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14 November 1924 — 5 June 2021

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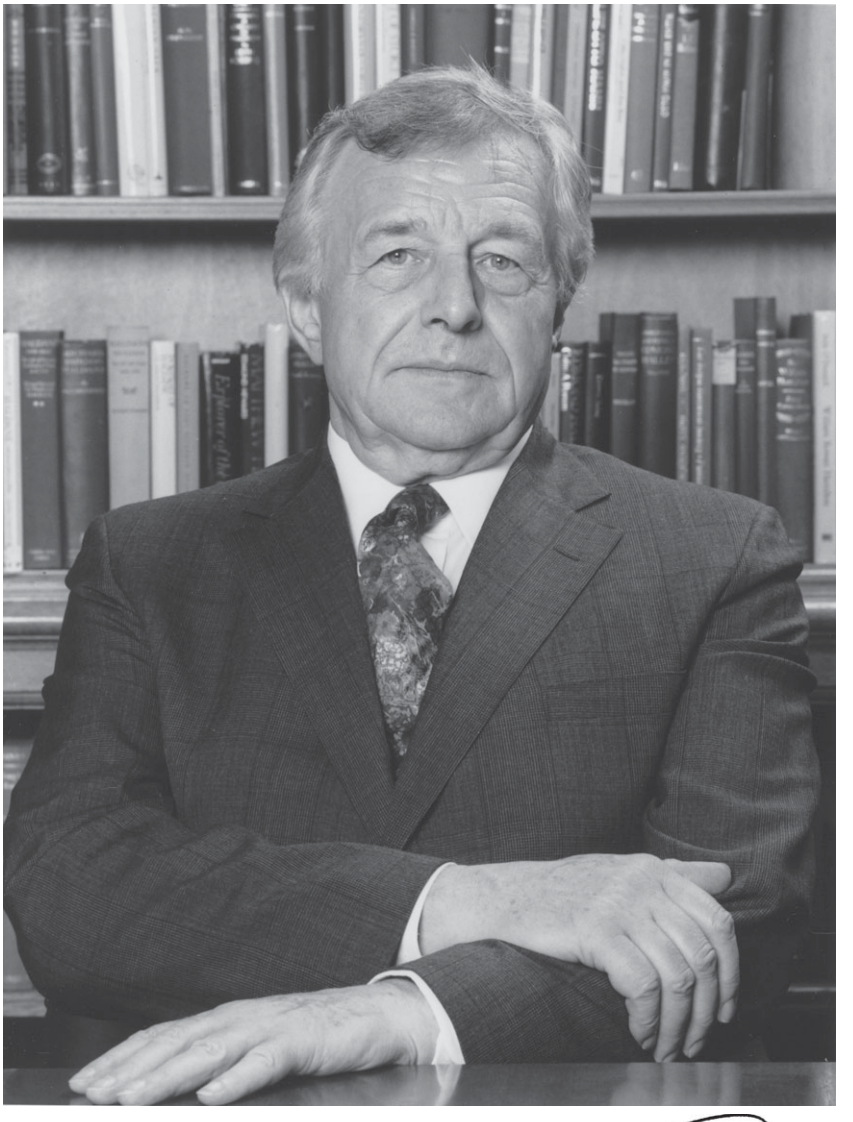

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WILLIAM JOSEPH WHELAN

14 November 1924 — 5 June 2021

Elected FRS 1992

By Angelo Azzi*

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William Whelan was an exceptionally celebrated scientist recognized equally for his work in research, education, publishing and international scientific organizations. He studied organic chemistry at the University of Birmingham. He taught at the University College of North Wales and the University of London and became head of the Department of Biochemistry of the Royal Free Hospital School of Medicine, University of London, in 1964. In 1967 he moved to the United States and served as professor and chairman of the Department of Biochemistry and Molecular Biology of the University of Miami Medical School for the rest of his career. Bill is known for his pioneering research on the structure of starch and glycogen. He discovered that glycogen contained the protein glycogenin, an enzyme with primer function in the synthesis of glycogen. This discovery filled a crucial gap in understanding the biosynthetic process that transforms glucose into glycogen. Bill's contributions, including his innovative methods for isolating and characterizing molecular structures like glycogen, have since become established scientific practices, and he established some of the fundamental concepts and nomenclature used in the carbohydrate field today.

Family, education, career

William Joseph Whelan (known as Bill) was born on 14 November 1924 in Salford, Lancashire, England. He was the oldest of four children of William Joseph and Antoinette Whelan. In 1914 Bill's father and grandfather went from Waterford, in Ireland, to Manchester, in England, where they found employment, and his father and mother met. His mother was a

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housewife and his father made skins for sausages. Educational opportunities had been denied to Bill's parents owing to family poverty, but they were offered to Bill. At age 11, he was bright enough to gain an entrance scholarship (though it did not cover the entire cost, which was partly paid by his father, though the family means were slim) to Stockport Grammar School, in the northwest of England, a venerable institution founded in 1487.

Bill had a slow start and was even put on probation, but then he improved and decided to take the science track. In 1940 he was taught by an inspiring teacher who made him fall in love with organic chemistry. Upon matriculation, Bill gained a distinction and was awarded a choice of scholarships. He accepted one by the Brewers' Society at the University of Birmingham (Department of Industrial Chemistry, which later became the Department of Biochemistry) and another one to study chemistry at the nearby University of Manchester. The head of the Department of Chemistry at Birmingham was Walter Norman (later Sir Norman) Haworth FRS, who was awarded the 1937 Nobel Prize in chemistry for elucidation of the structure of ascorbic acid. At that time, this was the premier place for research on carbohydarates in Britain. At the end of the academic year, Haworth invited Bill, among the more promising undergraduate chemistry students, to become an assistant (there was a shortage of technicians) to the graduate students in his research laboratory. During that time, Bill was engaged in the isolation of glucose 1-phosphate using potato phosphorylase and starch. Bill took a liking to enzymes and decided, given the opportunity, that this would be the direction to take in his PhD studies.

While pursuing his PhD in chemistry, Bill was assigned a classified project for the Royal Navy, intended to improve an antisubmarine device, that was a carbohydrate problem related to starch. In his studies, Bill applied enzymes to understand starch structure, but came to realize that he was using enzymes of unknown specificity on substrates of unknown structure, so he decided to employ a new column chromatography technique to make quantities of maltosaccharides of known structure, which then became model substrates for the actions of amylases, phosphorylase and other enzymes. Bill was subsequently regarded as a biochemist to the extent that the *Biochemical Journal* invited him to be an editor in 1952 and he was invited to join the Department of Biochemistry at the Lister Institute for Preventive Medicine in London in 1956. The Lister Institute at the time was one of the cradles of biochemistry and biophysics in Britain, with studies on the metabolism of carbohydrates and on enzymology. At the Lister Institute, Bill finally decided to get some formal training in biochemistry by taking an evening course at the Chelsea Polytechnic, taught by Rodney Porter (FRS 1964), who was to become a Nobel laureate in physiology or medicine in 1972. Bill received all his degrees (Bachelor of Science, Doctor of Philosophy and Doctor of Science) at the University of Birmingham. Later, the University of La Trobe, Australia, awarded him an honorary Doctor of Science degree.

At the first Federation of European Biochemical Societies (FEBS) meeting in London, in 1964, Bill met Feodor Lynen (ForMemRS 1975) (this Nobel Prize was again awarded jointly 1964 Nobel laureate in physiology or medicine), who then recommended him to the University of Miami administration as a candidate for the vacant chair of their Department of Biochemistry and Molecular Biology. In 1967 he accepted the appointment and emigrated to the United States. Bill's importance in putting the University of Miami's Department of Biochemistry and Molecular Biology on the map really cannot be understated. When he arrived there, no-one could have imagined that it would turn into the research centre of excellence that it is today. The high standards that he set, along with his love for science and

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encouragement of the next generation of researchers, played a fundamental role in making the department what it is today. He was instrumental in establishing highly innovative educational programmes at the University of Miami at the undergraduate, medical and graduate levels. Some of the programmes are still in practice.

Scientific research

The first chemistry studies

Samuel Peat was elected to the fellowship of the Royal Society in 1948, and almost simultaneously he was appointed to the chair of chemistry at the University College of North Wales at Bangor as successor to the distinguished chemist E. D. Hughes (FRS 1949). Peat took Bill with him from Birmingham, who was appointed to lectureships. The group of Bill, F. H. Newth and two research students concentrated their efforts on developing the work on starch-metabolizing enzymes that had been started in Birmingham, and created a rapidly growing research school that was soon recognized as one of the major centres of carbohydrate research. In that very year, 1948, Bill, working with Samuel Peat and his team, published an important paper titled 'Photochemical degradation of starch' in the journal *Nature* (1)*. This study shed light on the process of starch degradation through photochemical reactions. Owing to this early study on starch, fate determined that Bill would become a carbohydrate chemist and later a carbohydrate biochemist and a nutritionist.

Starch, a crucial food source for humanity, is found in various plant parts such as seeds, rhizomes, roots and tubers. It exists in the form of semi-crystalline granules, each possessing unique characteristics depending on the plant it originates from. While the size and shape of these granules differ among plant species, their internal composition exhibits strikingly similar features. They consist of growth rings, blocklets and both crystalline and amorphous lamellae. Starch granules are primarily composed of two polyglucans: amylose and amylopectin. Amylose has a relatively straightforward molecular structure, comprising glucose units linked by α-(1,4) bonds to form long chains with a few α-(1,6) branches. On the other hand, amylopectin, which makes up the majority of starch, shares the same fundamental structure but has shorter chains and numerous α-(1,6) branches. The chemical structures of amylose and amylopectin units are given in figure 1, and those of starch and glycogen in figure 2.

From chemistry to enzymology

Motivated by their initial success, Samuel Peat and his collaborators, including Bill, continued their exploration of starch in subsequent years. In 1949 they published another interesting paper titled 'The amylolytic enzymes of soya bean' (2). This research focused on understanding the enzymes responsible for the breakdown of starch, particularly in soybeans.

Two pivotal studies emerged from the scientific community in 1950 that further illuminated the properties of starch. In their collaborative work, Bill and F. Baker investigated the birefringence of amylose and amylopectin in whole structural starches. Their publication, 'Birefringence of amylose and amylopectin in whole structural starches', revealed the unique optical properties of different components of starch, providing crucial insights into their structural arrangements (3). Around the same time, Bill and E. J. Bourne conducted an

* Numbers in this form refer to the bibliography at the end of the text.

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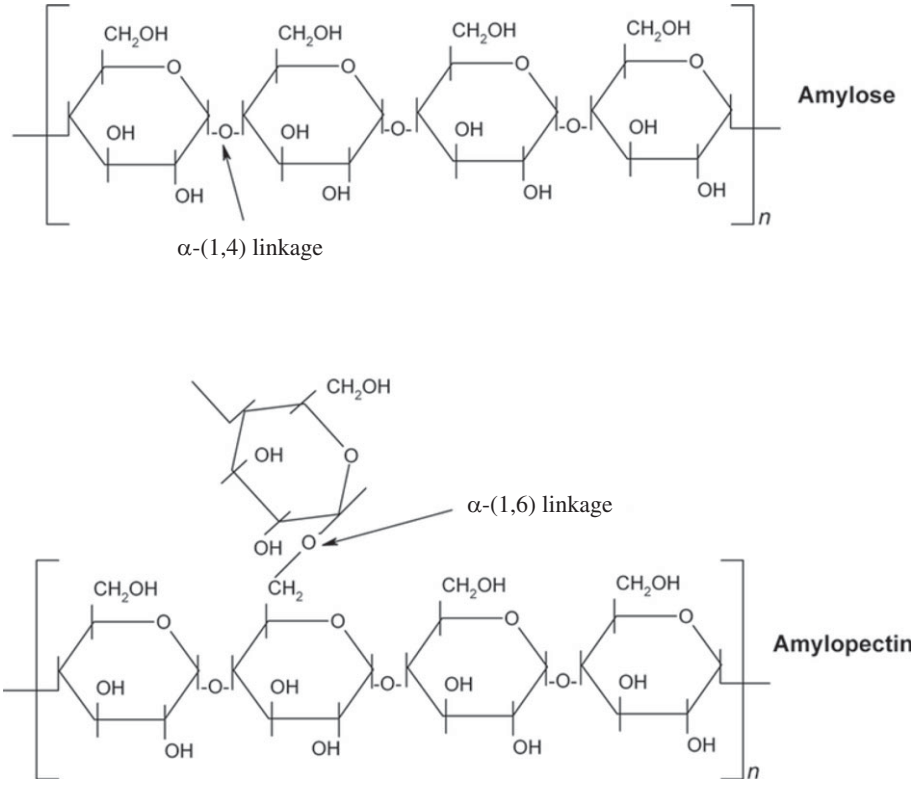

Figure 1. The chemical structure of amylose and amylopectin units.

investigation titled ‘Mechanism of the β-amylolysis of amylose’ (4). Their study focused on unravelling the intricate mechanism behind the β-amylolysis process, a specific type of enzymatic degradation of amylose, one of the key components of starch. Their findings shed light on the molecular-level interactions involved in this process, paving the way for future breakthroughs in enzymology and starch utilization.

In the 1950s, a team led by Bill embarked on a series of studies to unravel the complexities of enzyme-mediated carbohydrate breakdown and synthesis, providing several significant contributions. Bill, in collaboration with others, identified a novel ‘de-branching’ enzyme in beans and potatoes. This enzyme plays a crucial role in carbohydrate metabolism, specifically in breaking down branched structures within carbohydrates. Their findings shed light on the mechanisms involved in carbohydrate digestion and provided a foundation for further research in the field (5). In a subsequent study, Bill and colleagues investigated the role of the Z-enzyme in β-amylolysis, a process responsible for breaking down carbohydrates into simpler units (6).

Collaborating with J. M. Bailey, Bill focused on developing a method for selectively inhibiting enzymic impurities associated with potato phosphorylase. Their work aimed to refine enzymatic reactions and improve the purity and efficiency of carbohydrate breakdown processes (7). Working together with P. J. Roberts, Bill’s investigation into the end products of salivary α-amylase’s action on amylose contributed significantly to our understanding of the processes of carbohydrate metabolism. Their findings shed light on the specific

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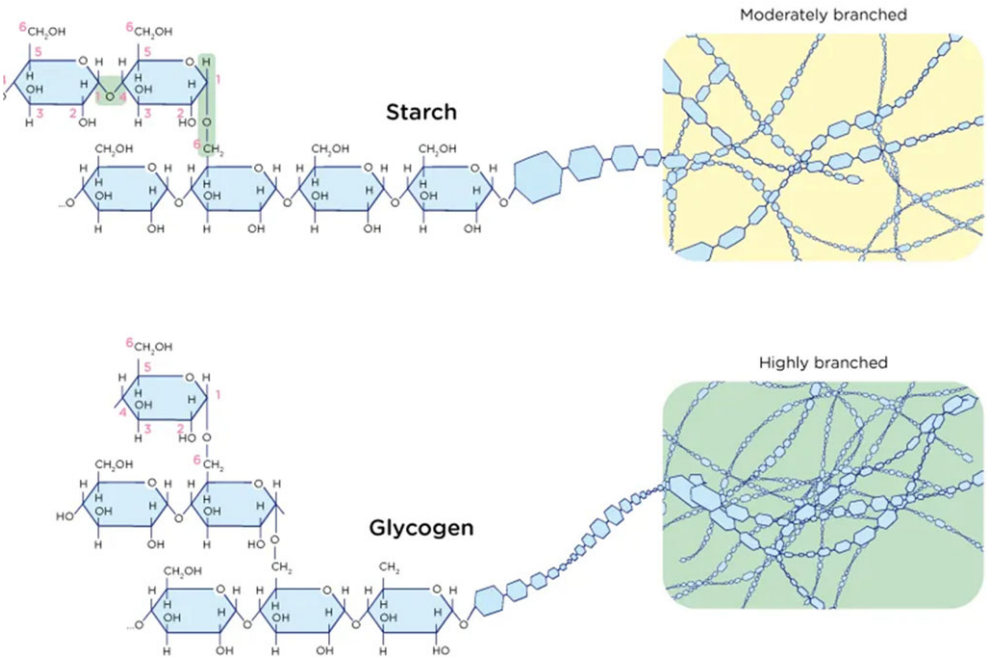

Figure 2. The chemical structure of starch and glycogen. Used with permission from www.jackwestin.com (http://www.jackwestin.com, accessed 5 July 2024) © Jack Westin Team.

breakdown products generated, and further elucidated the relatively complex enzymatic reactions (8). In the study of *Clostridium butyricum*, Bill and H. Nasr explored the properties and functions of the amylase enzyme. Their research provided insights into the enzymatic processes occurring in bacteria, expanding our knowledge of the diverse mechanisms involved in carbohydrate metabolism across different organisms (9). Bill's team, collaborating with other researchers, investigated the synthetic action of almond emulsin, an enzyme known for its unique properties in modifying carbohydrates. Their findings, published in *Nature*, highlighted the potential applications of almond emulsin in carbohydrate chemistry and catalysis (10). Bill and P. J. Roberts explored the actions of salivary α-amylase on amylopectin and glycogen, two important carbohydrates. Their research provided valuable insights into the specificity of enzyme–substrate interactions and the mechanisms underlying the breakdown of complex carbohydrates (11). Building upon previous work, Bill and Sarah Peat examined the role of the Z-enzyme in potato juice, which attacks the few β-1,3-links present in amylose (12), and they discovered the presence of D-enzyme, a disproportionating enzyme 1,4-α-D-glucan : 1,4-α-D-glucan, 4-α-D-glucanotransferase (13). In the research for the specific enzymatic steps and reactions required for synthesizing complex carbohydrates, Bill and J. M. Bailey elucidated the action pattern of potato phosphorylase, an enzyme involved in carbohydrate synthesis (14). In a subsequent study, the mechanism of action of D-enzyme, an enzyme involved in carbohydrate metabolism, was explored to shed light on its role in the breakdown of carbohydrates (18). In a comprehensive review, 'The synthesis and degradation of polysaccharides' (15), Bill explored the synthesis and degradation of

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polysaccharides, providing a detailed overview of the various enzymatic reactions and mechanisms involved. This seminal work consolidated existing knowledge and became a key reference for researchers studying carbohydrate metabolism.

Carbohydrase mechanisms, carbohydrate synthesis and glycogen structure

Carbohydrase is the name of a set of enzymes that catalyse five types of reactions, turning carbohydrates into simple sugars, from the large family of glycosidases. In 1957 Bill and J. M. Bailey collaborated to investigate the mechanism of carbohydrase action, specifically focusing on the action pattern of β-amylase (16). Their research shed light on the intricate steps and enzymatic reactions involved in the breakdown of carbohydrates, further enhancing our understanding of carbohydrate metabolism.

A paper by Bill and J. R. Turvey describes the preparation and characterization of isomaltodextrins, which are branched oligosaccharides. The authors investigated their properties and composition, providing valuable insights into these complex carbohydrates (17). The synthesis of amylose, a linear polymer of glucose molecules, using potato D-enzyme was also obtained (19). The action of human salivary α-amylase on amylopectin and glycogen was examined in several studies, which provided insights into the enzymatic breakdown of amylopectin, a component of starch (20–22). Limit dextrins were not only produced by α-amylase on amylopectin but also by muscle-phosphorylase, an enzyme involved in glycogen metabolism (23). Maltodextrins consist of D-glucose units connected in chains of variable length. The glucose units are primarily linked with α(1→4) glycosidic bonds, like those seen in the linear derivative of glycogen (after the removal of α-1, 6 branching). The research on maltodextrins investigated the actions of starch carbohydrases on chemically modified maltodextrins, which are intermediate products of starch hydrolysis. It examines how different modifications of maltodextrins affect the activity and specificity of starch carbohydrates (29).

In a study of 1970 (25), Bill examined the specificity of starch de-branching enzymes, focusing on their ability to break down different types of starch molecules. He investigated the efficiency of various de-branching enzymes in hydrolysing specific starch structures. Several papers used the incomplete conversion in determining the structure and properties of amylaceous polymers (24,28). Bill proposed a revised model for the structure of glycogen and amylopectin, which are highly branched glucose polymers. His experiments proved that the A and B chains of both glycogen and amylopectin are not arranged as in the regularly re-branched structure and suggested a structural modification to the existing Meyer–Bernfeld model based on new experimental findings (26).

Amylose branching by potato Q-enzyme

The study ‘Branching action of amylo-1,6-glucosidase/oligo-1,4→1,4-glucantransferase’ focused on the branching action of this enzyme and explored the enzyme’s ability to transfer glucose units and create branching points in glucose polymers (27). In another paper, ‘Purification and properties of potato 1,4-α-D-glucan : 1,4-α-D-glucan 6-α-(1,4-α-glucano)-transferase’(30), Q-enzyme evidence was obtained against a dual catalytic function in amylose-branching enzyme, and emphasized the need for further investigations to comprehensively understand the mechanisms and structural aspects of amylopectin synthesis in plants.

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There are two related papers. In the first paper, published in 1975 and titled 'Temperature-independence of the action of Q-enzyme and the nature of the substrate for Q-enzyme' (31), the authors discuss the temperature-independence of Q-enzyme's activity and elucidate the characteristics of its substrate. These findings provide important information about the enzymatic properties of Q-enzyme. In the second paper, published in 1976 and titled 'On the mechanism of amylose branching by potato Q-enzyme' (32), the authors present several key findings. First, they describe how potato Q-enzyme converts amylose into an amylopectin-like molecule through a random, endo-type trans-glycosylation of substrate chains. Second, they demonstrate inter-chain transfer during the formation of amylopectin branch linkages, as evidenced by radioactive label transfer between substrates of different molecular weights. Third, the authors determine that the minimum length of an amylose chain capable of acting as an acceptor in the trans-glycosylation reaction, under the experimental conditions, is 40 glucose units. They interpret this requirement as indicating the necessity for a stabilized secondary and tertiary structure in the substrate before it can be utilized by Q-enzyme, which can only occur when the chains exceed a certain length. The study proposes two mechanisms for inter-chain transfer: one involving the reaction of the enzyme with a chain possessing a stabilized (helical?) conformation, leading to the formation of an enzyme–donor chain intermediate, which then reacts with an acceptor chain to complete trans-glycosylation; the other mechanism envisions the substrate as a complex formed between two chains (a double helix?), with the enzyme encountering the complex and carrying out inter-chain trans-glycosylation reactions.

Initiation and regulation of glycogen biosynthesis

Several studies by Bill's group provided articles that focus on the initiation and regulation of glycogen biosynthesis in different organisms. 'The initiation of glycogen biosynthesis in *Escherichia coli*' (Barengo *et al.* 1975) explored the process of glycogen synthesis in *E. coli*, while 'The initiation of glycogen biosynthesis in rat heart' (34) investigated the initiation of glycogen synthesis in rat heart, specifically the formation of protein-bound glycogen. In another study (33), evidence was presented for the coordinated regulation of liver glycogen synthase and phosphorylase by a common protein phosphatase. The study suggested that this mechanism operates in parallel with adenosine 3′:5′-monophosphate-dependent protein kinase to control glycogen metabolism. The purification and properties of rabbit-liver glycogen synthase were also obtained (33).

In a seminal paper, 'A precursor of glycogen biosynthesis: α-1,4-glucan-protein' (Krisman & Barengo 1975), the mechanism of glycogen biosynthesis was investigated in the absence of added primers, leading to the proposal of the existence of a new enzyme called glycogen initiator synthase. This study suggested that the synthesis of glycogen occurs in two steps, involving the transfer of glucose from UDP-glucose to an acceptor protein. Another study (36) provided further evidence that the primer for liver glycogen synthesis was a protein to which glucose is covalently attached. Finally, a self-glucosylating protein as the primer for rabbit muscle glycogen biosynthesis (37) was identified as acting in the early stages of glycogen biosynthesis in rabbit muscle. The study identified a self-glucosylating protein that acts as a primer for glycogen synthase and branching enzyme, facilitating the formation of high-molecular-weight glycogen. Overall, these articles contributed to our understanding of the initiation, regulation and enzymatic processes involved in glycogen biosynthesis in different organisms.

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The discovery of glycogenin

Bill's most cited research has been on glycogenin. The molecular structure of glycogenin in the centre of a glycogen granule and a scheme of glycogen synthesis are given in figures 3 and 4. Glycogenin is an enzyme that catalyses its glycosylation process and forms a chain of maltosaccharides on itself. This chain acts as a primer for glycogen synthesis, particularly in muscle tissue. The most well studied form of this enzyme is called muscle glycogenin-1. In the first step, a monosaccharide primer is formed on a protein called muscle apo-glycogenin. The process of autoglucosylation starts at a specific site on the apo-glycogenin called Tyr-194, using UDP-glucose as a substrate. The catalytic site of the enzyme adds α-glucose residues linked in a 1,4 configuration. The length of the maltosaccharide chain can vary upon completion. This chain then acts as a primer for the synthesis of mature macroglycogen, which has a molecular weight of 107 Da, through an intermediate form called proglycogen with a molecular weight of 400 kDa. The enzymes involved in this process are glycogen synthase and branching enzyme. Initially, the autoglucosylation process is likely to be intermolecular. The sequence of events was initially proposed by Bill and colleagues in 1995 (42). The discovery of glycogenin as a protein that could be glycosylated from UDP-glucose dates back to the 1970s. In 1975, Clara Krisman, from the Leloir laboratory in Buenos Aires, conducted an experiment using ^{14}C-labelled UDP-glucose and a liver extract. The results showed the formation of a ^{14}C-labelled glucose product that precipitated with trichloroacetic acid (TCA), indicating glycosylation of a protein. Krisman concluded that this protein was involved in glycogen synthesis and served as the long-sought primer, which was previously assumed to be a carbohydrate. She postulated that the liver system produced a maltosaccharide chain on a protein primer with the help of a hypothetical enzyme called 'glycogen initiator synthase' (Krisman & Barengo 1975). In 1985, Bill coined the term 'glycogenin' for the protein undergoing glycosylation. This experiment was a crucial breakthrough in resolving the long-standing question about the nature of the primer for glycogen synthesis. Subsequently, Bill realized the fortunate circumstances regarding the affinities of two competing enzymes, glycogen synthase and 'glycogen initiator synthase', for UDP-glucose. The latter enzyme exhibited a significantly higher affinity. This allowed Krisman to use a lower concentration of ^{14}C-UDP-glucose in her experiment, which was below the K_m value of glycogen synthase for UDP-glucose. Had the situation been reversed, it is doubtful that protein glycosylation would have been easily discovered. Building upon Krisman's observation, together with Joseph Lomako, Bill investigated whether a protein remained bound to mature glycogen (38–41). They worked with rabbit muscle glycogen, ensuring the removal of any adventitiously bound protein. Through radiolabelling experiments, they identified a covalently bound protein with a molecular weight of 37 kDa, which was detectable by SDS-PAGE and radioautography after enzymatic or chemical removal of glycogen. It was later revealed that glucose was bound to a tyrosine residue in glycogenin, forming a novel glucose–protein bond. The discovery of this unique glucose–protein bond took several years owing to its novelty.

In 1984, at a symposium in Buenos Aires organized by Bill and Krisman, Bill reported the bond to tyrosine (35). At the same symposium, another colleague, Juana Tandecarz, presented her findings on a similar protein-labelling experiment using a potato extract and low ^{14}C-UDP-glucose concentration, which resulted in a TCA-precipitable protein with a molecular weight of 37 kDa. This reaction was activated by Mn^{2+}. Recognizing the connection between his muscle glycogen protein and Tandecarz' s findings, Bill invited her to Miami for further investigation. Alongside Ignacio Rodriguez, who had discovered the tyrosine bond,

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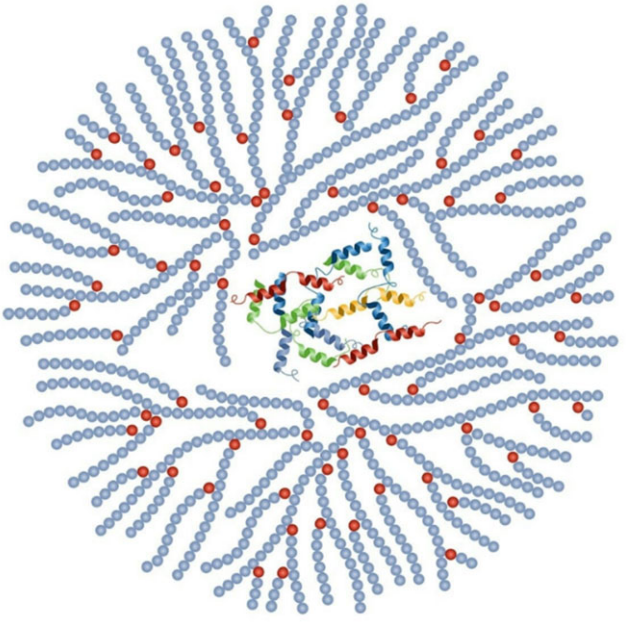

Figure 3. The chemical structure of glycogenin (image by Mikael Häggström/Wikipedia).

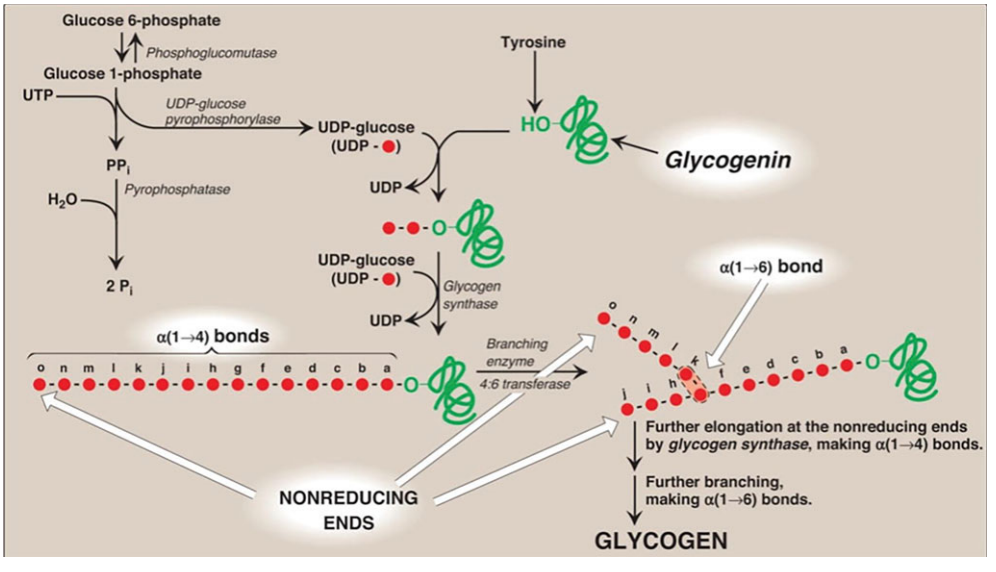

Figure 4. Scheme of glycogen synthesis. Copyright unknown.

Bill demonstrated the Mn^{2+}-activated ^{14}C-glucose labelling of a protein in a rabbit muscle extract. This labelled protein, with a molecular weight of 37 kDa, reacted with antibodies against the muscle glycogen protein. Subsequently, Bill isolated glycogenin and 'glycogen initiator synthase' from a muscle extract and discovered that they were one and the same protein (38), a finding simultaneously made by the Cohen laboratory in Dundee (Pitcher *et al.* 1988; Smythe & Cohen 1991).

Bill performed further experiments and observed the ability to radio-glycosylate multiple protein species, which were also detectable through Western blot analysis. He used muscle extracts from various sources, including grouper, lizard, frog, turtle, house cricket and oyster, as well as extracts from *Penicillus* algae, sweetcorn, sweet potato, banana, plantain, cocoyams and cowpea seeds. Unfortunately, he never published a full report on these findings; however, he did follow up on one of the observations. He focused on the protein in sweetcorn that underwent radio-glycosylation and produced a positive immunoblot. During purification, he identified it as another self-glycosylating protein with a molecular weight of 42 kDa. Interestingly, this protein had no homology with the muscle glycogen protein. It attached a single β-glucose residue to an arginine residue through another novel glucosyl–protein bond. However, the purified sweetcorn protein, which Bill named amylogenin (43), did not yield a positive immunoblot with muscle glycogenin antibodies. This suggested that more than one protein was detected in the crude extract, and during purification the protein responsible for the positive immunoblot was lost. Bill concluded that the isolation and characterization of a primer for starch synthesis (or for amylose and amylopectin synthesis) could have significant biotechnological applications. The amount of starch that a plant can synthesize likely depends on the presence of a primer. This relationship appears to hold true for muscle glycogen as well. In the current context of utilizing corn for ethanol production, overexpressing the starch primer could increase starch content at a minimal cost.

The glycaemic response

In later years, the research conducted by Bill and colleagues (44) focused on the glycaemic response to protein consumption and the rate of consumption of digestible carbohydrates. In a first study, they found that consuming various types of meat led to significant increases in blood glucose levels, possibly owing to gluconeogenesis from digested protein. Interestingly, the response was inversely related to the amount of meat consumed. In the second study (45), the researchers investigated the impact of the rate of consumption of digestible carbohydrates on glycaemic responses. Surprisingly, they found that the responses were equally distributed between rapid consumption and consumption in five equal portions over 12 minutes. Additionally, they observed significant variations in the glycaemic responses among different individuals consuming the same foods.

The third study (46) examined the glycaemic index (GI) as a measure of glycaemic response and its reliability in guiding individuals who wish to avoid large glycaemic responses and hyperglycaemia. Volunteers underwent multiple tests after overnight fasting, and their glycaemic responses to each food were compared. The results showed that each person displayed characteristic glycaemic responses unrelated to others. There were substantial variations in average areas under the blood glucose/time curves among different testers, highlighting the individual nature of the glycaemic response. Therefore, relying solely on published GI lists to control glycaemic response may be misleading. Overall, these studies

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emphasize the importance of considering individual variations in glycaemic response to both protein and digestible carbohydrate consumption, challenging the notion of a standardized GI as a reliable guide for controlling blood sugar and body weight.

International organizations

Bill was a tireless promoter of international collaboration between biochemical societies. He helped found FEBS and became its first general secretary in 1964. When he moved to Miami, he looked round for similar opportunities in the Americas, specifically to see whether an equivalent of FEBS might be formed. A long-time colleague, Bernie Horecker, was about to become the president of the American Society for Biological Chemists (ASBC, now ASBMB). A Canadian colleague, Donald Whittaker, was about to preside over the Canadian Biochemical Society. Bill had formed a close acquaintance, because of common research interests, with the most prominent biochemist in South America, Luis F. Leloir (ForMemRS 1972), who was to win the Nobel Prize in chemistry in 1970. Contacting them, and through them other biochemists around the hemisphere, brought to light a wide expression of interest in forming a Pan-American version of FEBS. By mid 1969, with Karl Gaede of Venezuela as the acting president, it was decided to form the Pan-American Association of Biochemical Societies (PAABS). It came into official existence on 1 January 1970, with Luis F. Leloir as the first official president. Bill was the secretary-general and another enthusiast, Raul Ondarza, from Mexico City, was the treasurer. Soon, PAABS included the Biochemical Societies of Canada, the ASBC and the Division of Biological Chemistry of the American Chemical Society, and Societies from Mexico, Venezuela, Colombia, Ecuador, Brazil, Peru, Chile and Argentina. PAABS enthusiastically mimicked FEBS by sponsoring an annual meeting, holding symposia and issuing a news bulletin, all of which Bill organised. In 1972, Bill resigned as secretary-general of PAABS (succeeded by Ronald Estabrook of Dallas) to become the general secretary of the International Union of Biochemistry (IUB, now International Union of Biochemistry and Molecular Biology, IUBMB) in 1973. Bill worked, in his new capacity, to have the IUB provide funds to PAABS and to the new Asian–Oceanian Federation (FAOB), starting in 1979. In 1982 an official membership category of Associated Organization was created in the IUB so that PAABS and FAOB gained recognition under the IUB umbrella. Since 1999, all four regional organizations, the others being FEBS and the African Federation (FASBMB), are associated organizations of the IUBMB. However, Bill expressed his disappointment over the years that PAABS (now PABMB) never flourished as he had hoped. Central America and the Caribbean, with the only recent exceptions of Panama and Cuba, have never been in the membership, while the societies from Venezuela, Colombia and Ecuador seem to have gone out of existence. All along during his tenure at the organizations, Bill brought to the IUB (as general secretary), and to the IUBMB (as president) his legendary and creative dynamism for promoting medical and biochemical education (figure 5).

A provision in the revised statutes adopted by the IUB sixth General Assembly in Tokyo in 1967 made an important step towards resolving the problem of China's representation in the IUB, by redefining an Adhering Body as representative of a scientific community, described as applicable to the biochemists of a country or an otherwise defined geographical area that has an independent budget for scientific purposes. However, it was not until 1979 that, as the result of an agreement brokered by Bill (then general secretary) and Bill Slater FRS (at

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Figure 5. Bill (standing), together with the IUBMB fellows at the Miami Winter Symposium 2014 (from Bill Whelan's private collection; copyright unknown).

that time treasurer), two Adhering Bodies from China (Beijing and Taipei), representing the biochemists from the two scientific communities, became members of the IUB. The IUB agreement was adopted by other scientific unions, and a little later by the International Council of Scientific Unions (ICSU) itself. In 1985, funds provided by an appeal among the world's biochemists were used to establish the Wood–Whelan Research Fellowship Fund, named to honour Harland G. Wood and Bill for their distinguished services to the IUB. The purpose of the fund was to grant short-term fellowships to enable biochemists to visit a laboratory to carry out an experiment or learn a technique. Additional donations to the fund were made by the ASBMB and by Bill himself. The programme was also supported by grants from the ICSU.

The Miami Winter Symposium

In 1968, as the new chair of biochemistry and molecular biology at the University of Miami School of Medicine, Bill founded the annual Miami Winter Symposium. Since it seemed to Bill that this south Florida watering place was not frequented by other biochemists, he conceived the idea of the symposia to bring distinguished scientists in contact with students and faculty of his department. That the event was held each year in January was an incentive to the visitors to share the plight of living in Miami in the winter. The experiment succeeded in its initial quest, and beyond. Faculty and students across the school attended. Visitors came from around the world. Nobel laureates, or laureates-to-be, were speakers (figures 6 and 7).

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Figure 6. Bill Whelan presenting Francis Crick FRS (left) with the Distinguished Service Award, Miami Winter Symposium 2003. Francis Crick did not attend the meeting and received the award in November 2002 (from Bill Whelan's private collection; copyright unknown).

The symposia started with metabolism, then concentrated on gene technology and became an international event in this area. The symposia now specialize in molecular medicine and its applications, bringing together investigators from academia and industry to participate in a programme that combines basic and applied aspects of the same research focus. Nature Publishing began a 25-year partnership in 1988 and later the symposia were managed by Elsevier. Successive later and continuing partners of the Biochemistry Foundation have been the University of Miami Miller School of Medicine, the Sylvester Comprehensive Cancer Institute, Scripps Florida and the IUBMB, the latter having committed a substantial annual donation in support of travel fellowships for young scientists from developing areas. In the Miami Winter Symposia, great science was presented: Bill's choice of speakers and topics has been extremely prophetic considering the number of scientists that received a Nobel prize after lecturing at a Miami Winter Symposium. Miami Winter Symposia created connections with great scientists, and an emphasis on helping younger researchers, resulting in a great experience for both speakers and attendees. The relaxed ambiance created by Bill, always prevalent at the symposia (along with long lunch hours and evening wine tastings), also attracted speakers, only too happy to meet and exchange ideas with attending delegates in a unique atmosphere. To date, the Miami Winter Symposium continues to be an excellent venue for the gathering of worldwide top-notch scientists in the biomedical field.

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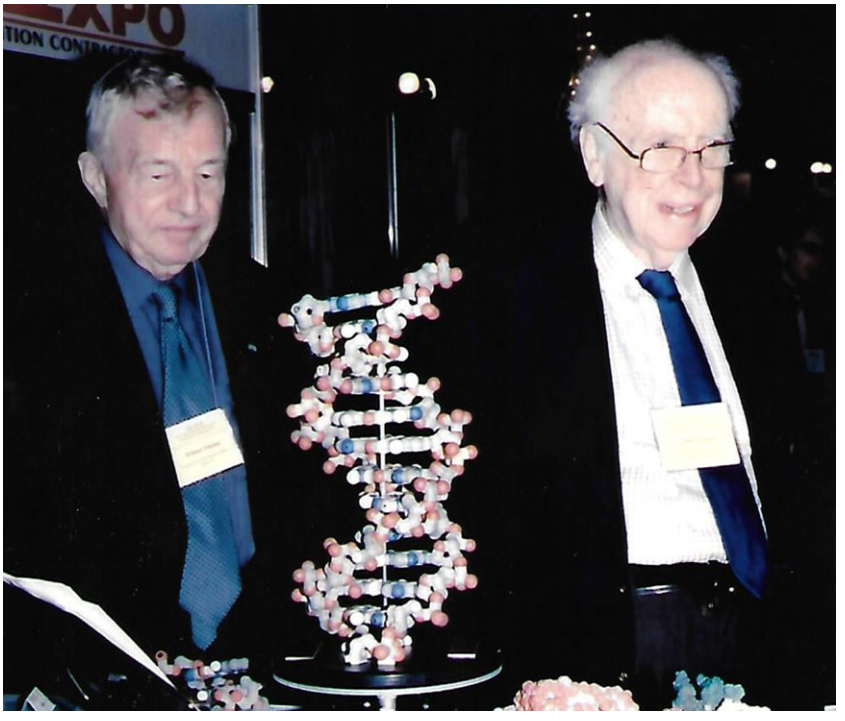

Figure 7. Bill with James Watson (ForMemRS 1981) (right), the Lynen lecturer at the MWS 1978, at the Miami Winter Symposium 2003 (from Bill Whelan's private collection; copyright unknown).

Publishing

As the first secretary-general of FEBS, Bill had proposed to move into the publication arena, and specifically produce a rapid communication journal modelled along the lines of the then relatively new *Biochemical and Biophysical Research Communications*. There were, however, three principal arguments against such a journal. The first was that it would not be possible to recruit an editorial board. The second was that there was not a market for such a journal. The third came from people who felt that short communications are ephemeral and simply overburden the literature, later being replaced by full reports. Bill could provide sufficient counterarguments, and found a publisher, North-Holland, for the new journal, *FEBS Letters*, and a new managing editor, Prakash Datta, who had thrown all his weight behind the proposal. The first issue of *FEBS Letters* appeared in July 1968.

In the 1970s, as a result of Bill's efforts with Bill Slater (as treasurer) to obtain an additional substantial source of income for the IUB, an approach was made to the publisher to link the Elsevier journal *Biochimica et Biophysica Acta* to the IUB, with payment of royalties to the IUB along the lines of the arrangements FEBS had with the publishers of its journals. The attempt was unsuccessful. However, Elsevier made a counter-proposal of offering the IUB sponsorship of a review journal, *Trends in Biochemical Sciences* (*TIBS*), that they had in mind. This was accepted by the IUB, Bill became editor of the journal and, with characteristic energy and skill, he made the journal a success, both scientifically

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and financially, for the IUB/IUBMB. *TIBS*, first published in 1976, was the first of a series of '*Trends*' journals published by Elsevier. *Applied Biochemistry* (now *Biotechnology and Applied Biochemistry*) was also started by Bill, as well as *Biochemistry International* (later *Biochemistry and Molecular Biology International*), specializing in the rapid publication of short reports, started by A. W. Linnane. When Bill was IUBMB president, *Biochemistry and Molecular Biology International* was moved from Academic Press, Australia to Taylor & Francis, and its name changed to *IUBMB Life*, published first in 2000 with K. J. A. Davies (USA) as editor. Bill became, together with Angelo Azzi, co-editor-in-chief. Bill also became editor of *BioFactors*, after founding editor Thressa G. Stadtman resigned. It must be underlined that Bill's efforts in creating and supporting IUBMB publications resulted in great visibility for the Union, important scientific promotion, and income that permitted the development of several scientific and educational activities.

In 1984, as the chair of the ICSU Press, Bill considered a magazine with a generic title and one that could move with the rapidly changing landscape, shifting with or ahead of the times. That materialized when Bill founded *BioEssays*, whose first volume appeared in December 1984, published by ICSU Press and The Company of Biologists, with an editorial of John Kendrew FRS.

In 1986, Barry R. Bloom, from the Albert Einstein College of Medicine and president of the Federation of American Societies for Experimental Biology (FASEB), was fundamental in the selection of Bill to become the first editor-in-chief of *FASEB journal*. Bill undertook the transformation of the *Federation Proceedings*, a quarterly compendium of meeting reports and reviews founded in 1942, into a new, monthly journal of interdisciplinary science whose first issue appeared in July 1987. The major achievement of the Whelan era (1987–1996) was to enlist the best and the brightest authors for invited reviews that form a veritable textbook of classic biology.

Recognition

The discovery of glycogenin led to Bill's election as a Fellow of the Royal Society in 1992. Previously, Bill had received many awards, including: the Alsberg Medal, USA (1967); the CIBA Medal of the Biochemical Society (1968); the Medal of the Japanese Society of Starch Science (1975); the Saare Medal, Germany (1979); Honorary Membership of the Royal College of Physicians, London (1986); and election as a Fellow of the American Society for the Advancement of Science (1989).

After becoming a Fellow of the Royal Society, he was elected as an honorary member of the British Biochemical Society (1993) and received the FEBS–IUBMB Millennium Medal (2000). In 2006, Bill received the University of Miami's Distinguished Faculty Scholar Award for lifetime achievement in research, and in 2003 he was elected as IUBMB Lifetime Special Member in recognition of his generous contributions to the IUBMB. He was recognized with many awards at the University of Miami and received the University of Miami Medal when he retired in 2019 at the record age of 96 years old.

Personal life and retirement

Of Bill's two sisters, Eileen and Sheila, only Sheila had children, and Bill's nephew, David May, was very close to him. In 1951 Bill married Margaret (figure 8). Margaret was a

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Figure 8. Bill and Margaret in London, 1951 (from Bill Whelan's private collection; copyright unknown).

teacher and a great supporter of education. She initiated the research and travel awards for graduate students at the University of Miami School of Medicine. They never had children, but 'adopted' medical students as their own. Bill often recalled that Margaret had been a role model for him. Sadly Margaret died in 1993, and in 2005 Bill remarried to Alina.

Bill's natural ability at public speaking made him popular with biochemistry students, who always gave high ratings to his lectures. It is remarkable that, until his retirement, Bill continued to be an active member of the Department of Biochemistry and Molecular Biology, participating in committees and faculty meetings, offering advice to faculty and delivering seminars on personal career perspectives and historical biochemical events.

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Figure 9. Bill Whelan and Eddy Fischer (right) at the Miami Winter Symposium in 2005 (photograph: Angelo Azzi).

Bill always made time for his family, friends and students and was very generous with them. He was particularly proud of his friendship with several extraordinary scientists, such as Edmond (Eddy) Fischer (ForMemRS 2010) (figure 9), with whom he exchanged weekly phone calls until the very end. Sir Hans Kornberg FRS was also one of his friends frequently mentioned in his conversations. Of Sir Hans, Bill especially liked his sense of humour and sharing his favourite quotes of Mark Twain. Bill always expressed great respect and affection for Frank Vella, IUBMB general secretary during Bill's presidency, and he highly regarded the 'other Bill', Bill Slater, and was often anxious about Slater's whereabouts when he was sailing alone without radio contact and no communication for weeks. Within the IUBMB family, Kunio Yagi, a past president of the IUBMB, was also one of his most regarded friends, and, above all, so was Harland Goff Wood, whom Bill considered one of the most influential and innovative officers of the IUB. Bill had also great esteem for Andy Sutherland, whose advice he often asked, and enjoyed spending time with him. Bill had a great admiration and respect for Phillip Frost, a friend and a sponsor.

Bill's business travelling was spartan, using public transportation and economic travel lodges. On the other hand, he also knew how to appreciate the upscale annual invitations to London and Hoboken sponsored by the publishers of the journals he was editor of. In addition, once a year, the week after the Miami Winter Symposium, Bill enjoyed relaxing and used to organize post-symposium trips for speakers, Nobel Prize laureates and staff. A popular destination was the Everglades, where, on several occasions, Bill hired houseboats to show the area at its best. After throwing an anchor overboard in a sheltered deserted bay, evenings were spent with a barbecue and a glass of wine, surrounded by wildlife and friends (figure 10).

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Figure 10. After the Miami Winter Symposium. (From the left) Bill, with his wife Alina, Jim Black, Sandra (Bill's secretary), and Andy Sutherland (from Bill Whelan's private collection; copyright unknown).

In later years, he loved to travel, and enjoyed sitting over dinner and sharing memories with friends and family. When travelling became physically challenging, he liked to sit in his armchair at home, in front of the balcony overlooking the Miami Biscayne Bay, while working on his iPad and sharing a bottle of chilled white wine with his lovely wife Alina and his friends.

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The frontispiece portrait photograph was taken in 1992 by A. C. Cooper and is © the Royal Society.

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Author profile

Angelo Azzi

Angelo Azzi is professor emeritus at the University of Bern, Switzerland, a faculty member of the Tufts University School of Graduate Biomedical Pharmacology and Drug Development Program and a volunteer professor at the University of Miami Miller School of Medicine. He graduated in medicine from the University of Padua (Italy), where he also earned PhDs in pathophysiology and biochemistry. His scientific career continued in Bristol (UK), Philadelphia (USA) and Bern (Switzerland). After retiring as chairman of the Institute of Biochemistry and Molecular Biology at the University of Bern, he moved to Tufts University (Boston, USA) as a senior scientist, where he remains active today.

In 1997, at the seventeenth Congress of the International Union of Biochemistry and Molecular Biology (IUBMB) in San Francisco, he was elected to the Executive Committee of the IUBMB as chairman of the Publications Committee. It was here that he first met Bill, the organization's president. Bill's extensive work in creating and editing journals was a significant source of knowledge and inspiration for Azzi. With Bill's encouragement, two dormant IUBMB journals, *BioFactors* and *IUBMB Life*, were revitalized. In 2000, when Azzi was elected president of the IUBMB, he persuaded Bill to join him as co-editor of *IUBMB Life*. Their professional collaboration blossomed into a strong friendship. This bond deepened further as Azzi supported Bill in organizing and continuing the renowned Miami Winter Symposia. Even after their editorship of *IUBMB Life* ended in 2020 and the Miami Winter Symposia concluded, visiting Bill at his home remained a valuable source of historical knowledge, inspiration and joy. Their exchanges of ideas and jokes continued to be a testament to a mind unaffected by time.

References to other authors

Barengo, R., Flawia, M. & Krisman, C. R. 1975 The initiation of glycogen biosynthesis in *Escherichia coli*. *FEBS Lett.* **53**, 274–278. (doi:10.1016/0014-5793(75)80035-4)

Krisman, C. R. & Barengo, R. 1975 A precursor of glycogen biosynthesis: alpha-1,4-glucan-protein. *Eur. J. Biochem.* **52**, 117–123. (doi:10.1111/j.1432-1033.1975.tb03979.x)

Pitcher, J., Smythe, C. & Cohen, P. 1988 Glycogenin is the priming glucosyltransferase required for the initiation of glycogen biogenesis in rabbit skeletal muscle. *Eur. J. Biochem.* **176**, 391–395. (doi:10.1111/j.1432-1033.1988.tb14294.x)

Smythe, C. & Cohen, P. 1991 The discovery of glycogenin and the priming mechanism for glycogen biogenesis. *Eur. J. Biochem.* **200**, 625–631. (doi:10.1111/j.1432-1033.1991.tb16225.x)

Bibliography

The following publications are those referred to directly in the text. A full bibliography is available as electronic supplementary material at https://doi.org/10.6084/m9.figshare.c.7344306.

(1) 1948 (With S. Peat & E. J. Bourne) Photochemical degradation of starch. *Nature* **161**, 762–763. (doi:10.1038/161762a0)

Downloaded from https://royalsocietypublishing.org/ on 27 October 2024

(2) 1949 (With S. Peat & S. J. Pirt) The amylolytic enzymes of soya bean. *Nature* **164**, 499–500. (doi:10.1038/164499a0)
(3) 1950 (With E. J. Bourne) Mechanism of the beta-amylolysis of amylose. *Nature* **166**, 258–259. (doi:10.1038/166258a0)
(4) (With F. Baker) Birefringence of amylose and amylopectin in whole structural starches. *Nature* **166**, 34. (doi:10.1038/166034a0)
(5) (With G. J. Thomas & S. Peat) The role of Z-enzyme in beta-amylolysis. *Biochem. J*. **47**, xl.
(6) (With P. N. Hobson & S. Peat) A 'de-branching' enzyme in bean and potato. *Biochem. J*. **47**, xxxix.
(7) 1951 (With J. M. Bailey & G. J. Thomas) Selective inhibition of enzymic impurities associated with potato phosphorylase. *Biochem. J.* **49**, lvi-lvii.
(8) (With P. J. Roberts) End products of the action of salivary alpha-amylase on amylose. *Biochem. J*. **49**, lvi.
(9) (With H. Nasr) The amylase of *Clostridium butyricum*. *Biochem. J*. **48**, 416–422. (doi:10.1042/bj0480416)
(10) 1952 (With S. Peat & K. A. Hinson) Synthetic action of almond emulsin. *Nature* **170**, 1056–1057. (doi:10.1038/1701056a0)
(11) (With P. J. Roberts) Action of salivary alpha-amylase on amylopectin and glycogen. *Nature* **170**, 748–749. (doi:10.1038/170748a0)
(12) 1953 (With S. Peat) The Z-enzyme in amylolysis. *Nature* **172**, 494. (doi:10.1038/172494a0)
(13) (With S. Peat & W. R. Rees) *D*-enzyme: a disproportionating enzyme in potato juice. *Nature* **172**, 158. (doi:10.1038/172158a0)
(14) 1954 (With J. M. Bailey) The action pattern of potato phosphorylase. *Biochem. J*. **58**, 560–569. (doi:10.1042/bj0580560)
(15) 1956 The synthesis and degradation of polysaccharides. *Lect. Sci. Basis Med*. **6**, 233–259.
(16) 1957 (With J. M. Bailey) The mechanism of carbohydrase action. 3. The action pattern of beta-amylase. *Biochem. J*. **67**, 540–547. (doi:10.1042/bj0670540)
(17) (With J. R. Turvey) Preparation and characterization of the isomaltodextrins. *Biochem. J*. **67**, 49–52. (doi:10.1042/bj0670049)
(18) (With G. J. Walker) The mechanism of carbohydrase action. 4. The mechanism of D-enzyme action. *Biochem. J*. **67**, 548–551. (doi:10.1042/bj0670548)
(19) 1959 (With G. J. Walker) Synthesis of amylose by potato *D*-enzyme. *Nature* **183**, 46. (doi:10.1038/183046a0)
(20) 1960 (With B. J. Bines) The mechanism of carbohydrase action. 6. Structure of a salivary α-amylase limit dextrin from amylopectin. *Biochem. J*. **76**, 253–257. (doi:10.1042/bj0760253)
(21) (With P. J. Roberts) The mechanism of carbohydrase action. 5. Action of human salivary α-amylase on amylopectin and glycogen. *Biochem. J*. **76**, 246–253. (doi:10.1042/bj0760246)
(22) (With G. J. Walker) The mechanism of carbohydrase action. 8. Structures of the muscle-phosphorylase limit dextrins of glycogen and amylopectin. *Biochem. J*. **76**, 264–268. (doi:10.1042/bj0760264)
(23) (With G. J. Walker) The mechanism of carbohydrase action. 7. Stages in the salivary α-amylolysis of amylose, amvlopectin and glycogen. *Biochem. J*. **76**, 257–263. (doi:10.1042/bj0760257)
(24) (With J. J. Marshall) Incomplete conversion of glycogen and starch by crystalline amyloglucosidase and its importance in the determination of amylaceous polymers. *FEBS Lett*. **9**, 85–88. (doi:10.1016/0014-5793(70)80319-2)
(25) 1970 (With G. S. Drummond & E. E. Smith) On the specificity of starch debranching enzymes. *FEBS Lett*. **9**, 136–140. (doi:10.1016/0014-5793(70)80337-4)
(26) (With Z. Gunja-Smith, J. J. Marshall, C. Mercier & E. E. Smith) A revision of the Meyer–Bernfeld model of glycogen and amylopectin. *FEBS Lett*. **12**, 101–104. (doi:10.1016/0014-5793(70)80573-7)
(27) (With F. Huijing, E. Y. Lee & J. H. Carter) Branching action of amylo-1,6-glucosidase/oligo-1,4→1,4-glucantransferase. *FEBS Lett*. **7**, 251–254. (doi:10.1016/0014-5793(70)80173-9)
(28) (With C. Mercier) The fine structure of glycogen from type IV glycogen-storage disease. *Eur. J. Biochem*. **16**, 579–583. (doi:10.1111/j.1432-1033.1970.tb01120.x)

Downloaded from https://royalsocietypublishing.org/ on 27 October 2024

(29) (With F. W. Parrish & E. E. Smith) Actions of starch carbohydrases on chemically modified maltodextrins. *Arch. Biochem. Biophys.* **137**, 185–189. (doi:10.1016/0003-9861(70)90426-1)

(30) 1975 (With D. Borovsky & E. E. Smith) Purification and properties of potato 1,4-α-D-glucan : 1,4-α-D-glucan 6-α-(1,4-α-glucano)-transferase: evidence against a dual catalytic function in amylose-branching enzyme. *Eur. J. Biochem.* **59**, 615–625. (doi:10.1111/j.1432-1033.1975.tb02490.x)

(31) (With D. Borovsky & E. E. Smith) Temperature-independence of the action of Q-enzyme and the nature of the substrate for Q-enzyme. *FEBS letters.* **54**, 201–5.

(32) 1976 (With D. Borovsky & E. E. Smith) On the mechanism of amylose branching by potato Q-enzyme. *Eur. J. Biochem.* **62**, 307–312. (doi:10.1111/j.1432-1033.1976.tb10162.x)

(33) (With S. D. Killilea, H. Brandt & E. Y. Lee) Evidence for the coordinate control of activity of liver glycogen synthase and phosphorylase by a single protein phosphatase. *J. Biol. Chem.* **251**, 2363–2368. (doi:10.1016/S0021-9258(17)33595-0)

(34) 1983 (With M. L. Blumenfeld & C. R. Krisman) The initiation of glycogen biosynthesis in rat heart. *Eur. J. Biochem.* **135**, 175–179. (doi:10.1111/j.1432-1033.1983.tb07634.x)

(35) 1985 (With I. R. Rodriguez) A novel glycosyl-amino acid linkage: rabbit-muscle glycogen is covalently linked to a protein via tyrosine. *Biochem. Biophys. Res. Commun.* **132**, 829–836. (doi:10.1016/0006-291X(85)91206-9)

(36) 1986 (With C. R. Krisman & R. A. Geremia) A (1–4)-α-D-glucan-protein involved in liver glycogen biosynthesis. *Carbohydr. Res.* **149**, 35–45. (doi:10.1016/S0008-6215(00)90367-7)

(37) 1988 (With J. Lomako & W. M. Lomako) A self-glucosylating protein is the primer for rabbit muscle glycogen biosynthesis. *FASEB J*. **2**, 3097–3103. (doi:10.1096/fasebj.2.15.2973423)

(38) (With J. Lomako) The occurrence of serine phosphate in glycogenin: a possible regulatory site. *BioFactors* **1**, 261–264.

(39) 1990 (With J. Lomako & W. M. Lomako) The biogenesis of muscle glycogen: regulation of the activity of the autocatalytic primer protein. *BioFactors* **2**, 251–254.

(40) (With J. Lomako & W. M. Lomako) The nature of the primer for glycogen synthesis in muscle. *FEBS Lett.* **268**, 8–12. (doi:10.1016/0014-5793(90)80959-M)

(41) (With J. Lomako & W. M. Lomako) The biogenesis of glycogen: nature of the carbohydrate in the protein primer. *Biochem. Int.* **21**, 251–260.

(42) 1995 (With M. D. Alonso, J. Lomako & W. M. Lomako) Catalytic activities of glycogenin additional to autocatalytic self-glucosylation. *J. Biol. Chem.* **270**, 15315–15319. (doi:10.1074/jbc.270.25.15315)

(43) (With D. G. Singh, J. Lomako, W. M. Lomako, H. E. Meyer, M. Serwe & J. W. Metzger) β-Glucosylarginine: a new glucose-protein bond in a self-glucosylating protein from sweet corn. *FEBS Lett.* **376**, 61–64. (doi:10.1016/0014-5793(95)01247-6)

(44) 2010 (With H. Ghanchi & M. Ricciardi) Protein causes a glycemic response. *IUBMB Life* **62**, 477–479. (doi:10.1002/iub.333)

(45) (With D. Hollar, A. Agatston, H. J. Dodson & D. S. Tahal) Blood glucose response to rate of consumption of digestible carbohydrate. *BioFactors* **36**, 491–493. (doi:10.1002/biof.125)

(46) (With D. Hollar, A. Agatston, H. J. Dodson & D. S. Tahal) The glycemic response is a personal attribute. *IUBMB Life* **62**, 637–641. (doi:10.1002/iub.365)

Downloaded from https://royalsocietypublishing.org/ on 27 October 2024