Bloomington, and Indiana University: first year (1967-68).

Arrival and first impressions.

We arrived in Bloomington, Indiana in September of 1967. It was never our intention to stay in Indiana for more than a few years, but as fate would have it, it is now nearly 50 years later. We have aged in this city and I expect we will be buried here (unless we move or have an accident elsewhere). We thought of Indiana as a temporary haven until something else opened up in a more interesting part of the country, or until we returned to Israel, still something we considered.

We drove from S. California with our portable belongings and two small children ages 4 and 2. As far as I remember the trip was uneventful, except that as usual Jonathan developed a fever, and we had to take him to the emergency ward in Salt Lake City. He chronically suffered from strep throat, and it was not until he had his tonsils removed a few years later that he got over this. Related to this, one of the first priorities on arrival in Bloomington was to find a pediatrician. We asked around and Dr Riley Shafer was recommended. As expected after a few weeks in Bloomington, Jonathan came down again with a strep throat. We took him to the physician's office and he was immediately admitted into the Bloomington Hospital. The pediatrician was panicky and told us he suspected meningitis. However we were very familiar with this pattern of Jonathan's illness and did not quite see what all the fuss was about. All Jonathan needed was antibiotics. At that time (1967) Bloomington Hospital was a small –almost a country hospital. The ward for children was not air-conditioned and there was no isolation ward, so that sick children were placed together, irrespective of their illness, i.e. a child with measles could be placed next to a child with a totally non-infectious disease. We became quite angry and declared that we were taking Jonathan home. Dr Shaffer in turn became very angry, and stated something to the effect "that I as a microbiology professor thought I knew everything, but I would be sorry". Anyway we took him out of the hospital, against Dr. Shafer's wishes with Jonathan screaming," I don't want to go home " all the way down the corridor, to our great embarrassment. After this we never consulted Dr. Shaffer again, although I did become acquainted with him later when one of my post-docs (Dr. Magda Souhrada, M.D. from Czechoslavakia) joined his practice. He was really a very conscientious and kind person, having had some tragic experience with children with fever and meningitis in his past. Eventually Jonathan had his tonsils removed, and the strep throat disappeared forever.

My initial impression of Bloomington was of a “laid back” town, surrounded by green hills and forests. The town itself was not distinguished architecturally, the downtown looking neglected. Like most mid-west towns the central square was dominated by the courthouse, surrounded by memorials to the dead of the USA’s many wars. On the courthouse square were a few department stores of that time, Woolworth, Ben Franklin and a Penny’s catalog store. In the 1960’s there were only a few apartment complexes within proximity of the university. There was one shopping center, the recently opened College Mall, mostly catering for students who made up a sizeable percent of the population. Most of the development, suburban type housing was in the eastern edge of town quite close to the university. There were few good restaurants, and almost no ethnic restaurants other than Chinese. There were many Pizza places and a few bars, the most famous being Nick’s on Kirkwood, the main student drag and next to the campus.

All of this has changed in the 50 years that we have lived here. It is now a city of close to 100,000 inhabitants, developed shopping on the west side of town, and the most amazing selection of ethnic restaurants better than I have seen anywhere outside of New York. During the spring and autumn the town looks pretty, not because of its architecture but due to the abundance of trees and flowing lawns. The university itself is beautifully landscaped.

In 1967 Bloomington was a town of about 50,000 “ native” inhabitants, and 30,000 students. Most of the buildings in town were either clapboard, red-brick or occasionally Indiana Limestone. It was obviously very different from Laguna Beach, or Irvine or Palo Alto but in many ways similar to Ithaca, N.Y. but without the steep hills. The campus on the other hand is beautifully landscaped the buildings uniformly built of local limestone, but looking as if it all developed in the 1930-1950s. Even the new buildings such as Simon Hall, just constructed in 2009 looks as if built in the 1940’s. I suppose this is what is termed Collegiate Gothic. The campus has extensive landscaping, with large lawns, trees, forested areas and flowerbeds, and a small arboretum on the site of the stadium previously used for the bicycle race, called the little five hundred. It is considered by many one of the most beautiful campuses in the USA, partly because of the uniform limestone architecture.

The economy of Bloomington was and is dominated by the university, although when we arrived there were some industries, an RCA plant, Otis Elevator and Sarkis Tarzian a company that made components for television and the film industry. None of these exist today. There were very few restaurants, the most popular being Sully's Oaken Bucket, a sports bar on the square. The Oaken Bucket was a trophy awarded to whichever team, Purdue or Indiana won the football game for that year. The trophy is an old beaten up bucket with chains attached to it, found somewhere in S. Indiana in 1925. Today the Malibu Grill occupies the site of the "Old Oaken Bucket" Even Indianapolis some 50 miles away did not have good restaurants and was locally known as "Indiana No Place". This has all changed, and Indianapolis is a thriving and very livable metropolis.

The downtown square has gone through many renovations with time. The courthouse has been spruced up and the dome redone. New more fashionable shops have appeared, and there are very good restaurants today on the square. Large apartment complexes are springing up everywhere. Kirkwood the main " college town" drag had a few bars and pizzerias, some of which such as Nick's are still functioning and served good pizzas and submarine sandwiches as well as good beer. Nick's was my lab's hang out for lunch during the first few years at IU. I had never had a submarine sandwich before and it was quite a treat. This is a sandwich with various kinds of meats, cheese slices and relish served usually on a large roll. We even had lunchtime lab meetings at Nick's with a black board provided by the restaurant. Nick's has been in the national news the last few years. Both Barak Obama and Hilary Clinton visited Nicks while campaigning for president. . When Mimi and I and the kids wanted to go out we would go to the Pizzeria next door, which was under the same ownership. The Hrisomalis family, newly arrived from Greece, started this restaurant and bar in 1924. However the family sold it in 1964. I have had a number of the younger Hrisomalis family members in my classes through the years. One of the granddaughters of the original Hrisomalis family and my son Yuval went to France as part of a group of teen exchange students. They family have gone from being restaurant owners to physicians and dentists within one or two generation.

On Friday and Saturday evening locals from the surrounding countryside come into town with their SUVs and trucks, and drive up and down Kirkwood, visiting the bars and looking for co-eds. Bloomington today is full of " sports bars" with multiple televisions set to different sports channels. These are few regular bars, without blaring television, where one can enjoy a beer or Scotch and some snacks. Fourth St, near campus is the main drag for " ethnic" restaurants, everything from Tibetan, Indian, Thai, Turkish etc. occupying many of the old houses. It is hard to believe that this change in eating habits has occurred during our time here. There is even a place to buy falafel, originally opened by the husband of an Israeli student. Today there are new cafes opening all the time, a new gastronomic fad.

The first really ethnic restaurant was the "Dow" run by an Ashram. It served a mixture of western and Indian food. The nephew of the Dalai Lama, whose brother settled in Bloomington opened a Tibetan Restaurant, the Snow Lion. The father, **Thubten Jigme Norbu** the brother of the Dalai Lama was on the faculty and his presence in Bloomington resulted in the immigration of quite a few Tibetans to the city. The story of Norbu and the eventual founding of the Tibetan Culture Center in Bloomington can be found at http://tmbcc.org/SITE/index.html. The Tibetan Cultural Center, on Snoddy Rd not far from our house is where monks clad in saffron colored robes live, and celebrate their religion and customs. The center also contains rare works of art and houses a museum and gift store.

Before settling down to work our first priority was to find housing. Before our arrival, Gene Weinberg, one of my new colleagues offered to find us an apartment, which he did in Barth Villa, an apartment complex on 2nd street, opposite the elementary schools, and within walking distance of Jordan Hall. In the 1960's the rent in Bloomington for an apartment was not different from the rent we paid for the house in Laguna Beach. Fifty some years later Barth Villa apartments are still standing and functioning. I passed them by today and they look the same as they did in 1967 whereas the house we rented in Laguna has been replaced with an apartment and worth millions of dollars.

We enrolled Yuval in pre-school, I believe it was called Small World, and Mimi remained at home with Jonathan. It was through Small World that we met other parents, some of whom are still our friends to this day. Jonathan learned to finger paint from a new friend, Alexandra Smith. We became friends with her parents David and Weezy Smith, a friendship that has lasted all these years.

We lived close enough to campus that I could walk or cycle to work, and the children eventually went to school, Rogers and Binford, across the road from our apartment. After the cultural wasteland of Stanford and Irvine, we enthusiastically attended concerts and operas. The opera was held in the University Elementary School Auditorium, and concerts mostly in Recital Hall. University elementary school, alas, is no more, and is part of the computer science and information technology component of the university. When we moved to Park Ridge in 1971 our children attended University School. This was an excellent school, with a extremely capable and well intentioned principal, Mr Rowland. Opera and major concerts are now held in the Musical Arts Center, built in 1972, a first class facility for opera. The education building in the heart of the campus was converted to the music school, in the 1990's, one of the largest, if not the largest in the USA with superb facilities for chamber music and small ensembles.

Although I mentioned that university school was excellent, the education system did have some flaws. Foreign languages were not taught, and we had to fight for the introduction of French into the curriculum of Middle school. Initially foreign languages were taught after or before the school day started or ended. There was opposition from Monroe county school administrators to the idea of teaching any foreign language. . Mimi also lobbied for a separate class for " bright" (should I say gifted) students. It took many years before this was achieved. I believe this has continued to this day, although the opposition at that time was due to the belief that this was elitist. The teaching did not improve, but the brighter children were in the one class and that seemed to work well socially. These children bonded and have remained friends for life.

<u>The department</u>

I had an appointment as an assistant professor in the bacteriology later called microbiology department (at that time part of the Biology Division). The Biology division was divided into Bacteriology, Zoology and Botany along very traditional grounds, and

Anatomy and Physiology, part of the Medical Sciences Program. Of these, the bacteriology department was the strongest, and had very good facilities, including a media kitchen and stock room that a few years later supplied the other departments as well as microbiology. This was run by Helen Arthur, a wonderful person, and very efficient top-notch administrator. She had helped plan Jordan Hall and knew the building intimately. She also was an expert on all the equipment and knew how to " fix" anything that did not work. All of the basic biology departments were housed in Jordan Hall, with the Medical School Departments, anatomy and physiology in nearby Myers Hall. Biochemistry was a component of the Chemistry Department which was always a problem since the biologist thought it should be part of our department. It did not get any autonomy until the 2000's.

Jordan Hall was a massive structure. The laboratories were large, and it was used for both research and teaching. Many of the teaching labs were in dire need of upgrading and modernization by 1967. The building was constructed between 1954-1956. The walls are so thick that today cell phone reception is almost zero. The walls of the corridors were tiled so that they could be washed down easily. The building not only housed laboratories, and class -rooms, but also a large library with open stacks. The one item lacking was a restaurant or snack room. The original building was U-shaped, however the U was filled in in 1984, increasing the space by 33% allowing for the addition of a large atrium, containing a cafeteria and computer spots.

In 1967 the Director of Biology was Frank Putnam, and Assistant Director Leland McClung. Frank Putnam was a renowned biochemist. He worked on the amino acid sequence of Bence-Jones proteins, serum proteins produced by multiple myeloma patients. These proteins are monoclonal antibodies produced by plasma cells. His research helped elucidate the structure of immunoglobins and antibodies. He arrived in Bloomington two years before I did and gave the department of biology direction. Biology had been a powerhouse of famous scientists. The Nobel Laureate Hermann Muller had died just a few years prior to my joining the department. On the faculty there was Tracy Sonneborn, an outstanding geneticist and teacher, John Preer, one of his students who continued the work on paramecium, and Marcus Rhodes and Drew Schwartz both renowned corn geneticists. They had been involved in the discovery with Barbara McClintock of transposons (jumping genes). Robert Briggs who developed the technique of nuclear transfer, which played an important role later in embryonic cloning, headed the Zoology Department. His research pioneered the way to today's embryo transplants.

Bacteriology had been a very renowned department with members like Salvatore Luria and Renato Dulbecco, both Nobel Prize winners. Jim Watson of DNA discovery fame had been a graduate student of Luria's. However they had left for other universities a few years before my arrival. The department had been decimated with the departure of many faculty including those mentioned above, as well as Howard Rickenberg (to Denver), and Jean Poindexter (to New York). Leland McClung, a world expert on pseudomonas. had headed the department the last few years.

There were four hires into microbiology that year: David White, Arthur Koch, Robert Ramalay and myself. David and Arthur remained here at IU. Bob Ramalay did not get tenure although he subsequently did very well at the U. of Minnesota. Someone else's gain as often happens, when tenure is denied. Unfortunately Arthur recently died of Alzheimer's disease, and David is not in good health. Arthur was a bacteriologist, studying theoretical questions relating to bacterial structure and motility. David had worked on myxobacteria, a " slimy" gliding bacteria that formed interesting structures that resulted from single cell cooperation to form a multicellular organism.

The department was quite strong with the new additions. Apart from Howard Gest, the chairman, and well known for his work on photosynthetic bacteria, there was Dean Fraser, a phage virologist, with whom I co-taught virology for a number of years, Walt Konetzka, a basic microbiologist, who had a wonderful reputation as a teacher, Tom Brock, one of the founders of the field of microbial ecology, Leland McClung, the worlds expert on pseudomonades and food toxicity, and Gene Weinberg, who studied iron metabolism in bacteria. Thus with the four new additions we were a group of ten. This was an all round good bacteriology department but no representation of animal virology other than myself. I would remain the sole virologist for many years, although I was not hired as one, but rather as a bacteriophage geneticist.

I was allocated a large suit of labs: two large rooms, an autoclave room for sterilizing material and adjoining animal facilities which were shared with other faculty. In these days there was no such thing as set up money (or at least I was not told about any,) since it was assumed that one would quickly obtain an NIH grant. I inherited a functioning lab from Jean Poindexter, who had just left the department. The only new pieces of equipment I requested were a -70 Freezer, and a Beckman isotope counter. Forty years later both these pieces of equipment are still in use, with the -70 freezer being shared by a number of virology labs in the new Simon Hall biochemistry/biology center. All other equipment was purchased from grants throughout the years.

First year of research

The strength of any research laboratory is the graduate students and post-docs who work in it. Microbiological Research is very labor intensive, and demands a core of people, including lab technicians, to prepare buffers, chemicals and grow organisms, whether bacteria, cell culture or virus. The problems that one deals with apart from scientific research are personal problems involving members of the lab. In many cases I had to act as father or big brother to graduate students, their spouses or " friends". In other cases I had to arbitrate petty arguments and spiteful acts among members of the lab. There are jealousies, "patriotism to the group" accusations of cheating, suspicion and paranoia. I won't go into these in detail but they can ruin the atmosphere and cohesiveness of the group. From the very first year I had to deal with marital problems of my graduate students.

I was quite happy that first year at Indiana University. I had a number of projects, the destructive effect of viruses on tumors (now known as viral oncolysis or virotherapy) research pertaining to virus replication, and the role of transfer RNA's in tumor development. I inherited a graduate student, RW from Jean Poindexter who had left the Department. RW was a very handsome young man from Florida, married to his high school sweetheart. However this marriage was to be disturbed by an undergraduate student who joined the lab and later became a graduate student. Although this affair did not result in marriage, RW and his wife split up. I very naively did not know what was happening and became involved. Despite his stormy personal life RW had a very successful scientific career .

A second graduate student soon joined the lab, this was G Z.. He was in many respects similar to RW, a very tall, suave, handsome young man, He could not decide whether he wanted to work with me or Tom Brock who had isolated different species of bacteria that lived in the hot springs of Yellowstone National Park. Although we produced papers together his main interest was in the Brock lab. Tom had isolated a bacterium that grew at 80-90 degrees, and I was interested in whether tRNA isolated from it could be charged at such a high temperature. This organism was called appropriately enough Thermus Aquaticus. If only we had recognized its potential. The enzyme that replicates DNA at high temperature (taq polymerase) was isolated from this strain, and became the basis of Polymerase chain reaction (PCR), a major and Nobel prize winning technique in biotechnology many years later. If only we had thought of this! I met GZ many years later now head of an ecology institute at Michigan State University.

Anyone entering my lab at that time would have been astounded to find large glass chromatographic columns of an inch or so diameter stretching from the floor to the ceiling of one of the rooms. We were separating different types of tRNA's on what was called MAK and BD columns by liquid chromatography. We needed a ladder to both pour the columns and load the samples. The various types of tRNA would be separated on the basis of charge and/or size. Allan Volkers, a post-doctoral fellow from Newcastle, England had joined me in this endeavor. He was my first post-doc. We were convinced that the difference in elution profiles would have some significance to cancer, since the tRNA's were isolated from liver tumors and compared to tRNAs of normal liver. Although there were differences, these were not followed up, since we did not have the chemical background and probably reflect modifications of specific bases or as known now epigenetic effects. Whether they have anything to do with cancer is in doubt. (see chapter on tRNAs)

At the end of my first year in Bloomington, I was invited to give a seminar in Denver by Howard Rickenberg, who previously had been a member of the department. He offered me a position at the National Jewish Hospital in that city. Both Mimi and I quite liked the city and debated seriously whether we should leave IU for Colorado. However I believe I was more against the move than Mimi since I worried I would not have access to graduate students, since the lab was at a hospital, and not on the campus of the University of Colorado. The appointment would have been a joint appointment with the U. Colorado Medical School and National Jewish Hospital. In this I was mistaken, since a future colleague, Norman Pace took the position and built up a very large and successful research group.

While on this visit I did meet a scientist who was to have a lasting influence on my research, and this was Ted (Theodore) Puck. He had started a new field, called somatic cell genetics, in which he developed genetic systems in mammalian cells (Chinese Hamster Ovary cells, known as CHO) in culture, analogous to what had been done with the bacterial strain E.coli. He convinced me, to take CHO cells back to Bloomington and to try to isolate mutants of the cell line. This was reminiscent of the type of work I started to do but unsuccessfully as a student in the Yanofsky lab at Stanford. I later took a course on cell culture in which Ted Puck and Phil Marcus taught the art of cell culture. I became close friends with Phil Marcus, who died last year. We would meet every year at the interferon society meetings and spend an evening together having dinner and attending the annual banquet. I learned a great deal from that course, and for a few years I was active in the society for cell culture.

I had received a 3 year grant to work on phage, which I used for the animal viral work. I received grants from the Damon Runyon Fund and American Cancer Society to work on tRNA modifications and profiles in cancer cells and a grant to work on mutants of Chinese Hamster Ovary cells. The isolation of mutants of the purine salvage pathway led to an interest in purine metabolism and the enzyme APRT which also became a focus of the laboratory. In retrospect it was a mistake on my part to pursue so many topics at the one time. I should have stuck with one or perhaps two of these projects instead of branching out in so many directions. Each one of these projects could have led to being an expert n a specific field and a lifetime of research. Thus my research was unfocused which had consequences later on.

First summer. 1968. Israel

After one year Mimi and I had still not settled down in Bloomington, and still thought of returning to Israel. After having set up the lab in Jordan Hall, we decided to spend the summer at the Weizmann Institute, in Rehovot, Israel giving myself time to look for a faculty position in Israel. I really did not consider industry (there certainly was not much biotech in Israel at that time) or a government job. I am not sure why other than that I already had an academic job and that seemed the direction to take.

We quickly settled into the Weizmann Institute, living in Beth Europa, and I enjoyed tremendously the atmosphere of the " machon" as it was called. I was working with Uri Littauer on tRNA modifications, a subject I had brought with me from John Holland's lab and my own lab in Indiana. I fitted into the Machon without any problem, my Hebrew was passable, and I think Mimi was happy. Beth Europa was a very beautiful modern apartment complex, and I walked through orange groves every day to reach the biochemistry building. Mimi renewed contact with her friends and family, and we celebrated Jonathan's 3rd birthday with lots of his second cousins. However my attempts at finding work in Israel were not so successful. This was a period when a new university was being set up in Haifa, and I was interested in a position there. I talked to those responsible for setting up a biology department and was more or less promised a position once the new director of biology came from Wisconsin. I argued (rather naively considering I was a junior assistant professor) that I had experience of Israel, and was willing to make sacrifices and accept a position now. I knew how tough Israel was as a place to live, which the guy from Wisconsin did not. I left at the end of the summer with some hopes that a job would materialize and we would move back. There were a number of obstacles in setting up a department of biology at Haifa University, the main one being the opposition from the Haifa Technion. The faculty of the Technion considered themselves very high powered (true) and did not want competition. Thus negotiations between the two bodies dragged on. The department of Biology at Haifa was not founded until 1971 and then called Evolutionary Biology. The medical school, which was going to be attached to this university was shifted to the Technion. Thus my attempt at moving at this time fell through. I think the main reason was that the individual hired to head the department left Israel after a few months. I might have found a position if I had been more persistent. It is interesting that in the last few years I have re-established contact with Haifa University and have given talks in the Department of Evolution. Also that summer of 1968, a year after the Six Day war, Israel was economically in bad shape although the moral was very high.

This was an interesting summer. There were many expeditions from the Institute into the newly liberated or now referred to as the West Bank, or Judea and Samaria areas of the country, giving us an opportunity to see archaeological sites previously closed. I remember one tour to Herodium the site of Herod The Great's winter palace in the desert of Judea. His tomb has recently (2016) been excavated at the site. It was quite safe to go into the " West Bank", and there was a lot of travel between this part of Israel and the " original Israel", mostly organized by the Israeli Nature Preservation Organization. Israelis flooded into the Arab cities to shop, drink coffee, and there was little obvious enmity. We took a number of trips of this nature, including one to a Bedouin encampment in the South of the country.

If a job had materialized I believe we would have returned to Israel. Even later, during a second Sabbatical in the 80's we considered the possibility of living on a moshav, a collective village, but by that time we were considered too old! The pull of Israel was always there, but we remained in Bloomington. I think it was the fear of bringing up children in Israel, with the constant threat of war that swayed us to stay in the USA.