the synaptic code!". And so there I was, to be trained in neurobiology.

[16:31:29:14] There was at the University of Aix-Marseille, a neurophysiologist, Professor Dr. Paul Dell, who himself had been trained in American labs in the early fifties, and who was in contact with Dr. Claude Klee at the NIH. Claude Klee was married to Werner Klee (also at the NIH) and she was a medical doctor from the University of Montpellier and had been a colleague of Dr. Dell. And Dr. Dell said to me "I'll put you in contact with Claude Klee who knows Marshall Nirenberg and then she will put you in contact with Marshall Nirenberg". I wrote a letter to Marshall (as he wished us to refer to him) as a newly trained electrophysiologist, seeking to apply this technique to *in vitro* models of neuronal development. I had learned extracellular recording techniques studying *in vivo* activity in cat sympathetic stellate ganglia, as a topic of research in the lab of Dr. Jean Gonella for my master's degree (University of Aix-Marseille) (J. de Physiol.,1971). Now with Marshall I wanted to learn intracellular recording technique in isolated neurons in culture. When I received a response from Dr. Nirenberg he said "OK, why don't you come, join the lab" and he had me come over to Bethesda. I was overjoyed and in preparation, read the early work of Drs. Phil Nelson (i.e."Excitable Cells in Tissue Culture", 1981) and John Peacock who in collaboration with Marshall were recording from electrically active neuroblastoma cells. So I didn't come as a post-doc, I came as a student scientist from the end of 1969 to the end of 1973! Useless to tell you that the environment in Marshall's lab was awesome; some of the researchers in the lab at that time, to name a few, were Al Gilman (Nobel laureate), Michael Shelanski, John Minna, Bernd Hamprecht, Bill Shain, Alan Peterkovski, Lloyd Greene, Bill Catterall, Zvi Vogel, Matt Daniels, Mary Stankowicz and Xandra Breakefield (who received a life time achievement award, at the SfN in 2013), also women technicians such as Kay Bradley. Note that recent symposia to honor Marshall and his work in neuroscience took place, first at the NIH in 2010 and then at the University of Kanazawa, Japan in 2011. The latter one was organized by Dr. H. Higashida (also a trainee in Nirenberg's lab) and I presented my then current work (regulation of enteric gliogenesis by the BMPs) with other ex-trainees of Marshall from the early 7O's. I also wrote an article (with Drs. M. Gershon and Lloyd Greene) in a special issue devoted to that symposium.

And the first meeting of the Society was in Washington D.C. Just like Dr. Larry Swanson (SfN President) had mentioned at last year's SfN meeting, that he was also attending as a 3rd year graduate student, here I was then, except that I was younger. … And learning how to grow and maintain neuroblastoma cell lines and record from them...
[16:32:31:06] I do remember, at that 1st meeting we all were contained in one auditorium, which felt like maybe 500 people attending, I think we may have been 1000 or so maximum?

Q: Did you present?

A: No, no. No I think I presented the first time when I was in Dr. Richard Zigmond's lab at Harvard in the Fall of 1977, and then subsequently when I was in Dr. Stanley Crain's lab. Stan, by the way, mentored Dr. Eric Kandel (SfN president and Nobel laureate) at Columbia (see Eric's book, "In Search of Memory", Norton and Company 2006). That was before Dr. Crain moved to Einstein and Stan told me that he "taught him [Kandel] how to make intracellular electrodes". [Laughs] Can you imagine? Ok. So yeah, it was with Dr. Crain that I became a member of the Society. We had several presentations actually. At least we went to the SfN meeting maybe 3 times where I presented when I was in his lab. But before that, let me go back.
[16:33:24:23] So at the NIH I met Dr. Gerald Fischbach (i.e. Ann. Rev. Neurosci.1997), who was subsequently one of the presidents of the Society, right? And he was at the NIH, one of the yellow berets then recording the distribution of cholinergic sensitivity on muscle fibers in culture before and after being innervated, with Dr. Steven A. Cohen, his trainee. And I was doing intracellular electrophysiology on neuroblastoma cell lines with Dr. Nirenberg, because he wanted to screen the degree of cholinergic responsivity in various neuroblastoma cell lines and somatic neuroblastoma x L cell hybrids under various differentiating treatments. Something like, dibutyryl cyclic AMP, an analog of cyclic AMP, which would promote differentiation. So we were comparing non-differentiated cell line versus the differentiated cell lines. Just their degrees of electrical excitability and their acetylcholine sensitivity. With Lloyd Greene we co-authored in 1974 one of the earliest articles demonstrating an enhancement in excitability of a neuroblastoma cell line after treatment with dbcAMP. Nowadays we know that the cAMP response element-binding protein (CREB) signaling pathway gets activated.
[16:34:19:03] So I met Gerry Fischbach at the NIH and Gerry said "OK, if you want to learn tissue culture…. [That was when he was offered an associate professorship at the time in the department of Pharmacology at Harvard] …come to join my lab and you'll learn how to grow primary neurons in culture. Because at the time I was growing cell lines *in vitro* in Nirenberg's lab. But you know, creating cell lines and carrying them on,

from one generation, to another is not at all like doing primary tissue culture of neurons that become post mitotic. So I joined Gerry's lab in Boston (1973-1975). And I remember I had, at the same time I was working with Gerry, to write the entire research work of my thesis in French, even though I had a number of publications in English (5 all together), which had been accepted from the Nirenberg time. I had to translate everything in French to defend the thesis, because I have a French national doctorate in Natural Sciences (D.Sc. 1975) from the University of Strasbourg. I don't have an American PhD, because of this combination of foreign student scientist program at the NIH and the French university system.

[16:35:28:03] So Gerry at some point said, "Ok have you finished translating this thesis into French because you should by now work longer on your current project in the lab!". Anyway, so I had actually a wonderful paper with Gerry (Dev Biol, 1980). We were one of the first people, I think, to show that depolarizing treatment with high potassium on dissociated chick dorsal root ganglion (DRG) neurons not only promotes morphological differentiation and neuritic outgrowth but also significantly changed the profile of their action potentials. You know the immature primitive action potentials have a delayed repolarization phase while the mature AP displays a much shorter repolarization. Drs. P.I. Baccaglini and N. C. Spitzer (J.Physiol. 1977) showed this developmental shortening in the AP duration in the system they were working with, the amphibian Rohan Beard sensory neurons. They showed that the calcium responses dominate early on and then as the AP matures, it displays a shorter duration. Nowadays we know that the shortening of the AP shoulder is due to increase in calcium-activated potassium current through voltage-gated channels. So we showed this effect with depolarizing treatment in the DRG neurons. And at the time, at the suggestion of my now spouse, Lloyd Greene, I said to Gerry, let's also look at NGF treatment to see what happens concomitantly with the high K^+ treatment. Lloyd provided us with NGF, while we provided him with chick embryo extract that I was in charge to prepare!

[16:36:25:09] So now you have two signaling pathways activated. This high potassium signaling, plus the NGF signaling and sure enough, we found enhanced survival/differentiation of the DRG neurons when they were co-treated with high K+ and NGF, compared to only high K+ treatment. The enhancement was due to activation of at least 2 distinct signaling pathways, which have now been defined. Depolarization signaling, which can induce calcium calmodulin kinase (CaMkinase II), PLD or MEKII (i.e. Bok et al., Mol Cell Neurosci 2007; Banno et al. J.Neurochem 2008), and NGF (or other neurotrophins) signaling which induces PI-3K, Akt and MAPK pathways (reviewed by Kaplan & Miller, Current Opinion in Neurobiology, 2000) or depolarization itself inducing neurotrophin signaling (i.e. BDNF release) via voltage gated calcium

channels, (i.e. Ghosh, Carnahan and Greenberg, Science, 1994). So that was this paper I had with Gerry.

Post-doc position with Richard Zigmond; this was omitted at the time of the video interview and should be inserted here:

When I returned from Strasbourg to Boston, after my thesis defense, (end of 1975), Richard Zigmond joined the Dept. of Pharmacology at Harvard and Gerry recommended that I spend a post-doc with Richard because his project involved electrophysiological approaches. In fact, I was Richard's first post-doc. He was interested in regulation of tyrosine hydroxylase (TH), the rate-limiting enzyme in catecholaminergic synthesis, using the sympathetic superior cervical ganglion (SCG) model. Since I was already familiar with sympathetic ganglia, this was an appropriate match for both of us. In contrast to the relatively large group of trainees in Gerry's lab, including at the time many subsequent notable neuroscientists (i.e. Steve A. Cohen, Lee Rubin, Darwin Berg, Eric Frank, David Farb, Dennis Choi and the only other woman, Ruth Siegel) it was just Richard, a technician and I. There is a paper I am particularly proud of that we published in the J. of Physiology (London) (1980) that demonstrates that electrical depolarization of the SCG neuron cell bodies alone, via antidromic stimulation of the post-ganglionic nerve, is not sufficient to induce TH activity. I found that such induction instead requires synaptic (orthodromic) stimulation, via the pre-ganglionic nerve in order to increase the specific activity of TH within the long term (3 days later) and that this can be blocked by a nicotinic antagonist. Nowadays, we understand the signal transduction pathways triggered by the binding of Ach to nicotinic receptors, which allows intracellular Ca^{++} entry, downstream protein kinase C or CamK-IV activation, and then activation of the transcriptional regulator CREB to result in such long term increased transcription of the TH gene.

We expanded this study with additional publications examining the corresponding increase of TH protein as well as the long-term increase of dopamine beta hydroxylase in the synaptically stimulated SCGs.

In relation to the history of SfN, note that the second time I presented at the SfN was in 1977 with Richard and then in the Fall of 1978 carrying in a Gerry Pack my 3 and 1/2 month old baby boy. There was no onsite childcare available at SfN meetings then!

And then I joined Dr. Stanley Crain in the Dept. of Neuroscience at Einstein, because with Lloyd, we moved from Boston to settle in New York. I spent 11 years at Einstein until 1991, becoming an Assistant Professor. There I became very interested in development of excitability in an intact

developing nervous system because Stan had this wonderful explant of fetal mouse DRG attached to a slice of spinal cord and had always been interested in opiate receptors and opiate sensitivities.
[16:37:24:15] A woman investigator, who collaborated with Stan in the Dept., was Edith Peterson and she was a champion of the establishment of explant cultures; Edith herself had been trained by the pioneer Margaret Murray at Columbia. I had a lot of respect for Edith and I learned from her the technique of culturing explants "in a hanging drop", you know. And we showed with Stan that when the DRGs were attached to the spinal cord, the sensory neurons became more sensitive to opiates, than if they were grown in isolation from the spinal cord (Chalazonitis, & Crain, Neuroscience, 1986). And we looked at these opiate responses at the time. But also we looked at long-term effects of NGF. I had an NIH grant on this. In those days it was fairly easy to have a grant, right? [Laughs] And we looked at long-term effects of NGF on the established DRG attached to spinal cord explants. That would be like looking at the influence not only of depolarization, but also the influence of maturation of the system that still responds to NGF even when the connections with spinal cord neurons have been established. We analyzed the DRG excitability, and sure enough with the long term NGF effect, we found reduction of the action potential duration. This was because the embryonic DRGs, even though they were attached to the cord, still had a very strong calcium current and continued to respond to the NGF differentiating treatment which would promote the narrowing of the AP.
[16:38:39:16] This was a little bit like what we had demonstrated with the dissociated chick DRG neurons and this maturation was still ongoing in the more complex system of explants. A publication in PNAS communicated by Dr. D. Purpura (at the time the chair of the Dept.) resulted from this work (Chalazonitis, Peterson & Crain 1987). And then I became, very interested in the topic of establishment of specificity of synaptic connections and I applied for a grant (which I got) and I will always regret not to have pursued this area of research. I had read seminal papers from McLachlan (1974), Nja and Purves (1977), and Jeff Lichtman, Dale Purves and J. Yip (1979-1980) who demonstrated that selective synaptic connections were being established between certain preganglionic motor neurons originating from selective spinal cord levels and sympathetic neurons in the guinea pig and other mammals. *interruption*. **[16:39:52:25]**

Q: This whole time you were a member of the Society?

16:40:27:10
A: Oh yes. Yes, yes.

Q: So what kinds of things were you doing with the Society for Neuroscience?

A: In those days, the eighties? Nothing except attending the meetings, presenting and sharing data with colleagues in my field of investigation. No, I was sort of describing that it was actually very exciting.

…Getting back to the project of studying specificity of connections between spinal cord neurons and specific sympathetic ganglia I said, "let's look at whether the pre-ganglionic motor neurons explanted from different levels of the spinal cord specifically establish connections with any other sympathetic ganglia along the sympathetic paravertebral chain or only with the sympathetic ganglion positioned at the corresponding level. I got an NIH grant and I collaborated with John Kessler, assaying the level of ChAT as a measure of the strength of synaptic interaction, in sympathetic ganglia co-cultured with defined spinal cord regions (dorsal, medio-ventral, ventral) or with defined neuraxis levels (cervical, thoracic, lumbar). The collaboration with Stan Crain was of course recording via electrophysiological and pharmacological means the degree of synaptic responses in the innervated sympathetic ganglia)… and sure enough, if you were to co-culture the medio-ventral region of the spinal cord at only the mid thoracic level, the establishment of cholinergic innervation with the superior cervical ganglion was the highest (compared with the dorsal or ventral region) and it was the highest when comparing co-cultures of spinal cord explant from the thoracic level with co-cultures of cord explants from inappropriate cervical or lumbar levels. Conversely, using the same assays we compared the degree of cholinergic innervation by spinal cord explants of either upper cervical, upper thoracic, lower thoracic or lumbar levels in co-culture with the SCG or two lumbar sympathetic ganglion (to achieve a ganglion mass equivalent to one SCG), and again the maximum synaptic interaction occurred at the upper thoracic level with the SCG and at the lower thoracic level with the lumbar ganglia. So the maximum specificity of interaction was happening in the explant co-cultures with the appropriate level of the cord *in vivo*. So there were positional cues that controlled the spinal cord neuritic outgrowth to establish the specificity of the connections with the matched sympathetic ganglia. These positional cues have been shown to be under control of the homeo-box genes (in Drosophila, *Antp*, G. Gibson and W.Gehring 1988) and then in vertebrates, HoxA-D. So the questions I was asking were way ahead of their time (a little bit like my mother did, in her days) because I didn't have any of the genetic information then and Drosophila biologists were not talking much with electrophysiologists, but that's what I was doing with Stan.

We published 2 papers in Brain Research in 1988 and 1989 on this work, when Brain Research was a journal of "high impact"!
[16:42:12:03] Actually, Tom Jessell (who was also a post-doc with Dr. Fischbach later on) was quite aware of this work and his lab has focused on the specificity of motoneuron identities and their connectivity with specific muscle targets under the control of selective Hox proteins (i.e. William, Tanabe and Jessell, 2003).

Yeah, so what I was doing for the Society? Nothing more than the younger generation now, coming in and attending the meetings and networking of course. The first time I met Stan Crain was actually the third meeting of SfN I attended, after my son's birth, when I carried my baby and Lloyd was also presenting.

So after 11 years at Einstein where I had been privileged to carry out significant developmental studies as a member of Stan's group, in a stimulating and supportive environment, I decided to leave. Several factors contributed to this decision. After we published with Stan an intriguing paper on the opioid excitatory effects on sensory neurons (Crain, Shen, Chalazonitis, Brain Res. 1988) Stan redirected his lab to focus on molecular pharmacology of the excitatory vs inhibitory opioid receptor signaling in mature neurons (e.g. Crain and Shen, Trends in Pharm. Sci, 1998). At the same time I distanced myself from the electrophysiological approach and became much more involved in the field of growth factors and their developmental effect on the neurons of the peripheral nervous system. Furthermore there was a lot of movement within the faculty of the Dept. of Neuroscience and a number of people that I had been collaborating with, besides Stan, left or were considering moving on. Rick Morrison and Jack Kessler for example. Jack and Rick are of my generation and each had trained in prominent labs: Jack with Ira Black (see Cellular and Molecular Biology of Neuronal Development, 1984) analyzing developmental perception of pain in sensory neurons with NGF or capsaicin (i.e. PNAS, 1980,1981) and Rick with Ralph Bradshaw and Jean de Vellis, analyzing neurotrophic effects of mitogens such as bFGF and EGF (i.e. PNAS 1986, Science, 1987) on cultured cortical neurons. So we looked at the effects of TGF-alpha, often produced by tumors, and compared them with the first member of the family of mitogenic growth factors, EGF. We thought that TGFα might also exert neurotrophic effects in cultured DRG neurons since EGF receptor-like immunoreactivity is found on some sensory neurons (Werner et al. 1988). We had one of the first papers showing that TGF-α, not EGF, promotes survival of spinal sensory neurons, but not nodose, trigeminal or sympathetic neurons. The effect was either direct or perhaps indirect via binding to a different type of EGF receptor (SfN abstract 1989; J.Neuroscience 1992). Next with Jack and Rick we analyzed the differentiating effect of two members of the

then emerging TGFbeta family of growth factors (TGFbeta-1 and TGFbeta-2) and it was one of the seminal papers on TGF-β neurotrophic effects. We showed its synergistic effect with NGF on promoting neuronal survival and differentiation (increased SP expression, neuronal clustering, increased neuritic growth and fasciculation) of DRG neurons in culture, with TGF-β1 being more efficacious than TGF-β2 (SfN abstract,1991; Dev Biol 1992). Subsequently many labs have examined neurotrophic effects of TGF-β in the PNS and CNS (dopaminergic neurons) in synergy with other neurotrophic factors (i.e. GDNF) (K. Krieglstein's lab and K Unsicker 's lab (i.e. J. Neurosci, 1998, 2003).

[16:43:18:10], …and then, as I said after I decided to leave Einstein around 1990, I met with Dr. Michael Gershon at Columbia. He was Chair of the Dept of Anatomy & Cell Biology from 1975-2005. Mike, besides his unforgettable teaching style to generations of medical students, first at Cornell and then at Columbia, has been a leader in understanding the development of the enteric nervous system (ENS), the control of GI peristalsis by sensory and motor enteric neurons, and GI disorders that involve the enterics. He has written a comprehensive book, quite popular, about research and discoveries in the ENS, entitled "The Second Brain-the Scientific Basis of Gut Instinct", 1998. – One reason he called it the "Second Brain" was because many of the neuronal phenotypes found in the CNS are expressed in the ENS, in contrast to those of the PNS. For instance serotonergic, gabaergic and dopaminergic neurons are found in the ENS. So Mike (who had worked as a post doc in Edith Bülbring's lab in Oxford, i.e. Bülbring and Gershon, 1967) is the one who discovered that serotonin/5-HT acts as a neurotransmitter in the ENS. He found that it is released from serotonergic neurons of the myenteric plexus (i.e. Gershon, Drakontides, and Ross 1965; recent review, Gershon, 2013) - and not just secreted by the entero endocrine cells (EC) cells of the mucosa of the gut to stimulate nearby intrinsic sensory neurons to induce peristalsis, as had been established early on in Edith Bülbring's lab. And I got turned on by this system, and I said maybe I want to look at the development of the enteric nervous system, which is not sympathetic, which is not sensory/DRGs but which is the other neural crest-derived nervous system, the intrinsic nervous system of the gut. In particular, very little was known in the early 1990s about whether neurotrophins or other neurotrophic factors are expressed in the developing gut and what their function would be in the immature ENS. You know, over the past 22 years with Michael we have really looked at a lot of signals all expressed in the developing ENS. To this end we took advantage of a powerful tool of immunoselection to separate the enteric crest-derived precursor cells from the other muscle, Interstitial cells of Cajal, or mucosal cells within the gut. We used an antibody against the neurotrophin binding receptor p75, (provided by Dr.Moses Chao, another SfN President) (i.e. Johnson, D. et al. 1986) that specifically recognizes the p75-expressing enteric crest-

derived cells. After isolation by this means, the cells are grown in a defined medium which had been used in the laboratory of Dr. N. Le Douarin, with or without the growth factors of interest. We have defined the role of several neurotrophic factors: NT-3 (J.Neurosci 1994, 2001), GDNF (Dev Biol. 1998), and the neuropoietic cytokines (CNTF, LIF) (Dev. Biol 1998) as well as laminin (Dev. Neurobiol. 1997), in the developing ENS. Then more recently, we approached the bone morphogenetic proteins (BMP-2 and BMP-4), which are not only major regulators of bone development but of many organs including the patterning of the primitive gut (i.e., D. Roberts Dev. Dyn. 2000). So we showed that BMP-2 and-4 regulate at fetal stages development of enteric neurons and in particular increase their responsiveness and dependence on other neurotrophic factors such as NT-3 (J.Neurosci, 2004). We also showed that BMP-2 or -4 signaling regulates in the adult, the diversification and maintenance of the ENS and thus exerts preponderant roles in the development of the ENS. **[16:44:19:13]** The BMP project was carried out in collaboration with Dr. John Kessler's lab. He pioneered studies on the multiple roles of BMP2: i.e. in sympathoadrenal cell lineage (Song, Mehler and Kessler, 1998), and in cortical neurons (Mabie, Mehler and Kessler J.Neurosci 1999). Dr. Kessler now in the Dept. of Neurology at Northwestern, where he was the Chair for many years, gave us the BMP over-expressing and noggin-over-expressing mice so we could analyze consequent alterations in the development of enteric neurons, their specific phenotypes, changes in GI motility (J. Comp Neurol 2008) and development of enteric glia (Dev. Biol. 2011). This was a 5-year project funded by the NIDDK. OK, we worked intensely on that project and 4 papers and one review (Dev. Neurobiol 2012) were published between 2004-2012, with corresponding presentations at SfN in 1999, 2003, 2005, 2007.

Recent (with Eric Huang) and ongoing (with Mart Saarma) collaborations omitted at time of the interview:

More recently a fruitful collaboration was established with Eric Huang's lab at UCSF to analyze the effect of a transcriptional cofactor that regulates BMP signaling, the homeodomain interacting protein kinase 2 (HIPK2), in development and maintenance of the ENS. Eric had shown that the TGFbeta-Smad-HIPK2 signaling pathway is required for the survival of midbrain dopaminergic neurons (Zhang et al. Nat Neurosci. 2007). Because at that time Sam Li and I had shown in the lab that neuronal serotonin stimulates development/survival of the enteric dopaminergic neurons (J.Neurosci 2011), I became interested to find out whether HIPK2 may also be implicated in development and survival of the enteric dopaminergic neurons. So I discussed with Eric at the international meeting on neurotrophins (organized in 2006 in my home

town Lyon, France) the project and Eric Huang gave us the mice with the HIPK2 gene deletion. In collaboration with Dr. Tuan Pham in Mike's lab we analyzed in whole mount preparations the enteric plexuses in these mice. Sure enough, neuronal loss occurs in both myenteric and submucosal plexuses and intensifies from the proximal (duodenum) to distal (colon), with in particular, a selective severe loss of enteric dopaminergic neurons. Most interestingly this was accompanied by an exacerbation of BMP signaling in both the myenteric and submucosal neurons. These neurons displayed increased autophagy whose incidence increased from the stomach to the colon, as well as loss of intraganglionic synapses. Wanda Setlik obtained these data at the EM level in the lab (J. Neurosci 2011; with cover issue #39).
Currently we are collaborating with the group of Dr. Mart Saarma (University of Helsinki) who has focused on the structure and function of a new family of neurotrophic factors: the mesencephalic astrocyte derived neurotrophic factor (MANF) and the cerebral dopaminergic neurotrophic factor (CDNF) (i.e. Lindholm and Saarma, 2010). Mart's group has shown that CDNF exerts a potent protective role *in vivo* on midbrain dopamine neurons and thus could be considered as potential therapy for Parkinson's Disease (i.e. Lindholm et al. Nature, 2007). Because patients affected with PD often display gastrointestinal disorders (such as constipation) before the movement disorders (i.e. Edwards et al., Movement Disorders, 1991; Cersosimo et al. J.Neurol 2012;) I discussed with Mart our interest to analyze the role of CDNF in the development of the ENS and in particular the dopaminergic neurons. We have used cultures of the enteric crest-derived cells treated with CDNF and other regulators of enteric differentiation. Currently we are analyzing the effect of CDNF in the maintenance of the enteric dopaminergic neurons using CDNF KO mice that Maria Lindhal in Mart's lab has been sending to us. So far we have presented data on this project at the SfN (2010 and now in 2013).

So, during my entire career I stayed with the peripheral autonomic nervous system and addressed the roles of many of the neurotrophic factors implicated in its development. That's what I did. And, um, for the Society, what have I done? So that's more recent:

From 1994-1997 I was Vice Chair and then Chair of the Neuroscience Chapter (Representative of the SfN) at the New York Academy of Science.
In 1996 I was organizer of the Brain Awareness week in the Greater New York area and I remember hosting the biology teacher with her Senior class from Mamaroneck, NY High School (which my son was attending), and guiding them through some of the Neuroscience labs at the Center for Neurobiology and Behavior at Columbia.

Then between 2007 and 2011 I was nominated to be a member of CWiN, the Committee of Women in Neuroscience with Rita Balice-Gordon the chair at the time, and I reconnected with Ruth Siegel who was also a member of that committee. And then more recently, the committee was chaired by Jill Becker and then with Ann Etgen when it merged with the diversity in Neuroscience committee, to become the Professional Development committee. Concomitantly, I served on the SfN Awards committee and mentored a number of students and post-docs at the SfN meetings

[16:45:16:03] As a member of the CWiN committee, along with a number of my female colleagues, I became very much aware of the situation and difficulties that women have to face. For some reason, even though most of my colleagues had been and are men, I didn't feel, it's very interesting, I didn't feel discrimination at all. But, there was I think a difference early on that I became aware of later on, which was how to be taken really seriously. I mean "politically" seriously, because intellectually, I have always been taken seriously. And you know we had a son and I had to struggle with that. I remember looking at my CV when I was with Dr. Crain, at the time, and for 2 or 3 years, nothing, no publications. That was at the time just after my son Ariel Greene was born. And it was a struggle, it was a struggle, but it is interesting, I didn't feel resentful about it.
[16:46:19:27] It's just in retrospect now, how much more seriously women are taken. You know. When you are at the childbearing age I'm talking about. And now of course there are plenty of very serious women in the field, that you can see around. In this regard, several of my female colleagues, developmental neurobiologists for whom I have felt great respect and who have made me feel included, have been over the years, Nicole Le Douarin, Chaya Kalcheim, co authors of "The Neural Crest" (Cambridge Univ Press, 1999), Dominique Toran-Allerand, Freda Miller, Barbara Hempstead and at Columbia, Taube Rothman. I would like to emphasize how Taube has been an enriching and supportive colleague throughout the research we performed together in Mike Gershon's lab.

But it was this gain by women of being taken seriously as leaders, which I think in retrospect, was not occurring in the early years.

[16:46:51:06]
Q: Did the Society do anything actively to support women?

A: Now?

Q: No, did it then?

A: Not really. Not really. No. I think that this movement is relatively recent. It was during the last 15-20 years. It was a change in awareness I think. Among women I'm talking about. Maybe men also. [Laughs] You see what I'm saying. But I don't have to complain about any of my colleagues, who as I say, have been in majority men. Without exception all my advisors who have been prominent scientists and heads of labs that I have worked with, or colleagues that I have collaborated with, have always respected my ideas and encouraged me to proceed. So, yeah, I think the Society is doing much more now, for example, day care. And that was all through the "committee of Women in Neuroscience" CWiN.
[16:47:52:24]

[16:48:20:14]
Q: Looking back what was neuroscience back then.

A: The most exciting thing you could do! [Laughs] And it is interesting, you don't necessarily predict the actual results, even if you have a plan /a specific experimental approach, it was an ongoing process and it's still the same feeling that I have now. As it is ongoing and the results arise, you're going to ask the next questions and you're going to do the next experiments. Of course you had to write the grant and specific aims, but I think the excitement was generated as the results were coming in. You see what I'm saying? As the results were coming in. I think of course it was in the framework that you had written down in the grant.

[16:49:13:28]
Q: So what was the framework? What were the driving questions of neuroscience then?

A: Well for the developmental neurobiologist that I am it was an understanding of how the particular neuronal system under study develops in response to specific developmental cues. And of course there were trends. You had to be lucky; maybe, the questions you were asking, were they making the trends? Were they part of the trends already? The research enterprise is very trendy, by definition. Research is dynamic and it's trendy. The technology of course changes from one generation to the next and is getting fantastic now (i.e. optogenetics, connectomics, computational neuroscience) and therefore you can have different questions now than you had then. Um, but it was the excitement in the lab and as I say, as you were getting the results, then you knew what the next steps should be.
[16:50:11:06] Afterwards there was always something to do after getting the results. Then in cases when things did not work the way you had predicted, or you had the wrong hypothesis, you had to think of alternate approaches. I don't know, maybe I was lucky. I don't remember negative

things or whether we shouldn't have carried out such and such approach. The one thing I regret is not to have been able to pursue some of the projects that I worked with. Like the questions of establishment of neuronal specific connections. Partly because maybe I was shy. Maybe, I didn't feel comfortable enough to lead a big group. The task would have been so demanding as to interfere with my personal life. I always interacted with a few number of people, who happened to be around. That started actually in Marshall Nirenberg's lab when I met Lloyd, Lloyd Greene. **[16:51:09:21]** Actually, I performed the first *in vitro* recordings on cultured chick sympathetic neurons and I tested their responsivity to acetylcholine. Lloyd carried out the cultures so that we could compare the excitability and cholinergic responsivity of these primary neurons to those of the neuroblastoma lines (Brain Res; 1974). And that early work was cited in Stan's book in 1976.

[missing some time – changing tape. Discussion of mother's scientific career]

My main motivation to participate in the video interview for the History of SfN was actually to pay a tribute to my parents: Angelique Arvanitaki (1901-1983) and Nicolas Chalazonitis (1918-2004). They were pioneer neurophysiologists using axonal and ganglionic preparations in invertebrates to understand the biophysics of neuronal electrical activities and their modulation. Both of my parents came to France as Greek immigrants (my mother via Egypt, where she was born). They came as students and attended the Universities in Lyon; my mother in the late nineteen twenties-early thirties and my father just before WWII. They both obtained French doctoral degrees and spent the rest of their lives in France.
[16:57:02:27]
So here is a measure of my mother's ambition: she goes as an undergraduate to the "Faculté des Sciences" in Lyon and she wants to register for the course in astronomy and the professor says to her "it is illegal for me to refuse you as a student, but I'm not going to let you pass the final test because I don't want to teach the course for only one person". Never mind all the other men students, she was the only student (and a woman to boot) who wanted to study astronomy. So she says "OK, I won't take astronomy; OK, I'll take the basic science courses." So then she went to study chemistry and mathematics, electricity and physics. So she had a basic science degree and then she joined the laboratory of the Physiology professor in Lyon by the name of Henri Cardot. C-A-R-D-O-T. Henri Cardot.
[16:57:55:24] And she had a wonderful relationship with him. He understood that she was extremely driven; she was working all the time. She obviously wanted to do something no other Greek woman, never

mind Greek of Egypt, had done. I don't know where she got that from; I really don't because her siblings were not ambitious. Neither my uncle, nor my aunt. But Angelique was. I have this joke about my grandmother telling her, because she was reading a lot at night when she was still living in Cairo "you should sleep a little bit, you're going to destroy your brain by reading all night long". [Laughs] Can you imagine? I don't know where she got that drive from. Was it, or was it not genetic? Maybe it was the cosmopolitan environment in Cairo with all these Europeans communities (French, British, Greeks, Italians, Jews etc.) cohabitating at the beginning of the XX century? I don't really know.
[16:58:57:29] One thing she understood, because she had a long vision, was that there would be no future in Egypt for a Greek woman who wanted to further her education. So in the late twenties she decided to leave for Lyon in France because she was fluent in French having attended the French "Lycee"/high school in Cairo. In the laboratory of Dr. Cardot at the University of Lyon she learned extracellular recording from axons isolated from marine invertebrates: Sepia *officinialis*, crabs, and the fibers of the myocardium of the land snail Helix. She built her own amplifiers (Arvanitaki, Bull. Soc. Fr. de Physique, 1932). Can you imagine? She focused on the oscillatory activities, either intrinsic or evoked of these nerve preparations. This work was carried out between 1930-1937 at the Mediterranean biological station of Tamaris and the laboratory of Dr. Cardot in Lyon. During that time she collaborated with a prominent French neurophysiogist, Dr. Alfred Fessard. She passed her Science doctorate thesis ("Proprietes Rythmiques de la Matiere Vivante" Ed. Louis Lapicque, La Sorbonne; Arvanitaki, 1938). I have a binding of the publications of her lifetime, before and after she met my father.
[17:00:01:02] And then in 1939, my father, who was a Greek from mainland Greece, from Athens, arrived in France with a fellowship from the Greek government at the time, to study at the veterinary school in Lyon for a doctorate degree in veterinary medicine, with the understanding to return to Greece and practice there. He never did. Ok. So there was a Greek community then, in Lyon, and I think that through this community Angelique met my father. So my father was 17 years younger than her. And it was a crazy love, more on my father's part than my mother's. My mother at the time, when she met him, she was in her late 30s, getting on 40 years old. And knowing her in retrospect, she probably thought "what the heck, if I want to have a child or some children, OK this guy is so crazy about me" even though she warned him and said "you shouldn't marry me because of our difference in age" she did and said **[17:01:18:29]** "Alright, let's get married". They got married in '42 and I was born in '43, which is going to make me – you can deduce how old I am. Tomorrow actually…
(the interview was on Nov 10th and my BD is Nov 13th).

So my father passed his DVM in veterinary medicine, and then he went on to obtain a degree in chemical engineering. And then he also in time became a “Docteur es Sciences”/PhD in 1954. And he worked with my mother. He said “I'll work with you; I want to work with you”. They started to publish together in 1947. And she was his guide. His compass, because you know, they were both Greeks supporting each other, both stressed out by the German occupation and the World War 2 environment. Think about it.
[17:02:14:23] Um, the Germans invaded Paris in '39. My parents were in Lyon, which was not invaded until November of 1942. So the French resistance started in Lyon in 1940 actually because it was in the south and still in the “free zone”. Um, and it was the Vichy Government collaborating with the Nazis which was going on in the north. Interestingly, my father did not become a French citizen until the ‘50s. He was a Greek citizen, but my mother had no citizenship as she was born in Egypt and it was like a protectorate. So when she came to France she immediately applied for French citizenship. She was not Greek by citizenship, not what so ever. See Greeks like my mother’s father, who had emigrated out of Turkey at the end of the XIX century to become refugees in Egypt, were not from mainland Greece and had a kind of protectorate status there without citizenship. So she became French much earlier than my father. **[17:03:18:23]** But what is amazing to me, and I would like the young generation of neuroscientists to appreciate this, is that during the occupation by the Nazis, they (my parents) continued going to the lab. It was walking distance from their apartment and they had government passes and had to come back home at certain times because there was an imposed curfew. The lab was by the way in a basement. That's something else again, because the physiology professor who at the time was the chair of the Physiology department in Lyon, not Dr. Cardot of course, the chair was Dr. Daniel Cordier and he may have been jealous. I don't know. Maybe to him there was something bizarre about this couple of Greeks? And they were working with their electrophysiology set ups, sort of isolated in this basement lab. And they were going to the lab every day, and in retrospect it probably was a psychological buttress for them to face the occupation. **[17:04:18:24]** At some point, they were by the way, interrogated I think by the Vichy auxiliary police, which came and searched their apartment; that was in 1944 after I was born. This came about, because of some students, Greek students who were of course in the resistance movement who had been sheltered by my parents. One of them had left my parents’ address in his pocket, which was not something he should have done. He got killed by the Vichy “auxiliary Police” or perhaps the Gestapo. They found the address in his clothing and they came to my parents’ apartment. They searched and they didn't find any weaponry. Apparently there <u>was</u> something hidden. I don't know. My mother said she had put “it” under

the mattress of my crib at the time! What I'm saying is there was a constant stress situation and they took refuge in research.
[17:05:19:28] Go tell that to any present day scientist. Ok. So this is pretty remarkable I think in retrospect.

One of the breakthrough contributions of Angelique was her discovery of electrical transmission in May of 1940. She called it "ephaptic" transmission " (from the Greek, "contact"). She demonstrated by extracellular recording that if two axonal membranes were apposed contiguously with one another and one axon was stimulated, the recordings showed that the contiguous axon was also activated. It had to be contiguous, and that was a model for electrical transmission. She called it an "experimental axo-axonic synapse". Actually, Dr. Michael V. L. Bennett, who is one of the founders of the field of electrical junctions/gap junctions and connexins (i.e. Bennett, J. Neurocytol., 1997) and Chair of the Dept of Neuroscience at AECOM in the eighties, knew my parents quite well. However English speaking colleagues became aware of this work, I would say not until 1942.
[17:06:21:00] I think this was due to one of the contemporary American biophysicists of the day, Dr. Ralph W. Gerard (University of Chicago then), who was one of the founders of SfN and after whom a SfN award in Neuroscience is named. So Dr. Gerard is the one who translated into English (from French) the ephaptic transmission paper. It was published in the J. Neurophysiol., in 1942. Dr Gerard had indicated in a footnote that "the manuscript was prevented to be published by war developments" and from that moment on the ephaptic transmission paper was read. And, my parents' work became known by English-speaking physiologists. They traveled in 1947 to attend the first Congress of Physiology in London, the first organized after World War 2. I got traumatized because I remember both of them leaving and I thought they would never come back. I was 2 1/2 year old at that time…. And here I'm talking to you at the Society for Neuroscience in 2013!
[17:07:16:15] So all during my growing up years, often when I was in my room and I would hear my parents talking about the data at home and all that, I felt shut off because I could not follow their discussions. I was a kid, it was beyond my understanding. And I did not want to be involved in science very much.
My mother, she was thinking, she was thinking. After she graduated, Angelique switched to Aplysia, the sea hare, and in 1941, there was another breakthrough in Dr. Cardot's laboratory; she started recording from identifiable neurons isolated from the abdominal ganglion of Aplysia. And the first time she dissected an Aplysia *fasciata* or *depilans?*, Angelique saw these huge neurons. The biggest ones can be like 500 microns or more in diameter; she was so excited. And she told me that in her first encounter with Aplysia, she recorded all night long! And she

found that if one neuron cell body was placed contiguous to a second isolated neuron, its intrinsic rhythmic activity could entrain a rhythmic activity in the second neuron. Significantly this paper, which was published in the "Archives Int de Physiology" in 1942, was actually privately translated into English, circa 1950, by Stanley Crain when he was getting familiarized with recording techniques, as a graduate student, then in the lab of Dr. Harry Grundfest at Columbia University. Stan gave me a copy of his translation, which I have kept along with my mother's original paper in French!

My parents, published together until 1973. Note that after WW2 and after Dr. Cardot had passed away, they moved in the early fifties their Aplysia work from the Tamaris marine biological station, to the Oceanographic Institute in Monaco. They had a large lab there with a view out to sea, since the Institute had been built on a rock in 1910. They would come in the late Spring, and Fall at the time when the wild (then not farmed) Aplysia *fasciata* , *depilans* or *punctata* would come close to the shore and be collected easily by local fishermen. Later on the Mediterranean Aplysia became rare and they had to import Aplysia *Californica*. In my mind as a neurobiologist, their main contribution was to show using intracellular recordings, that within the isolated abdominal ganglion, there were identifiable neurons with distinct morphology and size, displaying identifiable spontaneous firing modalities (i.e. tonic, bursting at various frequencies. My parents also analyzed the photoactivation of some of the neurons which were pigmented (i.e. Arvanitaki & Chalazonitis J.Physiol Paris 1958, Bull Inst Oceanogr, Monaco, 1960). These specific characteristics would be called nowadays "phenotypes". Dr. Eric Kandel has described this contribution in the international context of single cell electrophysiology of the time (see his book Cellular Basis of Behavior, Freeman and Company, 1976). This work spurred on the US side of the Atlantic a detailed mapping of the identifiable functional properties of the neurons of the abdominal ganglion of Aplysia californica (Frazier, Kandel, Kupfermann, Waziri, Coggeshall, J. Neurophysiol., 1967) and all of the neurons were renamed: from L1-L11 on the left side of the dorsal face of the ganglion and R1-R15 on the right side. When I compare with a photography of the abdominal ganglion in Aplysia *Fasciata* my parents gave me, I am pretty sure (and Dr. Kandel can correct me!) that they had named "B1, B2, B3, B4" those corresponding to what were later called L2, L3, L4, L6, and "Gen" the one now called L11. On the right side of the ganglion the largest one they had named "A", now R2, a smaller one "A'" now R14 and "Br" now R15.
[17:08:18:28] My parents were not considering synaptic input in those days. That is, which presynaptic axon is connecting via a neurotransmitter, onto which post-synaptic cell. What my parents focused on was the spontaneous activity of the neuron(s) within the

isolated ganglion. But as is presently known, the Aplysia ganglion preparation DID allow the mapping of pre-and post synaptic connections, identification of the neurotransmitters involved, identification of reflexes as forms of complex behavior, and ultimately, analyses of short-term and long-term habituation and the molecular mechanisms of retention of these behaviors (Cellular Basis of Behavior, E. Kandel 1976).
[17:09:09:17] So in the 50s, I think, we would have called my parents biophysicists, in that they were interested in understanding what parameters could generate these intrinsic different patterns of activity, independently of synaptic interaction. And what could modulate these activities; for instance: temperature, pH, pO2, pCO2, photoactivation, laser light etc. In retrospect, all of these stimuli could alter the efficacy and/or molecular structure of ion channels within the axonal or neuronal membranes and thus promote changes in their bioelectrical properties. Of course they were aware of A. L. Hodgkin and A. F. Huxley's work. I mean, if you give me the list of the international physiology colleagues of the time, my parents interacted with or discussed the work of all of them who have been leaders in the field, i.e. early on, K.S. Cole, B. Katz, J.C. Eccles, RW Gerard, H.K Hartline, T. Bullock, Francis Schmitt, Alex Mauro etc. So by 1959, there was a famous biophysicist by the name of Britton Chance at the Johnson Foundation (Univ of Penn). He was not a neurophysiologist necessarily; he was a biophysicist in addition to be a world champion in sailing races. He worked a lot with respiratory enzymes and oxidative phosphorylation
[17:10:12:17] and bacterial photophosphorylation, more from a biophysics point of view (i.e. Science 1954). He was aware of my parents work. I remember that he came to visit their lab in Lyon around 1958 and I actually opened an iron gate for him to access the basement lab directly, because the regular entrance of the University might have been closed! After this encounter there was a lot of enthusiasm expressed by my parents and they accepted Dr. Chance's invitation when he said "why don't you come and spend a sabbatical year in Philadelphia at the Johnson foundation" where he was then director. And "You know, we'll work together. We'll do things together on phototransduction etc.". and they said "OK". Dr. Chance passed away a few years ago (in 2010). So we crossed the Atlantic in the Fall of 1959. We came on the original "Queen Mary"/Cunard Lines. Can you imagine? It took us several days and we did not feel any "jet lag"! I remember I was looking at the skyline of New York City as the boat was approaching Manhattan harbor, which did not have the looks it has now, but I remember that still. It was fantastic and the three of us were so happy. And that was of course, a life-changing year for us. As I came with them and, even though I would be one year behind in the French school education system, I know how lucky I was to benefit from such an experience. At the advice of Dr. Chance I did not go to a public school in Philadelphia, but attended a private Quaker school, the

Friends' Select School, in downtown Philadelphia. This opportunity was eye opening for me, you know, compared with the French public school system. It was completely different. First, it was co-ed. I had been in a Lycee/French High School attended by young women only. At FSS there were all these "clubs" that you could attend in addition to the formal classes and we called all our teachers by their first names such as "Teacher Olive", the Science teacher, "Teacher Margaret", the English teacher etc… And I loved it of course. And so did Angelique and "Nick", as they were called by their first names, in contrast to the formal "Drs. so and so" used by the French academics. I remember coming back from FSS one afternoon to Dr. Chance's lab and being amazed at the shape of this ancient horseshoe crab/Limulus which was used for experimentation. My parents got to meet a lot of their physiologist colleagues at that time. And we discovered America. They were invited at the NIH by Dr. Ishiji Tasaki to give a lecture and Angelique delivered it. In the attendance were two post-doctoral trainees, Dr. Eric Kandel at the NIMH then ("In Search of Memory" Norton & Company, 2006) and Dr. Felix Strumwasser (i.e. J. Psychiat. Res.,1971). Both were so "imprinted" that each decided to use the Aplysia abdominal ganglion preparation intensely in their respective labs. Then in the early spring of 1960, I accompanied my parents to Chicago and while they attended a FASEB meeting (there would not be an SfN meeting until 1971), I was fascinated by the car traffic on Michigan Avenue flanked by the towering skyscrapers. In June then, we flew from Philadelphia to Seattle in one of the first jet plane connections, to attend the "International Symposium on Nervous Inhibition" organized in Friday Harbor on San Juan Island in Puget Sound by Dr. Ernst Florey; he was a pioneer of invertebrates neurophysiology, originally from Austria. My parents presented (i.e. Chalazonitis, N. in "Nervous Inhibition" ed Florey, E.,1961). We discovered the beauty of the northwest forests and the calm inlets of Puget Sound. Then we left Philadelphia to spend the summer months until October of 1960 in Woods Hole and my parents were guests at the MBL in Dr. Tasaki's lab. The relaxed and congenial atmosphere of Woods Hole was heartwarming. We had rented a small cottage nearby. They were parties on week ends, sailing events and my parents socialized with the best in neurophysiology, at the time: Drs. Harry Grundfest, Stephen Kuffler (I met the 4 children of Steve Kuffler and his wife, artist Phyllis, and with Suzi, Damien, Genie and Julian we have been friends until the present), also Drs. Felix Strumwasser, Mike Fuortes, Michael Bennett, Karl Frank (his son Eric, was my contemporary when we were in Gerry's Fischbach lab), and my apologies to those that I have forgotten to name. To me it was wonderful. **[17:11:15:01]** And I could see how happy my parents were, you know, for them they felt so welcome, it was such an open environment for the research. There was no discrimination, no Greek background, this and that to deal with. It was openness. And when in the Fall of 1960 we sailed back to France this

time on the US ship “The United States” I told myself that I would be returning some time. So OK, why after all that exposure to scientific life did I become a scientist? They didn't really push me, but I think, deep down my mother, sort of hoped all along that I would become a (neuro)scientist. She didn't want me to play cards with my Grand Mother! She didn't want me to learn Latin or ancient Greek, absolutely not. No.
[17:12:20:23] But the experimental disciplines, yes. So Dr. Eric Kandel is at Columbia right? So he teases me sometimes, “Oh, you remind me of Angelique” etc. (because of a facial resemblance with my mother). So one time I'm in the elevator with him, we greet each other and then he addressed other younger people standing around, and he says, nodding at me “her mother shaped my career” and the other guys wonder whom is he talking about? [Laughs] And he would tease my husband, as he introduced him as the “son-in-law of Dr. Arvanitaki “. You know, but it's an ongoing joke and Lloyd Greene told him once, “Eric, look I loved my mother-in-law, but I've done things on my own too!”. **[17:13:19:00]** So the other day (October 30th 2013) I attended the Stephen Kuffler 100th anniversary Memorial Symposium at Rockefeller University, and Dr. Kandel says to me, “you really should write a biography about your mother.” I said “OK, alright”, and I thought to myself maybe, I'll decide, even though I am aware that it will be an emotionally demanding task as a daughter’s point of view.

Q: This is a wonderful story.

A: And what can I say, I just became a grandma this September. I think both of my parents would have been delighted. I've been lucky, I've been very lucky. Interestingly this past summer one of Stan Crain’s grandsons did an internship with me in the lab and we all went to State College Pennsylvania to visit Stan and his wife Bea who live there now, and it was a joyful reunion. I really didn't want to do neuroscience when I was a teenager. I think it crept up in me as I graduated, things made sense to me. I became interested in questions. Not the ones my parents were interested in. You see what I'm saying, different preparations, different approaches.
[17:14:06:12]
So after, that sabbatical year, my parents finally got funds and recognition on the French side. They were offered a large, well-equipped lab in the newly built Institute of Neurophysiology of the C.N.R.S. in Marseille and we moved from Lyon to the ancient Mediterranean port in 1962. They had a staff of electronic engineers and an electron microscopist; Ph.D students and post-doctoral fellows (i.e. M. Gola, G. Romey). They also had visiting foreign fellows (i.e. Drs. Y. Watanabe, and H. Takeuchi and in Monaco, Dr. C. Spyropoulos). In the seventies my mother received an honorary degree from the University of Athens (she

had never been to Greece until then!) end in 1967 was recipient of the "Palmes Académiques" at the French Academy of Sciences. She also received an honorary degree in Japan-don't recall which University! Several scientific biographies have mentioned Angelique's and Nicolas' work and I was contacted by their authors for supplemental information: one chapter on "Arvanitaki and Cardot" (by Prof C. Bange) and another on "les neurons geants d'Aplysie" (by Dr. François Clarac) in a book entitled "L'Essor des Neurosciences, France 1945-1975" that includes French Neuroscience (2008). Another publication devoted to the contributions of Professor Alfred Fessard and includes his pre-WW2 (1936) collaboration with Angelique, (by Dr. Suzanne Tyč-Dumont et al. J, of the History of the Neurosciences : Basic & Clinical Perspectives, 2012).

So, I didn't like Marseille too much, you know, but I was getting my master's degree and I didn't want to do anything with the Aplysia (!!) As I said at the beginning of the interview, I listened to Dr. Paul Dell one of my professors, who was in connection with the NIH. He advised me to get trained for my Ph.D. research in an American lab. And Angelique and Nicolas strongly supported this plan.
[17:15:00:02] So you know, it has been good. Really. It's really interesting to me to think, that I have never felt discriminated as a woman at all. But why didn't I? I didn't become a lab chief. You see what I'm saying. **[17:16:03:07]** Despite the fact that I have instructed other researchers and I've been a research mentor to many people in the labs of prominent American neuroscientists. I never thought of my parents as "heads" in the administrative sense, because they were not strictly affiliated with universities but were only performing basic sciences at the CNRS and were never chairs of Departments. American women neuroscientists of the new generation are, or have been like, for instance, Carla Schatz, Jill Becker, Lorna Role, Story Landis, Lynn Landmesser, chairpersons in addition to research leaders. Chairs and full professors and leaders now, like Cheryl Dreyfus, a long time colleague and friend of mine, who got her Ph.D. with Michael Gershon and who was also a post-doc in Stan Crain's lab at AECOM. Also Carol Mason my present colleague in the Dept of Pathology and Cell Biology at Columbia, who is the current President of SfN. I was not a leader. So I was a leader at the bench. A local leader I would say.
[17:17:01:14] But it's wonderful, I think neuroscience is the scientific discipline to continue making the public aware of (such as the government emphasis on "the Brain Initiative"). And this should be definitely starting in high school. The Society has evolved tremendously now, since the start of the XXI century.

Q: How so?

[17:17:39:01]
A: It has now integrated so many more disciplines: i.e., molecular genetics, models of neurodegenerative diseases, brain cancer, the search for therapies, etc. The networking now available to its members and its increasing attendance; it has become not only international, but global, you see what I'm saying. You meet Asians and Indians in addition to Europeans, Australians and South Americans. While between the seventies and the nineties it used to be mainly attended by neurophysiologists, Anglo-Saxons and a few Europeans who were also in contact with the Americans.

Q: Thank you.

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