Mammals, Milk, Molecules, and Micelles

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Abstract

After a brief description of my family background and school days, my professional career as a dairy scientist is described under three headings: research, teaching, and writing. My research activities fall into four areas: biochemistry of cheese, fractionation and characterization of milk proteins, heat stability of milk, and dairy enzymology. Finally, I offer some advice to young scientists.

SCHOOL YEARS

I was born on November 20, 1937 and reared on a dairy farm near Mitchelstown, County Cork, Ireland; my ancestors had farmed there for more than 200 years. Although Ireland was not involved in World War II, it did suffer shortages, especially of manufactured goods and foods not produced in Ireland, which were rationed until the early 1950s. As with most Irish farmers at that time, my family was self sufficient in the principal foods, so although we lacked luxury foods, we did not suffer from malnutrition. Because coal was not available, peat was used as a substitute. However, there are no peat bogs in the Mitchelstown area, forcing us to harvest poor-quality peat from the local low hill. We depended on oil lamps and candles for light (electricity was not available in rural Ireland until the early 1950s). Although the 1940s were not a nice period in Ireland, life there was often better than in most of Europe at that time.

I attended a small (approximately 80 students and 2 teachers) local primary school (Knockadea) from 1943 to 1950. Like my schoolmates, I was not very studious and preferred outdoor pursuits to reading; however, my grandmother ensured that I did my homework. I helped on the farm from an early age and did work such as hand-milking cows, feeding calves, and tending to pigs and hens.

In 1950, I transferred to a secondary school at Mitchelstown, to which I cycled approximately eight kilometers on a poor-quality road in all sorts of weather. The transition to secondary school involved larger classes, new subjects, and specialized teachers (some of whom were not very stimulating). At my first Christmas tests, I came out at the top of the class, a position I maintained throughout my five years in secondary school. The school was relatively small and at that time had a high attrition rate (not unique to this school). From a class of approximately 45 in my first year, only six completed the five-year course. Students dropped out for various reasons, especially on reaching the school-leaving age (14 years at that time), and took up trivial jobs or eventually emigrated to the United Kingdom or the United States. Our school was not very distinguished academically, athletically, or socially, and some students transferred to more prestigious schools. It was an all-boys school (as most Irish secondary schools still are), but we managed to meet the girls from the neighboring all-girls school.

During the course of my secondary schooling, I would have taken up farming as a career, and my father would have been happy for me to do so, but my mother, and especially my grandmother, did not approve of me going into farming, which was reasonable, considering that I had performed reasonably well at school and was the oldest of eight children, including two younger brothers, who did take up farming. At the National (School) Leaving Certificate Examinations at the end of secondary school, I achieved good results and could have chosen any university or other program I wished.

UNIVERSITY DAYS

At that time, there was little advice on careers; I do not recall any in-depth discussions on careers, but I registered at University College, Cork (UCC) in October 1959 to study for a Bachelor of Science (BSc) degree in Dairy Science. Ireland has a long history of dairying, especially in the production of butter, most of which was exported through the Cork Butter Market, established in 1760 to coordinate the export of butter. Starting around 1860, buttermaking technology underwent a series of improvements, and schools were established throughout northern Europe to train farm buttermakers. Such schools were established at Cork and Dublin in 1880. Buttermaking worldwide changed suddenly from a farm-based to a creamery-based industry following the development of the centrifugal separator by Gustav de Laval in 1878. Industrialization of buttermaking

created the need for suitably qualified personnel to manage creameries. A six-month course for creamery managers was introduced at Cork and Dublin in 1893. This course was extended and improved progressively and moved to the Royal College of Science for Ireland (RCScI; a technological university), Dublin in 1915. In 1924, the RCScI was transferred to University College, Dublin, but the Creamery Managers' Course was transferred to UCC, where a Faculty of Dairy Science was established in 1924. The Creamery Managers' course was designed to train managers for cream-separating stations and small central creameries where butter was manufactured. To meet the need for more in-depth trained personnel, a four-year course was established at the RCScI in 1915, and this course, leading to a BSc in Dairying, was also transferred to UCC.

The first year of this course consisted of mathematics, applied mathematics, physics, chemistry, and a language; surprisingly, biology was not included. At the end-of-year examinations, I obtained good results and placed third in my class. A component of the BSc in Dairying course was 20 weeks work placement, spread over the summer vacations. I obtained a placement at a small local cooperative creamery, Garryspillane. On my first day on the job, the manager gave sledge hammers to me and another student, and set us to break up a concrete floor in preparation for the installation of a new pasteurizer—this was valuable experience for a budding dairy scientist! Things improved thereafter, and I learned the basics of the Irish dairy industry.

The second year of the course consisted of chemistry, electrical engineering, and civil engineering (still no biology); presumably, the engineering elements reflected the need that a small creamery should be as self sufficient as possible. Practicals in engineering included free-hand drawing and metalwork. I retained third place in the class at the summer examinations in 1957. During summer 1957, I spent a few weeks at a factory in Coleford, Gloucestershire, England, which produced the blackcurrant juice product Ribena. This was my first overseas travel, and it included new experiences [living in a POW camp, drinking crude cider (scrumpy), and visiting Tintern Abbey (the ruins of a magnificent abbey razed by Henry VIII)]. However, I spent most of that summer in Ireland, managing a traveling creamery, a small cream-separating station mounted on a truck, serving small, widely dispersed milk suppliers in southwest Ireland.

Our third year at UCC consisted of courses in dairy technology, dairy bacteriology, dairy engineering, physical chemistry, accounting, economics, and dairy husbandry. I spent the summer of 1958 at various dairy factories: Wall's ice cream factory in Acton, London, the branch creamery of Garryspillane, the cheese (natural and processed) factory of Mitchelstown Co-op, and the Condensed Milk Company in Limerick, which produced concentrated and powdered milk.

The fourth year of the course consisted of dairy chemistry, dairy bacteriology, dairy technology, economics, and accounting. These courses included long, and not very efficient, practicals. At the summer examinations in June 1959, I placed at the top of the class. In Ireland, a professor from a foreign university is involved in each subject as an extern examiner. In Dairy Technology, the extern examiner gave each student a very thorough oral examination, and I believe that I scored very well at that examination, which I attribute to my wide-ranging work placements.

Following the results of my final examination, I decided to undertake postgraduate studies in microbiology. I approached Professor Michael Grimes. However, he was about to retire and was not accepting new postgraduate students. He suggested that I speak to Frank Kosikowski, Cornell University, Ithaca, NY, who was a Fulbright Fellow at UCC in 1958–1959. Professor Kosikowski (Kosi) arranged for me to start on a PhD program at Cornell in August 1959. During that summer, I did relief work at Mitchelstown Creameries; one day, the general manager told me that the manager of their largest branch was about to leave and asked if I was interested in the position. I told him about my plans to go to the United States, and he said, "Go West, young man," which I did.

POSTGRADUATE STUDIES

In August 1959, I left for the United States. My parents probably would have preferred that I took the job at Mitchelstown Creameries, but they raised no objections. At that time I had done very little foreign travel, just two brief periods in England and in both cases with friends; I had never been on a plane. My parents and 82-year-old grandmother accompanied me to Shannon airport to see me off (I presume that they felt like millions of Irish parents during the previous century who saw their children emigrate). In this, the prejet era, the flight from Shannon to New York took about 20 hours, with a fueling stop at Gander, Newfoundland. Idlewild (now JFK) airport is an intimidating place even for an experienced traveler, but I passed through immigration and customs and took a shuttle bus to the Port Authority Bus Terminal, where I boarded a Greyhound bus to Ithaca, NY. I remember being very impressed by the road system in New York and New Jersey and the skyline of Manhattan. At that time there were approximately 20 Irish postgraduate students at Cornell [mainly in Agriculture], one of whom, Tony O'Sullivan, a Dairy Science graduate from UCC, offered me temporary accommodation in an apartment shared by five Irish students at 208 William Street. One of the occupants returned to Ireland shortly after I arrived, and I replaced him. I spent the next five years in that appartment, with a series of housemates.

The day after my arrival, following a quick tour of the campus with Tony O'Sullivan, I met Professor Kosikowski at the Department of Dairy Industries (changed to the Department of Food Science a few years later). Cornell is a very picturesque campus situated on a hill between two deep gorges and overlooking one of the Finger Lakes, Cayuga (the college anthem goes: Far above Cayuga's water, there's an awful smell, some say it's Cayuga's water, we know it's Cornell). Cornell is mainly a private university (Ivy League) founded in 1865, with four state colleges (at that time called Agriculture and Life Sciences, Veterinary Science, Home Economics, and Industrial and Labor Relations) attached. Its College of Agriculture is regarded as one of the best in the United States, especially in Animal Sciences. The Head of the Department of Dairy Industries, which was established in 1902, was D.F. Holland; other staff were F.V. Kosikowski, B.L. Herrington, F.W. Shipe, V. Krukowski, W.K. Jordon, Jim White, and Dick Marsh. Two well-known retired members, A.C. Dahlberg and E.S. Guthrie, frequented the Department.

At an early meeting, Kosi outlined my academic program. I was to concentrate on coursework for the first year. Kosi, who was familiar with my background, advised that I should major in Dairy Science (later Food Science), with minors in Biochemistry and Microbiology. He felt that I had an adequate knowledge of dairy science and technology and recommended that I take only his own course on cheese, for which I was also a teaching assistant (TA). I also took a postgraduate-level course on dairy chemistry by B.L. Herrington, which involved reading and discussing *Principles of Dairy Chemistry* by R. Jenness and S. Patton, published in 1959. I served as a TA for eight of the ten semesters I was at Cornell, three times for Kosi's cheese course and five for B.L. Herrington's Analytical Methods course.

I had no problem achieving the required grades in coursework and was happy to take a range of undergraduate and postgraduate courses in microbiology and biochemistry. As I progressed, my preferences shifted from microbiology to chemistry, and I took courses in organic, analytical, and physical chemistry.

Although research was a minor part of my program during the first two years, I was associated with and assisted senior postgraduate students and became familiar with a range of analytical techniques. My first publication (Fox 1963) arose from such work. For various reasons, I had to determine the salt (NaCl) content of cheese frequently, using a modification of the Volhard titration, which is laborious and smelly. In the Analytical Methods course, for which I was TA, we studied various potentiometric titrations, including for halides. It occurred to me that it might be

possible to use a potentiometric titration for the determination of NaCl in cheese. I investigated this principle, and it proved to be very satisfactory. The potentiometric method is now a standard International Dairy Federation (IDF)/AOAC method for determining the salt content of cheese. I think that I have always been good at recognizing opportunities for research, of which this is an early example.

Around 1960, Kosi's group was involved in two main areas: cheese flavor and a bioassay for antibiotics in milk. Kosi had been studying cheese flavor for several years, especially proteolysis and amino acid catabolism. By 1959, with Dick Scarpillino and Bob Hall, he was using gas chromatography (GC) to study the volatiles in cheese. I became fairly adept with GC and considered developing a research project using GC to study cheese ripening, but Kosi discontinued this work.

In approximately 1960, the United States Department of Agriculture (USDA) permitted the treatment of cheesemilk with H_2O_2 as an alternative to heat treatment. Kosi disapproved of this and was interested in developing a method to detect milk that had been treated with H_2O_2/catalase (when present, H_2O_2 could be detected using any of several redox indicators, but this approach was not applicable when the H_2O_2 had been reduced by catalase). He asked me to take on this project. Essentially, the project became a study of the effects of H_2O_2 on various chemical and physicochemical properties of milk. Although we did not develop a method for the detection of H_2O_2/catalase-treated milk, I did learn a number of useful techniques and worked for the first time on milk proteins, which have been the focus of most of my research for the past 45 years. The results of my work were published in Fox & Kosikowski (1967). I have often thought that it would be interesting to repeat this work, using the better techniques now available, but I never did.

In early 1964, I decided that I had done sufficient work for a PhD thesis, and I started writing. When I presented a draft of my thesis to Kosi, he was not impressed; he said, "You come from a country that has produced many famous writers, now go and emulate them"—I have been trying to do so since, with some success. Eventually, I got my thesis into an acceptable form and arranged for my PhD examination, which went well. κ-Casein was discovered in 1956 by von Hippple & Waugh, who proceeded to explain the colloidal stability of milk and to develop a model of the casein micelle. I have always been fairly conscientious about reading the literature (and still impress on my students the need to do so) and had recently read Waugh's publications on the casein micelle—at the viva voce, I spoke eloquently on the casein micelle, which, I believe, impressed my examiners. The structure and properties of the casein micelle are still active areas for research. I have kept abreast of this work and have written occasionally on the subject (e.g., Fox & Brodkorb 2008).

In early 1964, Kosi received a Public Health Service grant to investigate the effectiveness of bactofugation to reduce the bacterial population in cheesemilk; he asked me to undertake the study as a research assistant. I spent about four months on the project, which showed that bactofugation is very effective (Kosikowski & Fox 1968). This was the first publication on the use of bactofugation to decontaminate milk, a technique which is now widely used, especially for Swiss-type cheese, to remove *Clostridium tyrobutyricum*, which causes gas blowing, as an alternative to nitrate.

In addition to being professionally fruitful, the five years I spent at Cornell were very enjoyable. Notable events included drinking beer at the Palms bar in Collegetown, parties at 208 William Street (and elsewhere), dating girls from Cornell, Wells College, and Cortland Teachers College, occasional visits to the Irish club (AOH) at Syracuse and to New York City, Boston, the Gettysburg battlefield, and Washington DC, as well as dinner at Thanksgiving, Christmas, and other times with staff members or married postgraduate students. I attended annual meetings of the American Dairy Science Association (ADSA) at the University of Maryland and at the University of Arizona, Tucson, where I gave my first public oral presentation [I made a very interesting journey by car

from Ithaca to Tucson with a Professor of Dairy Husbandry and his wife; I returned from Tucson to East Lansing with three graduate students from Michigan State University (MSU), in about 30 hours of continuous driving].

GOING FURTHER WEST

In early 1964, I successfully applied for a postdoctoral position with Dr. Hans Lillevik, Biochemistry Department, MSU, East Lansing, scheduled to commence in September 1964. After completing my PhD, I returned to Ireland in May 1964 for a vacation and to assess job prospects. I took interviews with the Irish Dairy Board (no offer) and with the (State) Agricultural Institute [An Foras Taluntas (AFT)]. I worked on the bactofugation project from May to August and planned to go to MSU early in September. Shortly before I was due to go to MSU, I received an offer from AFT for a research position at their Dairy Research Center at Moorepark; I requested a postponement (which I received) and went to MSU, which was a good move. [During my postdoc at MSU and subsequent postdoc at the University of California-Davis (UC Davis), I got hands-on experience of several valuable research techniques, became familiar with other aspects of dairy chemistry and became generally more confident as a result of a successful outcome to my research.]

The Department of Biochemistry at MSU had recently been formed; Dr. Lillevik had been a member of the chemistry department, where I was based for a few months, awaiting completion of a new biochemistry building. Lillevik was basically a physical chemist who had worked with Leroy Palmer at the University of Minnesota, St. Paul, and done a postdoc with K. Linderstrom-Lang at the Carlsberg Laboratories, Copenhagen. He was a very interesting, philosophical character, with a very disciplined approach to research. My project was to improve methods for the isolation of individual caseins. Lillevik collaborated with Bob Brunner in the Department of Food Science, whose students were working on the isolation and characterization of several minor milk proteins. I had many interesting and stimulating conversations with Lillevik and Brunner, and learned to do starch gel electrophoresis (recently developed), free boundary electrophoresis, anion exchange chromatography, and analytical ultracentrifugation.

I attended the 1965 annual meeting of the ADSA in Lexington, Kentucky and made an oral presentation. I believe I impressed a group of professors from UC Davis who were recruiting a young dairy chemist to replace the recently retired Dr. Gene Jack. I had a number of discussions with them, as a result of which they encouraged me to apply for the position at Davis. I declined to do so immediately but accepted a postdoctoral position with Dr. Nick Tarassuk at UC Davis on the isolation of lipase from milk and agreed to discuss the matter again after six months.

I returned to Ireland in late August 1965 and was married on September 11 to an Irish girl, Olive Lenihan, whom I had first met in New Jersey and later in Chicago, where she was a nurse. We returned to the United States on September 12 and set off by car from Chicago to Davis, stopping off at various places along the way.

Tarassuk had been working on milk lipase for many years. In 1965, he had a postdoc, M. Yaguchi, who had done a PhD on lipase with Tarassuk and was convinced that κ-casein had lipase activity because they coeluted from DEAE-cellulose. Yaguchi was about to leave Davis to take up a position at the National Research Council, Ottawa, Canada, and I was to replace him. Basically, my job was to confirm or refute the κ-casein hypothesis. I had a fortunate break, as A.G. Mackinlay and R.G. Wake of the University of Sydney had just published a paper describing a new method for the isolation of κ-casein, using the mild dissociating agent, dimethylformamide, in DEAE chromatography. Using this chromatography system, I succeeded in separating lipase from κ-casein and eventually isolated a homogeneous preparation of lipase, which we characterized (Fox et al. 1967, Fox & Tarassuk 1968, Patel et al. 1968). I failed to recognize that milk lipase is the

lipoprotein lipase (LPL) of blood serum (in 1962, E.D. Korn showed that milk contains a LPL which was studied in detail by T. Olivecrona and collaborators in the 1970s).

After six months at UC Davis, the search committee asked if I had reached a decision; I replied that, for better or worse, I had decided to return to Ireland, which I did on January 1, 1967. I often wonder if I made the best decision—certainly, I would have had better facilities at UC Davis, not just in my own laboratory but also elsewhere in the department and in the university generally. A university like UC Davis has many major advantages over Moorepark or UCC, including great libraries and experts on various topics, not just at UC Davis but even more so at its sister university at Berkeley. However, I have no regrets.

ESTABLISHING A RESEARCH CAREER IN IRELAND

AFT was established in 1958 by the Irish government, which transferred some research facilities from the Department of Agriculture to AFT and established some new centers. One of the latter was the National Dairy Research Center (NDRC) at Moorepark, which was established on a large estate about 40 km from Cork that had been a British Cavalry base from 1890 to 1922. The NDRC comprised five departments: Dairy Husbandry, Dairy Chemistry, Dairy Microbiology, Dairy Technology, and Pig Husbandry. I was assigned to the Dairy Technology Department, of which Tony O'Sullivan was head. Moorepark was established on a greenfield site and by 1967, the facilities were still very rudimentary; when I joined, the Dairy Technology Department was housed in a Nissen/Quonset hut, but we moved into new laboratories in September 1967.

Although the lack of equipment and a very poorly stocked library were major problems, there was a very good pioneering spirit at Moorepark, and I managed to get some research projects started, including a search for rennet substitutes, factors that affect the proteolysis of caseins by rennet, and the dissociation of casein micelles by urea and their reformation on removal of the urea by dialysis (Fox 1969a,b, 1970; Fox & Walley 1971a,b; McGann & Fox 1974). This work showed that bovine pepsin is a very good rennet substitute and was used widely, alone or mixed with chymosin, until the introduction of fermentation chymosin in approximately 1990 [which I also assessed (O'Sullivan & Fox 1991)]. The reformation of casein micelles from urea-treated milk was quite a clever idea that I regret not pursuing. Much later, we investigated the dissociation and reformation of casein micelles from ethanol-treated milk (O'Connell et al. 2001, 2003) or by pH adjustment.

As the mission of AFT, including the NDRC, was to improve Irish agriculture, we were expected to do some applied work. I got involved with cheese factories, in whey utilization and especially in the manufacture and use of casein. After attending an IDF symposium on casein and caseinates in Paris in 1967, I decided that I would try to develop these products in Ireland, where at that time there was only one small factory making rennet casein for the manufacture of plastics. I wrote a monograph on casein and caseinates (published by AFT) and discussed casein production with several dairy companies, including those that became Glanbia and Kerry Foods. I like to think that I had some influence on the development of the modern casein industry in Ireland, which is now one of the principal global manufacturers of functional protein products.

PROFESSOR OF FOOD CHEMISTRY

In 1969, Professor G.T. Pyne in the Dairy Chemistry department at UCC retired. He had joined the Faculty of Dairy Science, UCC, upon its foundation in 1924 and served as lecturer and later as Professor of Dairy Chemistry. He did excellent research on milk proteins and milk salts (his work on milk salts is still cited), but he never built up a significant research group and never

invested much in equipment—he relied on ideas rather than on equipment. For his work on the heat stability of milk, he used a saucepan with an oscillating device made from the motor of an old record player, heated by a micro-Bunsen burner controlled by a technician and heat-sealed glass vials prepared by his technician from glass tubing; he was a good example of quality over quantity. He was quite active in university politics and frequently served as Deputy President.

Starting in 1960, UCC changed from Dairy Science to Food Science and following Pyne's retirement, the Professorship of Dairy Chemistry was changed to Professor of Dairy and Food Chemistry [and in 1987 to Food Chemistry]. There were six applicants for the Professorship, two others of whom had also worked on milk lipase but failed to isolate it due to its strong association properties. I was appointed and took up office on October 1, 1969 at the age of 32 (one of the youngest Professors appointed by UCC).

The department I inherited had two technicians, no postgraduate students, limited laboratory space, very little equipment, and two lecturers, one of whom, D.T. McSweeney, also served as Supervisor of Examinations; the other was Patrick Morrissey (also appointed on October 1, 1969), who had recently been awarded the PhD degree for work on the rennet-induced coagulation of milk under Pyne's supervision. Classes commenced a few days after my appointment, and my primary initial task was to keep ahead of lectures and practicals. This task was made more challenging, as I included lectures on the structure and biochemistry of muscle and meat, which required much reading.

Three postgraduate students registered in 1970 and commenced work on (*a*) the isolation and characterization of pepsins (O'Leary & Fox 1973, 1974, 1975; Fox et al. 1977), (*b*) proteolysis in cheese (Fox & Guiney 1973, Phelan et al. 1973), (*c*) fractionation of caseins (Fox & Guiney 1972), and (*d*) heat stability of milk (Frank O'Mahoney, supervised by Pat Morrissey). In subsequent years, Pat took over the meat area, which he developed to a high level, and I took over work on the heat stability of milk.

Gradually, the situation regarding equipment improved. Laboratory space was very restricted until 1979 when the Food Science faculty moved into a new building, which permitted the intake of increased numbers of undergraduate and postgraduate students and an increase in research activity. Laboratory facilities were increased again in 1993, resulting in another surge in student numbers.

In comparison with the United States and many European countries, money for research at Irish universities was very limited. We piggybacked on grants made available by the university for teaching, and by carefully selecting projects, we survived. European Union (EU) funds became available after approximately 1980, and in 1995 the Irish Department of Agriculture and Food, for the first time, earmarked substantial grants for food research, but by then it was too late for me!!!

Throughout my career, I worked on four main areas: cheese biochemistry, milk proteins, heat stability of milk, and food enzymology; summaries of my contributions in these areas, with selected references, are given below.

Cheese

Arising from my association with Dr. Kosikowski, because of the potential of cheese as a research subject, the importance of cheese to the dairy industry (about 35% of all milk), and its desirable organoleptic, convenience, and nutritional properties, cheese has been the principal subject of my research since the 1960s. I have published about 180 research papers, 70 reviews (e.g., Fox et al. 1996a,b; Hayaloglu et al. 2002) and seven books [*Fundamentals of Cheese Science* and *Cheese: Chemistry, Physics and Microbiology* (a two-volume book in its third edition)] on the science and

technology of cheese. The principal aspects on which I have worked, with selected references, are:

1. Rennet substitutes were one of my early projects, on which work continued for several years (Fox 1969b; Fox et al. 1977; O'Leary & Fox 1973, 1974, 1975; O'Sullivan & Fox 1991; Bansal et al. 2009).
2. Methods for quantifying proteolysis in cheese. Some of the methods developed are widely used and have attained almost standard methods status (Kuchroo & Fox 1983, Kuchroo et al. 1983, Shalabi & Fox 1987, Folkertsma & Fox 1992, O'Shea et al. 1996, Pripp et al. 2000).
3. The contribution of various agents to cheese ripening: rennet, indigenous milk enzymes, starter lactic acid bacteria (LAB), nonstarter LAB (NSLAB), and secondary microorganisms. To study the contribution of each of these, we developed or modified methods for producing NSLAB-free cheese, starter-free cheese using gluconic acid-δ-lactone to acidify the curd or rennet-free curd by inactivating the residual rennet in the curd by increasing the pH or using specific inhibitors [pepstatin or α_2-macroglobulin (in blood serum)] (O'Keeffe et al. 1978; Farkye & Fox 1991; Shakeel-ur-Rehman et al. 1998a,b; Bansal et al. 2010).
4. Cheese-related microorganisms (Mullan et al. 1981; Farkye et al. 1990; Law et al. 1992, 1993; Wilkinson et al. 1994, McGarry et al. 1994; O'Donovan et al. 1996; Fernandez-Espla & Fox 1998; Lynch et al. 1999; Brennan et al. 2001, 2002)
5. NaCl is critical for cheese ripening and quality; we studied the following aspects: variations in the concentration and distribution of NaCl in cheese, correlation between salt concentration and cheese quality, factors (physical and compositional) that affect the diffusion of salt in cheese curd, and the influence of NaCl on the growth of *Penicillium roqueforti*, *Penicillium camemberti*, and *Lactococcus* spp. in cheese and on the quality of Cheddar, Blue, and Camembert cheese (Godinho & Fox 1982; Guinee & Fox 1984, 1986, 2004; Morris et al. 1985).
6. Specificity of chymosins, pepsins, plasmin, and microbial rennet substitutes on individual caseins (Mulvihill & Fox 1979b, McSweeney et al. 1993).
7. Identification of the large water-insoluble and small water-soluble peptides in Cheddar cheese; about 200 peptides were identified (Singh et al. 1995, Mooney et al. 1998, Fernandez et al. 1998).
8. Intervarietal comparison of cheese (Hewedi & Fox 1984; Madkor et al. 1987; Zarmpoutis et al. 1997; Gobbetti et al. 1997b, 2002; McGoldrick & Fox, 1999; Hayaloglu et al. 2005; Di Cagno et al. 2007; Vernile et al. 2009; Bansal et al. 2009).
9. Acceleration of cheese ripening by elevating the ripening temperature or adding exogenous enzymes; production of enzyme-modified cheese (Folkertsma et al. 1996; Wallace & Fox 1997; Shakeel-ur-Rehman & Fox 2002; Kilcawley et al. 1998, 2006).
10. Rennet-induced coagulation of milk (Huppertz et al. 2005, O'Connell et al. 2006, Bansal et al. 2007).
11. Factors that affect the quality of cheese (Gobbetti et al. 1999; Shakeel-ur-Rehman et al. 2000, 2004; Guinee et al. 2002).

Heat Stability of Milk

In comparison with other biological systems, milk is very heat-stable, which allows heat sterilization without major physical changes. Unconcentrated milk withstands all commercial heat treatments, but the stability of concentrated (>2×) milk is marginal, as a result of which sterilized concentrated (evaporated) milk was not commercialized until 1884 (by Thomas Myenberger); attempts to do so by Nicolas Appert in 1809 and by Gail Borden in 1856 were unsuccessful. The variability

and unpredictability of the heat stability of milk were of concern to the dairy industry in the nineteenth century, but the first published work on the subject was by Sommer & Hart in 1919. In the early twentieth century, evaporated milk was an important product in Ireland and was one of the research areas of G.T. Pyne; I continued these investigations. The study of heat stability was attractive because, in addition to being commercially important, it is fundamentally interesting and challenging but because few laboratories have been involved, progress is slow and simple equipment is sufficient (progress depends more on ideas than on equipment).

Aspects investigated included variability, correlation with compositional factors, interspecies (bovine, ovine, caprine, equine, porcine, and human milk) comparison, each of which has a distinctive HCT-pH profile (Fox & Hoynes 1975, 1976), effect of various additives (phosphates, polyvalent organic acids and their salts, amides, including urea, and carbonyls, including sugars and polyphenols) on heat stability (Shalabi & Fox 1982; Tan-Kinita & Fox 1996; O'Connell & Fox 1999, 2001b; O'Sullivan et al. 2002) and the mechanism of the maximum-minimum in the HCT-pH profile (Fox 1981, Mohammed & Fox 1987, Singh & Fox 1987, O'Connell & Fox 2001a). I published 60 research papers on the heat stability of milk and reviewed the literature three times (Fox & Morrissey 1977, Fox 1982, O'Connell & Fox 2003). Singh & Fox (1987) and O'Connell & Fox (2001a) proposed that the pH dependency of the heat stability of milk is due to the effect of β-lactoglobulin on the dissociation of κ-casein from the surface of the casein micelles; κ-casein-depleted micelles are sensitive to calcium-induced coagulation. In the pH range 6.5 to 6.9, β-lactoglobulin reduces the dissociation of κ-casein but increases pH to >6.9, thereby creating a maximum-minimum in the HCT-pH profile, and this hypothesis has been widely supported.

Milk Proteins

Most of my research has been on properties of milk proteins. In addition to work on cheese and the heat stability of milk, I have worked on the fractionation, isolation, interspecies comparison, and functional properties of milk proteins, the structure and properties of casein micelles, and the effect of high pressure on milk proteins. I have published approximately 60 research papers (e.g., see Fox & Morrissey 1972; Fox & Guiney 1972; O'Connor & Fox 1973; McGann & Fox 1974; Mulvihill & Fox 1979a; Murphy & Fox 1991; Lucey et al. 1996; O'Connell et al. 2003, 2006; Malin et al. 2001; Zobrist et al. 2005; Huppertz et al. 2006b) and 25 reviews (e.g., see Fox 2003, Huppertz et al. 2006a, Fox & Brodkorb 2008, Uniacke-Lowe et al. 2010) on milk proteins. Volume 1 of *Advanced Dairy Chemistry* is devoted to milk proteins.

I started the work on functional milk proteins (casein and caseinates) during the 1960s, when the transition from industrial to food-grade products occurred, and this area later became a major theme for our department, especially for Professor D.M. Mulvihill.

Although the lactoproteins of all species that have been studied are generally similar, there are large interspecies differences with respect to concentration, types, and properties. Sporatically, I have worked on the proteins of bovine, ovine, caprine, human, porcine, equine, asinine, canine, elephant, eland, wildebeest, and monkey milk. The proteins of equine and asinine milk are more like those of human milk than are ruminant milks and are attracting attention for the nutrition of human infants who are allergenic to bovine milk proteins (see Uniacke-Lowe et al. 2010). There are approximately 4500 species of mammal, but the milk of only about 50 species has been studied sufficiently for the data to be considered reliable. There is great opportunity for research on the milk proteins of various species, which is important from evolutionary and classification viewpoints, the nutrition of orphaned infants, the preservation of endangered species and, at least in some cases, the elucidation of commercially important properties.

Food Enzymology

Milk contains about 70 indigenous enzymes, which are important from the spoilage, stability, protection, or digestion viewpoints (see Fox & Kelly 2006). I became involved in enzymology when I worked on milk lipoprotein lipase at UC Davis; I have published 57 research papers and 31 reviews on various aspects of food enzymology and edited a two-volume book, *Food Enzymology*. I have worked on indigenous lipoprotein lipase, plasmin, cathepsin D, and the acid phosphatase of milk (Fox et al. 1967; Fox & Tarassuk 1968; Patel et al. 1968; Grufferty & Fox 1988a,b; Akuzawa & Fox 1998).

Microbial enzymes are important in several dairy products, and I have worked on the extracellular proteinases, peptidases, and lipases of *Pseudomonas fluorescens*, *Arthrobacter nicotianae*, *Brevibacterium linens*, *Corynebacterium variabilis*, *Lactococcus* spp., *Lactobacillus* spp., *Propionibacterium shermani*, and *Micrococcus* spp. (Stepaniak et al. 1982; Fox et al. 1989; Garcia de Fernandez & Fox 1991; Requena et al. 1993; Gobbetti et al. 1995, 1997a, 2001; Baral et al. 1995; Stepaniak & Fox 1995; Rattray et al. 1996, 1997; Rattray & Fox 1997; Fernandez-Espla & Fox 1997; Fernandez-Espla et al. 1997; Smacchi et al. 1999).

Exogenous enzymes are used widely in the processing of foods, including milk (see Fox 2002). The principal exogenous enzymes I have worked on are rennet substitutes, proteinases, and lipases for the acceleration of cheese ripening, and proteinases and transglutaminase to modify the functional properties of milk proteins.

TEACHING

Teaching is an integral part of the work of a university professor, and when I joined UCC, teaching (lectures and practicals) was the principal part of the job. During my career as Professor of Food Chemistry, I taught courses such as Introductory (General) Chemistry, Analytical Methods in Chemistry, Chemistry of Food Constituents, Food Analysis, Dairy Chemistry, and Food Enzymology. My lecturing style varied with the level of the course. I tried to introduce a tutorial system, but the students disliked it, perhaps because they had too many courses to cope with. For students taking Food Chemistry in their final year, I introduced a library project on an assigned topic and a minor research project instead of set practicals. These projects are now integral parts of food science and technology courses at UCC. I enjoyed formal teaching, and I believe the students appreciated my style and effort.

I regarded research as an aspect of teaching (if my research generated some commercially useful results, that was a bonus, but it was not the primary objective). I supervised about 65 MSc theses, most of which were published. Most of these graduates work for Irish food industries, but some are spread around the world. I supervised the research of 35 PhD candidates (some jointly with colleagues) and about 15 postdoctoral fellows. A high proportion of my PhD students and postdocs have entered academic life at universities or research institutes in Ireland, the United States, Australia, New Zealand, Netherlands, Norway, Spain, Italy, Greece, Egypt, South Africa, Japan, and Iraq; some of these have been very successful and are highly ranked by the ISI. It is very gratifying to me that many of my students are in academic positions—they are my academic progeny who continue my research and teaching work.

WRITING AND EDITING

In the course of my academic career, I have written extensively. In addition to approximately 350 research papers, I have written 170 reviews, coauthored two textbooks, and edited or coedited

30 books, some of which are in the third edition. I was one of the founding editors and served as one of the editors for eight years of the *International Dairy Journal*, one of the leading journals for dairy science and technology.

I became involved in the publication of textbooks by accident in 1980, when I met George Olley of Applied Science Publishers at a symposium. In the course of our discussions, George asked if I thought that there was a need for a textbook on dairy chemistry, to which I replied yes. He asked if I would edit it, and I agreed, thus beginning 30 years in book preparation. The principal themes have been: *Advanced Dairy Chemistry* (three volumes, three editions); *Cheese: Chemistry, Physics and Microbiology* (two volumes, three editions); *Food Enzymology* (two volumes), written for postgraduate students, lecturers, and researchers and the leading books in the field; and the *Encyclopedia of Dairy Sciences* (four volumes, two editions), intended for undergraduates and anybody interested in reading around their area of specialization in the general area of dairy science and technology. I have also coauthored two undergraduate textbooks, *Dairy Chemistry and Biochemistry* and *Fundamentals of Cheese Science*, based on my lecture courses at UCC.

OTHER ACADEMIC ACTIVITIES

As a visiting professor, I have given lectures on Dairy Chemistry at the University of California, Davis; Agricultural University, Uppsala, Sweden; Massey University, Palmerston North, New Zealand; the University of Minnesota, St. Paul; University of the Orange Free State, Bloemfontein, South Africa; the University of Wisconsin, Madison; Escola Superior Biotecnologia, Porto, Portugal; Northeast Agricultural College, Harbin, China; National Agricultural University, Vicosa, Brazil; University of Campinas, Brazil; University Complutensa, Madrid, Spain; Universidad Nacional del Litoral, Santa Fe, Argentina; California Polytechnic State University, San Luis Obispo, California; the University of Melbourne, Australia; University della Basilicata, Potenza, Italy; South Dakota State University, Brookings.

I have served as Extern Examiner for PhD candidates at the Universities of Glasgow, Edinburgh, Strathclyde, Bradford, Reading, and Leeds; Agricultural University, Uppsala; Aarhus; Agricultural University, Wageningen; the University of the Orange Free State, Bloemfontein, South Africa; Massey University, Palmerston North, New Zealand; Agricultural University of Norway (Aas); and the University of Bourgogne, Dijon, France.

I was a member of the Permanent Committee of Commission F (Dairy Science, Nutrition, Education) of the IDF, 1977–1979 and President of IDF Commission F, 1979–1983. I served as a member of the Irish Council for Educational Awards, 1972–1980.

AWARDS

- Research and Innovation Award. (Irish) National Board for Science & Technology (1983)
- Miles Marschall Award of the American Dairy Science Association (1987)
- Medal of Honor, University of Helsinki (1991)
- Senior Medal, Agricultural & Food Chemistry Division, Royal Society of Chemistry, London (2000)
- Highly Cited Award of the Institute of Scientific Information; *In recognition of Prof Fox being the most highly cited researcher in Agricultural Science during the period, 1995–2002* (2002)
- International Dairy Federation Distinguished Service Award; *In recognition of an outstanding contribution to dairying, worldwide* (2003)
- Gold Medal, (UK) Society of Dairy Technology; only three such awards are made per decade (2007)

COMMENTS AND ADVICE

I am approaching the end of a fairly productive career in dairy science and technology as a teacher, researcher, and author. Several factors have made this possible; I would highlight the following and have the audacity to offer my experience as advice to young scientists.

- I have a reasonable level of intelligence, but at all stages I had classmates or colleagues who were brighter than me. I believe that the principal reason for my success has been that when I got an opportunity to improve my situation, I was in a position to avail of it and did so.
- At all stages of my career I had options; I believe that I made the correct choices and have no regrets.
- I have been an empirical scientist who relied on experimentation rather than on theory. In retrospect, I could, and perhaps should, have been more rigorous and quantitative. However, had I done so, my approach would have been narrower, and I would probably have overlooked or ignored many of the areas I did explore.
- I have had a long career, 47 years since my first publication. I did not suffer from burn-out; I still find research as exciting as when I started. I regard my research, and especially my writing, as a hobby. I like to work steadily and consistently and if possible to avoid pressure.
- I avoided administration as far as possible. As head of a small university department, a certain amount of administration was inevitable, but I did not make it my raison d'être. I did serve on some university and national committees, but I never found committee work attractive—too much discussion and compromise.
- During most of my career, facilities and resources available to me for research were very limited, yet we managed to operate a productive research program. An objective measure of this is that I was the most highly cited researcher in Agricultural Science, worldwide, during the period 1995–2002. Thirteen years after retiring, I am still ranked 67th in the ISI Highly Cited list of Agricultural Scientists.
- I believe that reading widely and keeping up to date with the relevant literature are essential. When I read a paper or attend a lecture, several ideas for research evolve. Kosi used to tell me that when one had a research idea, it was best to do the research first and then read the literature, presumably to guarantee originality. I do not know how Kosi's ideas evolved but I prefer to read the literature first—there is not much point in reinventing the wheel!
- I keep a fairly broad research base—if one's research area is too narrow, it will soon become essentially exhausted; also, students can be offered a choice.
- Endeavor to attract good postgraduate students, they will keep you young and fresh! A poor student requires more input for less output than a good student. Of course, this is a chicken-and-egg situation, good students look for well-established and active professors. I interacted closely with both undergraduate and postgraduate students and operated an open door policy.
- One of the more effective ways of attracting recognition is via the development of good/novel analytical methods—they are usually the most highly cited papers. Another route is via good critical reviews, which many researchers, especially young scientists, use as an introduction to a subject. At least some universities do not recognize reviews as publications for the purpose of promotion, which I find strange—it requires much more effort to write a good review than a research paper.
- Not everybody is equally good at writing but everybody can improve; work at improving your writing skills.
- Discuss science with colleagues within and outside your immediate environment.
- Avail of facilities and equipment in other departments/laboratories in your university or institute.

- If possible, work at interfaces; even work at interfaces between relatively closely related areas can be rewarding. Take up and apply new equipment and methods.
- Research is expensive in terms of personnel, facilities, and financial resources. It is a continuous struggle to find funding for university research. In comparison with other areas, e.g., military and medical, agriculture and food science are low-priority areas. Most research on agricultural and food science is done by national institutes and to a lesser extent by universities. The large international food companies, e.g., Nestle, Unilever, and Kraft-General Foods, have excellent research facilities, but these represent only a small proportion of the global food industry—most food is processed by small or very small companies that have little or no R & D facilities. In my experience, public funding for food research is becoming more industrially orientated. Obviously, this approach has certain benefits, which are probably short term. It seems desirable that some funds should be ring-fenced for more basic research in food science and technology, i.e., research that has no immediate application. Such basic research is best undertaken by universities.

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Errata

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