

THE AIM OF MY LIFE IS TO STUDY THE NATURE

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I was born in 1923 on the 6th of July in Budapest, Hungary. My beloved grandfather was a resident in Buda and was the owner of a tailor shop in the inner-city in Pest. He had four sons, among them my father, who started his studies in the high school of fine arts in his teens, being a very talented painter. But his career was interrupted after a quarrel with one of his professors and became a member of a “bad” society of painters like Lajos Gulácsy, his father sent him abroad to learn some more practical things like textile industry in England and Germany. Returning home he started his new path as a director of a textile factory in Gács, a small village, now Holic, Slovakia. He became acquainted with my mother in a nearby town Losonc (Lucenec) and married her in 1919, when she was 19 and he 28 years old. Before his marriage he painted a picture with Buddha sitting in the center before a splendid vessel and at Buddha’s sides there were two naked women, one of them resembling very much to my mother. On the back side of the painting was a Chinese inscription, which could be deciphered many years later only by the grandmother of one of our International Training Course fellows (who came from Beijing), because it was written with ancient Chinese letters as follows: “If you would like to know the future and you went to the palmist and he could not tell you the truth, you should turn to Buddha and he will tell it to you”.

My parents lived in a part of the castle of the former counts of Forgách. There was a big park, where I spent often my time with our dog Tommy, who was a French bulldog and took care of me so effectively, that nobody could approach my pram. My grandparents visited us often during the summer and we also spent in Budapest several weeks. My grandfather took me then every afternoon to the confectionery to eat “indianer” (moor’s head), my favourite pastry and hid me once into the wardrobe,

when the doctor visited us to look after my throat-ache, because I was very much afraid of medical men at that time. One day my grandfather felt unwell during our common walk, the ambulance carried him into a hospital where he died soon.

I started primary school in Baja, a small town in Southern Hungary, near the Danube, where my father became director of another textile factory and founded soon a football team in the factory. In the school I learned Hungarian very quickly, as before I knew only German, because my parents and my nurse spoke only German in my presence. But the real fun of Baja for me was the Danube, we had a motorboat and almost every weekend we visited the islands in the neighborhood. My favorite island was named Maurice which had a sandy bank and where I liked to swim and stroll among the willow trees. Once in a thunderstorm a ship of the Danube fleet saved us, for having fun I decided to hide myself in a chimneystack and I was very proud that the whole crew was looking for me, until they succeeded to find me.

Unfortunately for me we moved one year later to Bucharest, Romania where my father was director of a bank and there he fell in love with his secretary. I had to learn Romanian and French in the German school. We moved back to Hungary with my mother, she divorced and started to learn pharmacy at the University of Szeged and I became resident in a cloister in Buda, where I spent eight years. Fortunately as my mother finished her studies, she worked as a pharmacist in Budapest and I became a day-boarder. Later she could not pay the high boarding-school fees and finally I ended as extern, not receiving my school reports until she paid all debts (including she got one during my stay in the hospital where I was put because a scarlet-fever epidemic), and this ended just before my final examination at the secondary school. Nevertheless we had quite high-qualified teachers, we learned English, German and French, beside Latin and were not allowed to speak Hungarian not even during the recreation. I had two girlhood friends Júlia and Éva and just to irritate our teachers we spoke often Latin. The parents of my friends were physicians and Éva also wanted to be doctor, but Júlia decided to study in the faculty of liberal arts. As my father returned with his new wife also to Budapest, my father and my mother decided that I should become secretary learning typing and stenography, which I denied immediately. I tried to enter the Medical Faculty of the University in Szeged, where the father of my friend Júlia was professor of surgery, after I was rejected at the Medical Faculty in Budapest in spite of my excellent final examination. With his help I finally succeeded to enter the medical faculty in Szeged in October 1941, together with Éva and we shared also a common room in the university college.

The University of Szeged had several advantages: first of all it was much more democratic, and liberal than the Budapest University. This was due not only to Albert Szent-Györgyi who received the Nobel prize not long before and became Rector of the University, but also to Professors like Miklós Jancsó, István Rusznyák and György Ivanovich. We all were excited by their lectures. Szent-Györgyi's two assistant professors Kálmán Laki and Brunó F. Straub were also our favourite lecturers. In contrast to these advantages among the youth organization of the university there was a fascistic group who provoked fights against students of Serbian and Jewish origins and they were expelled for several weeks from the lectures in the spring of 1942.

In 1944 when the war came more and more nearer to Hungary the Jewish population of the country was deported to Germany, Éva and her family were transported to Auschwitz, where they were all killed in a gas-chamber, only her younger brother returned to Budapest after the war and became a famous writer. I named later my daughter Éva in her memory and my commitment to neurochemistry originated from her interest in the research of schizophrenia.

In October I entered the Medical Faculty of the University in Budapest, because the Red Army occupied soon Szeged, but in December the University was also transported to Halle, Germany and I received also a "SAS" summons to follow them. Therefore I succeeded to go to a Neurological and Mental Hospital in Buda as a patient with a diagnosis of hyperthyreosis. There I met two medical students, one from Szeged and one from Budapest from our course and one professor from Szeged. I spent the Christmas eve with my mother at home and returned at night by tram in the direction of the hospital, but at the place where I had to change trams, there was no tramway, instead a German soldier stopped me and told me to return. As I spoke fluently German I asked him just to go a few blocks ahead to arrive home on Xmas eve. These scenes repeated themselves several times until I walked lonely on my way to the hospital escorted only by the fireworks of the Russian "Katyousha". Around midnight I arrived safe at the hospital where we had a big party eating and drinking the vermouth I brought with me. Late in the morning, when I revived I was told, that everybody has to move from the sanatorium to the main building of the hospital, because the Red Army occupied the sanatorium for their headquarter. The main building was already full when we arrived, therefore we shared a big guestroom together with the professor. As there was no heating we had no problems of dressing, everybody slept in his or her coat, the professor slept even with his hat on, which on one side where he used to sleep, rose up. Our dressing- and washroom consisted of a basin enclosed with a folding-screen. Once when the German soldiers tried to break out from the castle and I was trying to wash myself, a shooting came through our window, a splinter fell in the basin and the folding-screen collapsed, but I remained half-naked, sane and everybody burst out laughing in spite of the grave situation.

During the siege of the castle I tried several times to go home but I was every time repelled by the soldiers, once I arrived till the St John's hospital, where I got rid of my watch. Later I succeeded to visit my father, who inhabited a villa near the cemetery of Buda. Finally as the siege ended I got home to my mother. We were all very happy to be alive and she prepared very fine paprika horse meat. A shooting before our house killed the poor animal. When I returned to the mental hospital we decided to go back to Szeged as soon as possible because we were sure that the University in Szeged will start earlier than in Budapest. This was easier to imagine, than to fulfill.

First we had to cross the Danube, but the bridges were all destroyed, and so we had to go to Budakeszi where a pontoon-bridge was built by the Red Army, which could be used some times also by civilian people. Then we had to go to the western railway station, where trains used to go to Szeged, but no regular trains were there going to Szeged. Finally the professor speaking with the stationmaster told us that

there is a Red Cross train carrying children to Orosháza because there was more food there, and we could enter that train as medical suite. So we arrived in the evening to Orosháza, but there was only the next day we could reach a train from Orosháza to Szeged. The professor remembered that one of his students whose father was district doctor in this town, lived here. We visited him and they invited us to sleep in their house. After the beet soup and the 100 gr black bread we received as daily portion in the hospital we were eating a Lucullan repast there was plenty of broiled beef with noodles and vine, but around midnight I met the professors and the students before the lavatory grooming and vomiting. The next day we arrived in Szeged and the professor invited us to live in the institute until we could get a place in a dormitory. The lectures started already, but soon they were interrupted because a typhus epidemic broke out, and every student had to delouse the people who entered Szeged. I was ordered to go in a customhouse which was built at the end of the Csongrádi avenue controlling the women and my colleague checked the men. After a few weeks our supervision ended and we continued our studies. The next semester I became demonstrator at the Institute of Pharmacology, than I spent a year as assistant in the Institute of Anatomy and Histology, mean timely I was an externist at the Neurological Clinic, after this I succeeded to enter the Institute of Medical Chemistry which was then directed by Professor Brunó F. Straub. After Albert Szent-Györgyi left Hungary from the Institute of Medical Chemistry and Biochemistry in Budapest, Straub was appointed in his place and I went with him in 1948. We continued there our research on muscle biochemistry with my later husband George Feuer.

In Budapest we started a new way of life in the institute. As Straub was living there, he was present always and everywhere: the lab was our first home from early morning till midnight, when we used to climb over the closed iron gate of the university in the Puskin street and walk home on foot to Buda, because the latest tram already left for the coach-house. I was one of the poor assistants, who measured the whole day the action of ATP on actomyosin and was able to measure about 50 samples a day on the viscosimeter, so I passed as Stakhanovist of the viscosimetry in our institute. At that time there were no free Saturdays and some times he called us to come in even on Sundays to prepare some muscle proteins, but then he invited us to lunch with him at the Teddy Bear Bistro and we felt us very honoured. In the late afternoon we even went with him to the espresso of the Szentkirályi-street where we ordered presso coffee and rum, instead of the five o'clock tee we used to drink in the Institute. There we discussed not only the experiments, but politics and art too. Alas these happy days did not last for a long time because after a while Straub got under the influence of the "triumvirate" who were the main party members of the institute and he was obliged to take part in the "higher politics". Therefore after a year we decided with George Feuer, who became meanwhile my husband, to go to the newly founded Academic Institute of Biochemistry, which was temporarily housed in the institute of public health and Imre Szörényi, an academician of the Soviet Union who returned to Hungary, was nominated as director and we could devote there our time entirely to research.

I was glad, because beside muscle biochemistry we could also start neurochemistry, which was my favourite theme. First of all we visited the Institute of Physiology in Pécs, whose director professor Kálmán Lissák invited us to study the methods they applied in the field of neurophysiology in their laboratories. I wanted to study the mechanism of the synthesis and breakdown of acetylcholine and their role in the central nervous system. This was also the topic of my candidate's dissertation, which I succeeded to defend in 1956. My dissertation was later translated into French and appeared under the title "Métabolisme des médiateurs chimiques du système nerveux" as a common edition of Masson et Cie, Paris and Akadémiai Kiadó in 1970. But again new troubles appeared, Szörényi wanted that the whole institute should investigate muscle mechanisms and I should determine the endgroups of the muscle protein actin. As I was not a chemist, but a medical doctor, committed to neurochemistry, I left the academic institute for the State Institute of Neurosurgery, where I got a lab and a Warburg apparatus and I could use the poor equipment of the clinical lab. The man who invited me was professor A.V. Terian, head of the Institute of Neurosurgery in Moscow, who was in charge to start the neurosurgical work in the Hungarian institute. I was stimulated by the possibility to get human brain tumours directly from the operating room and so I started my research on brain tumours with full of confidence in myself. This work lasted fifteen years and ended in 1971, when I returned to Szeged as the head of a membrane research group in the Institute of Biochemistry of the Biological Research Center directed by Straub F. Brunó. The results of these 15 years was summarized again in a book entitled "Biochemistry of brain tumours" as a joint edition of McMillan Press Ltd., London and Basingstoke, University Park Press, Baltimore, London, Tokyo and Akadémiai Kiadó in 1974, with the foreword of Abel Lajtha. The book was also translated into Russian and a Japanese edition was also planned. The book contained not only the newest results of brain and brain tumour biochemistry from the literature but also the experiments which I performed on the more than five hundred brain tumours, besides other brain tissue mainly from cases of epilepsy and aneurysm. These were enzyme activity measurements, as well as isoenzyme demonstrations.

I succeeded to demonstrate that the isoenzyme pattern, i.e. of lactic dehydrogenase changes in a characteristic way, which starts already in the neighborhood of the tumour. The experimental part of the book consisted of the theses of my dissertation for the academic title "Doctor of Medical Sciences", which I received in 1968. During the fifteen years in the Neurosurgery I spent two years abroad to learn new methods, which I could use in my tumour experiments at home. I spent a half-year in 1956/57 in Berlin at the Pharmacological Institute of the Humboldt University where I studied the metabolism of different choline esters (butyryl-, succinyl-, acetyl-) by chromatographic methods. In 1963/64 I was working in New York Montefiore Hospital at the Department of Anaesthesiology and Pathology where I got acquainted with gel electrophoresis in order to demonstrate isoenzyme and protein changes in brain tumours. In collaboration with Marks and Lajtha in the New York State Research Institute for Neurochemistry and Drug Addiction, Ward's Island we investigated also enzyme activities in different cell fractions of brain tumours.

Finally I spent a half-year in 1966 in Paris at the Laboratory of Eutonology, Boucicaut Hospital doing pharmacological investigations on chlorpromazine free radicals, GABA and gamma-hydroxybutyrate. Due to my colleague Agnes Ullmann from Budapest, I was also invited to the seminars in the Pasteur Institute organized by Jacques Monod, where I took part in vivid discussions with Jean-Pierre Changeux on the identity or difference of acetylcholine esterase and receptor.

In 1968 at the Biological Institute of Tihany we set together for the first time to discuss the future themes of the Biological Center of the Hungarian Academy of Sciences in Szeged. Straub as director general headed the meeting. In the Institute of Biochemistry three groups were envisaged which were named shortly nucleic acid, protein and lipid groups. I preferred the investigations of receptors above all, but as I was chosen as head of the lipid group I had to offer the study of the biochemical role of phospholipids as well, which was preferred by Straub. After voting for the themes it turned out that my beta-adrenergic receptor plan won more voices, than the phospholipid: obviously the receptor plan was presented much more enthusiastically by me.

It was in 1971 June that I started my new research field in Szeged. Among my first pupils were Ágnes Nagy, who came with me from my lab in Budapest, Katalin Maderspach who was also biologist in Budapest, Csilla Torday a chemist from Szeged, Zoltán Kiss was a biologist who finished the University in Szeged and Anna Borsodi, who came a year later, was also a biologist from Budapest. My first idea was to investigate the metabolic enzymes of noradrenaline in order to compare their active group with the beta-adrenergic receptor, because both proteins reacted with the same molecule. Cooperation with the Pharmacological Institute of the Medical University in Szeged was given, because at that time they were interested in the effect of inhibitors of beta-adrenergic receptors. We compared our results on rat heart measuring activation and inhibition of adenylate cyclase activity with their in vitro and in vivo results and found a strict parallelism. We obtained similar results with histamine and serotonin in blood-vessels, stomach and developing heart measuring also adenylate cyclase activity in cooperation with the Biophysical Institute of the BRC, the University Medical Clinic, the Pharmacological Institute in Szeged and the Biological Institute in Tihany. A series of common publications appeared in the seventies from these experiments that are cited even nowadays.

In the seventies scientists from Sweden and USA succeeded for the first time to demonstrate opiate receptors in the brain by radioligand binding methods, soon after that in Scotland a group isolated the first endogenous opioids from brain, which they identified as pentapeptides. As I was nominated meanwhile in 1977 as deputy and later as director of the Biochemical Institute of the BRC, I was able to turn my interest toward the opiate receptors, which played an important theoretical and practical role as analgesics, euphoric and sedative drugs causing addiction and tolerance.

In order to start work on opiate receptors we needed a reliable good radioligand, which was prepared by Géza Tóth in the isotope laboratory of the Biological Research Center. This was a tritiated form of the antagonist naloxone, and a good research team for the purification of opiate receptors was set up. This group was rep-

resented by the quartette of Anna Borsodi, Sándor Benyhe, József Simon and Mária Szűcs. The peptides and columns were prepared in the Organic Chemical Institute of the Eötvös Loránd University in Budapest, we had cooperation with them, which is continuing till now. We decided to concentrate on the isolation and purification of kappa-opiate receptors, because by activation of only this receptor one cannot evoke the symptoms of addictions. We started with the purification from frog brain, since this preparation turned out to be more stable than mammalian brain products and it contained relatively more kappa-opioid receptors. We succeeded for the first time to publish the method of pure kappa-opioid receptor isolation. With this preparation Katalin Maderspach in our group produced a monoclonal antibody of it and localized the receptor in rat, chicken and later in human brain using an immunofluorescent method in collaboration with the First Institute of Anatomy of the Semmelweis University in Budapest, and some other institutes at home and abroad. Finally owing to the isotopic department we managed to prove with MERF, a labelled heptapeptide derived from proenkephalin A, that it is bound to the kappa2-opioid receptors, which is regarded now as a heterodimer of delta- and kappa-opioid receptors. Later it turned out that MERF and some of the opioid peptides (including those reported in the literature by others as dynorphin, Met-enkephalin, beta-endorphin, bovine adrenal medullary peptide, etc.) are not bound exclusively to opiate receptors, but display other nonopiate actions as well, which are not inhibited by naloxone, for example. MERF is bound also to the sigma2-receptor. Unfortunately we did not succeed to clone our purified kappa-opioid receptor. Our application for a research grant was denied in 1984 by the Academy. It took almost ten years when the first publication of the cloning of kappa-opioid receptor appeared in the literature.

Meanwhile our research trend turned more and more to practical fields, the reason of it was mainly financial. Emphasis was put on the selective, specific peptide and alkaloid ligands, which were not or less addictive than morphine. Mainly Anna Borsodi and her group represented this direction, Mária Szűcs investigated the biochemical mechanism of addiction, whereas Katalin Maderspach explored the kappa-opiate receptor distribution in the developing brain tissue culture. All three of them succeeded to defend their theses of Doctor of Biological Sciences of the Academy. Hopefully Sándor Benyhe holding a “candidate degree” will follow them.

Summarizing these efforts although my original programme was only partially realized, a lot of valuable results and publications originated, which are cited often in the literature. I hope my group will continue this type of research, because the spreading of the drug abuse in our country renders these investigations indispensable.

My daughter Eva Feuer was born in 1953, she entered the University also in Szeged and studied in the special mathematic faculty organized by the late professor László Kalmár. By now she is head of the Department of Quality Management in the Computer and Automation Research Institute of the Hungarian Academy of Sciences. Her daughter Gerda Tóth is a student of the Medical University in Budapest.

I feel, that my passion for ornithology was based also on my love of Nature. I always envied flying birds, because they seemed so free for me. I tried to get closer

to them by learning ethology and by taking sound registrations and sonograms of different bird voices (alarm- and mating calls), which I published in scientific journals. My hunting dog an English setter, who accompanied me always on my exploratory paths, brought on the alarm calls of the waders.

As I got older and could not follow the birds on the riverside of the Tisza and the heron colonies in the rushes of the lakes, I decided to acquire a farm in the neighborhood of Szeged. When I found the right place it was some 40 km away from my flat, but it was surrounded by a pine-forest with a small house with mud walls and thatched roof and a draw well. The house was almost covered by a huge mulberry tree, under its shadow I could sit in silence and observe the singing birds, the prey birds, woodpeckers, jays and orioles and many others. Great and blue tits nested in my garden in hollows and green finches built their nest on the apricot trees. My dogs were always happy to get in the car when we went to the farm, they had a free life there, hunting after the lizards and mice which succeeded always to hide somewhere in safety.

Since 1985 I have retired officially, but I am still active, although since 1993 I received no grant anymore. Beside the books I wrote I had 125 scientific papers and received about 750 citations. I was titular professor of the József Attila University in Szeged giving lectures on neurochemistry from 1973–1997. At present I am involved in the Ph.D. training course of the medical faculty delivering lectures on molecular neurobiology. My main activity is now the follow-up of the scientific literature, but my most important goal did not change, I am still interested in the cognition and study of Nature...