

Fran Bubanović: The Visionary of Medical Chemistry and Biochemistry in Croatia

Vladimir Damjanović,¹ Kristina Mlinac-Jerković,^{1,2,*} Svjetlana Kalanj Bognar,^{1,2} Jasna Lovrić¹

¹ Department of Chemistry and Biochemistry, School of Medicine, University of Zagreb, Šalata 3, 10 000 Zagreb, Croatia

² Croatian Institute for Brain Research, School of Medicine, University of Zagreb, Šalata 12, 10 000 Zagreb, Croatia

* Corresponding author's e-mail address: kristina.mlinac@mef.hr

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Abstract: Professor Fran Bubanović was the founder of the Department of Chemistry and Biochemistry at School of Medicine established a hundred years ago, in 1917, within the University of Zagreb. Fran Bubanović was an exemplary scientist, great science communicator and teacher. He trained many generations of physicians in chemistry and biochemistry. The aim of this essay is to give insight into his scientific collaboration with the Nobel Prize winner Svante Arrhenius and other world-renowned scientists, his teaching work in chemistry, his university textbooks in the field of medical chemistry and biochemistry since he had a profound impact on education of medical students in basic science. We hope that this essay will bring an additional dimension of Fran Bubanović as a superb university teacher and scientist whose legacy still remains unequalled. Therefore, he is legitimately called “the father of medical chemistry” in Croatia.

Keywords: Fran Bubanović, medical chemistry, medical biochemistry, medical chemistry education.

INTRODUCTION

A hundred years ago (1917), under dramatic global political circumstances and imminent end of the Austro-Hungarian Empire, School of Medicine in Zagreb was founded. The Department of Chemistry and Biochemistry was amongst first established departments which underlies the importance of (bio)chemical education for future medical doctors from the very beginning. First classes in (bio)chemistry started in the following academic year, 1918/1919. As this centennial approaches, we are remembering Professors who had pioneering role in creating the medical studies in Croatia and former Yugoslavia and who left a major impact on chemistry and biochemistry education. We cannot even begin to ponder those names without giving the greatest credit to Fran Bubanović (Figure 1), who is known as “the father of medical chemistry” in Croatia.^[1]

Fran Bubanović was born on November 19th 1883 in Sisak, Croatia. He finished his high school education in Zagreb, and continued the studies in natural sciences which were at the time held at Faculty of Philosophy University of Zagreb (1901–1905). After graduation he started teaching chemistry in high schools first in Zagreb, and then Bjelovar.

Bjelovar was also his starting point for international scientific training because it was the Bjelovar county major who sent Bubanović abroad. In 1917 Bubanović was sent to Vienna, to Austrian physician and biochemist Otto von Fürth with purpose to prepare for organizing and leading Chemistry Department at newly founded School of Medicine in Zagreb. After his return to Zagreb in 1918, he stayed at School of Medicine until his retirement in the academic year 1954/1955. He died in Zagreb on February 6th 1956.^[2–5]

SCIENTIFIC WORK

In 1909 Bubanović left Bjelovar on a scholarship and went to Groningen in the Netherlands to the laboratory of Professor Hartog Jacob Hamburger, a Dutch physiologist and chemist. Professor Hamburger is most known for determining the composition and for using physiological solution, which is still sometimes referred to as Hamburger's solution. In coauthorship with Hamburger, Bubanović published a paper regarding the permeability of red blood cells against cations^[6] which was afterwards accepted as his doctoral thesis in 1910 at University of Vienna. As a result of several published papers^[7–9] during his stay in Groningen,



Figure 1. Fran Bubanović (1883–1956), the founder of Department of Chemistry and Biochemistry at School of Medicine University of Zagreb.

he was invited to Nobel Institute in Stockholm, Sweden and in 1911 started his fruitful scientific collaboration with one of the fathers of physical chemistry, Nobel Prize winner Svante Arrhenius. Although their collaboration was relatively short, it turned into a lifelong friendship^[10,11] between Bubanović and Arrhenius families, where Arrhenius was even a godfather to his daughter. Arrhenius as his supervisor significantly influenced Bubanović's professional work. One of the most notable papers from this collaboration regards haemolysis.^[12] Bubanović's bibliography^[2,13] shows us that his scientific interests were liquid state physical chemistry, cellular physical chemistry, membrane permeability and analytical methods in chemistry and biochemistry.^[1] From that we can see that although he aimed to understand the basic chemical principles, he also strived to apply that knowledge to a living organism and to understand the broader meaning of chemistry in biomedical science.

During his career, Fran Bubanović published 23 scientific papers.^[9] The majority of those papers were published by 1930. After that period Bubanović focused on his teaching work and university textbooks. His most notable scientific papers, the ones published in collaboration with

Hamburger, Arrhenius and Fürth by 1918, were his most cited papers. After he started to organize and lead the Department of Chemistry and Biochemistry, he didn't want to impose his scientific interests on his younger colleagues and assistants (Tomislav Pinter, Josip Mikšić) who were free to pursue their own interests. Although he had the legitimate right, as the Department head and their supporter, to be a co-author on their papers, he never resorted to that option. We can only speculate how his scientific career would progress if he hadn't been consumed so much with teaching work.^[2]

His first very notable papers were published in collaboration with H. J. Hamburger.^[6–8] The results of experiments conducted for those papers (Figure 2)^[6,7] showed that red blood cells are equally permeable to both cations and anions which significantly contributed to understanding the process of haemolysis which led to Bubanović being invited to Nobel Institute in Stockholm. He also investigated the influence of fat-soluble substances on phagocytosis.^[8] That paper represents significant contribution to physiology and pathophysiology at that time. Other prominent contribution to science was published together with S. Arrhenius^[12] and that paper (Figure 2) also focused on haemolysis, specifically on different selected substances which increase or decrease the haemolysis rate in hypotonic solutions. The collaboration with O. von Fürth resulted in investigation of diffusion of electrolytes in colloidal gelatinous system^[14,15] which led to a more profound understanding of observed vs. theoretical behaviour of different electrolytes in colloidal solutions. A list of all Bubanović's scientific papers can be found in references 2, 3 and 13.

POPULARIZATION OF SCIENCE

It is often said that Fran Bubanović is one of the greatest Croatian science communicators. This area of his activities has been extensively covered by other Croatian chemists and scientists.^[4,10,11,16–20] The purpose of all of his efforts in science popularization was to bring natural sciences closer to the general public in a way that complex chemical principles and laws can be understood and applied in everyday life by a non-scientist. He published more than a hundred popular papers and about a dozen books and booklets on diverse topics. He was a firm believer in educating the people and even today, he is most known for his work on science popularization. His greatness and progressive feeling for social justice is evident from the fact that his vast knowledge was not reserved only for the academic environment, but also for the broad community and the people who couldn't afford higher education. He will most definitely be remembered for his science communication efforts which can be attributed to the fact that he was an

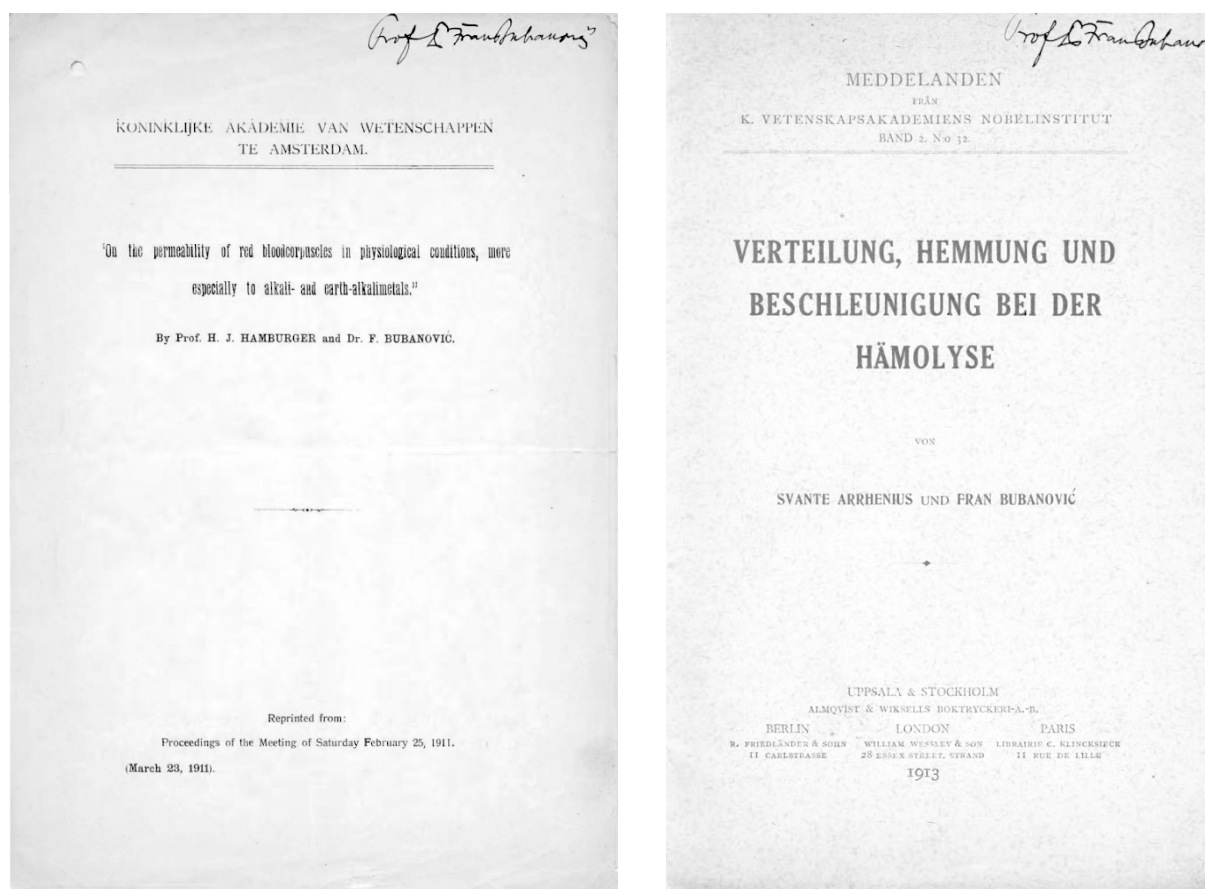


Figure 2. Cover pages of Fran Bubanović's papers with Hartog Jacob Hamburger and Nobel prize winner Svante Arrhenius.

extremely literate and eloquent person. Being the great lecturer that he was, he was able to explain the most perplexing topics in an easy and understandable manner. A list of all Bubanović's science popularization texts can be found in references 2, 3 and 13.

TEACHING AND IMPACT AT SCHOOL OF MEDICINE ZAGREB

In the academic year 1918/1919 Fran Bubanović established the Department of Applied Physician Chemistry which was at that time the most modern university chemistry department. In the very first semester after School of Medicine was founded, chemistry classes were held at Division of Pharmacy, Faculty of Philosophy by Professor Gustav Janeček until the newly founded Department at School of Medicine was operational. It contained a lecture hall, student laboratory, many scientific laboratories and a library with capital works and up to date issues of scientific journals. Within a few short years, education in chemistry and biochemistry at the Department was at the highest level for that time in means of instruments and equipment,

available chemicals and well educated staff.^[21] It should also be noted that from the first years until today the Department changed its name several times and is now known as the Department of Chemistry and Biochemistry.

In addition to founding the Department of Chemistry and Biochemistry and introducing the (bio)chemistry courses, Bubanović also had other major roles in the history of School of Medicine. From 1918–1941 he was the Head of the Department of Chemistry and Biochemistry, from academic year 1952/1953 – 1954/1955 he was also the Head of the Physiology Department and, most notably, he served as Dean of School of Medicine in two terms: academic years 1921/1922 and 1930/1931. Until today, that makes him the only non-physician Dean of School of Medicine!^[22]

In the period from 1918/1919 until 1940/1941 Bubanović teaches chemistry and biochemistry not only to medical students, but also to chemistry and pharmacy students at the Division of Science and Division of Pharmacy, respectively, held at the time at Faculty of Philosophy University of Zagreb. In addition, he taught chemistry to veterinary medicine students at the Faculty of Veterinary Medicine.^[22,23] Taking all of this into account, we may claim that Bubanović taught chemistry at every possible course in

Zagreb at the University level. An interesting fact is that during his career Bubanović was retired in a period from 1941–1945 which coincided with the formation of Independent State of Croatia during the Second World War. He was retired because he belonged to the freemasons order until 1939.^[1,24] The fact that he left the freemasonry saved him from being prosecuted and sent to a concentration camp – instead he was simply retired. He came out of retirement after the end of Second World War and the formation of Yugoslavia.

During his academic years Bubanović and his colleagues introduced many courses for medical students. From the very beginning, chemistry and biochemistry classes were held as two-semester courses with a relatively high study load per week, especially when compared to today's curriculum at School of Medicine in Zagreb. Each of these courses had both theoretical and practical part. In addition to obligatory courses, a large number of elective courses were also taught. To mention a few of his colleagues who were critical for the functioning of the Department during the Bubanović period, we should note Josip Mikšić (the first Bubanović's assistant), Tomislav Pinter (who will become the Department Head after Bubanović in 1946) and Mihovil Proštenik (who will become the Department Head after Pinter in 1971). During Bubanović's involuntary retirement (1941–1945) the Department was led by Stanko Miholić (1941) and Ibrahim Ruždić (1942–1946). After Bubanović, who coordinated both chemistry and biochemistry classes, the chemical group of courses were led by Tomislav Pinter, while biochemical courses were coordinated by Mihovil Proštenik.^[22,24]

CAPITAL WORKS ON MEDICAL CHEMISTRY AND BIOCHEMISTRY

After listing the achievements and contribution of Bubanović to science, science popularization and teaching at School of Medicine, it would be reasonable to assume that all of this work is more than enough for a one man's lifetime. However, probably the greatest contribution of Bubanović to Croatian medical chemistry and chemistry in general is thousands of pages of textbooks on chemistry. Bubanović was a firm believer that there is no quality education in small nations if there are no adequate textbooks in their mother tongue.^[1] As soon as 1921, just several years after School of Medicine was founded, Bubanović published "*Chemistry for medical students; chemical analytical practicals*" (original title "*Kemija za medicinare; kemijske analitičke vježbe*").^[25] That historical textbook is the first textbook of School of Medicine altogether, not only in basic science! This work is divided in three parts:

inorganic, organic and physiological. Inorganic part describes qualitative analysis of selected metals and non-metals. Organic part deals with the reactions of some biologically relevant compounds, while physiological part contains some examples of qualitative and quantitative biochemical analysis of urine and gastric juice. His capital work is the "*Chemistry for students of chemistry, medicine, veterinary medicine and pharmacy*" (original title "*Kemija za slušače kemije, medicine, veterine i farmacije*").^[26] This textbook had three editions: the first edition was published in three volumes from 1930–1931 and it is very important to note that it was the first university textbook of chemistry in Croatia. On a bit more than 1700 pages, the first volume contains: I. Theoretical or general part and II. Inorganic chemistry. Volume two is composed of: I. Organic chemistry and II. Biochemistry. Volume three consists of: I. Chemical analytical practicals and II. Chemical analysis of urine. The second (published 1946–1948) and third (published 1948–1950) editions had two volumes each and every volume contains two issues. In 1949 Bubanović has been awarded with a prize from Yugoslavia government for his work. It should be pointed out that at that time most of the relevant textbooks of chemistry and biochemistry were written in German or English. Therefore, by writing this textbook, Fran Bubanović enabled students not only from Croatia but from whole former Yugoslavia, minority of which spoke foreign languages, to study chemistry on the highest possible level.^[1] This textbook still remains the only textbook of a Croatian author which covers complete overview of general, physical, analytical, inorganic, organic chemistry and biochemistry! Had Bubanović left us only with this one textbook, we would be immensely indebted to him, let alone his entire legacy. It is absolutely fascinating that a single person was able to write a textbook which encompasses all chemistry disciplines. That only strengthens our perception of Bubanović as a man with a huge literary talent and encyclopaedic knowledge of natural science.

Volume one (Inorganic chemistry) of the later editions is composed of issues: 1. General part of inorganic chemistry and 2. Specialized part of inorganic chemistry. Volume two (Organic chemistry) is comprised of issues: 1. General overview of organic compounds and 2. Specialized organic compounds (biochemistry). In issue 1 of volume 1, Bubanović covers the essential concepts and laws of chemical changes, determination of molecular and atomic masses, nomenclature and classification of chemical elements and compounds, thermochemistry and thermodynamics, electrochemistry, chemical equilibrium, kinetics, atomic and molecular theory, colloidal state of matter, solid state of matter and crystal systems, and stoichiometry. Issue 2 of volume 1 covers the properties, reactions and compounds of the following groups of elements: noble gases, alkali and alkaline earth metals, boron, carbon and

nitrogen group of elements, chalcogens and halogens, and the d-block groups of transition metals (*e.g.* copper, zinc, titanium, chromium, nickel, cobalt and iron group). Issue 1 of volume 2 covers the general overview of the chemistry of the following organic classes of compounds: alkanes, halogenoalkanes, alcohols, aldehydes and ketones, carboxylic acids, ethers, esters, amines, amides, nitriles, sulphur and phosphorus containing organic compounds, alkenes, alkynes, substituted carboxylic acids, aromatic compounds, polycyclic and heterocyclic compounds and plant alkaloids. Issue 2 of volume 2 encompasses the chemistry and biological role of lipids like fats and oils, cholesterol and its derivatives, phospholipids and sphingolipids, carbohydrates (naturally occurring mono-, di- and polysaccharides), proteins, vitamins and hormones as well as enzymes.

In addition to textbooks that cover the theoretical part of courses held at the Department of Chemistry and Biochemistry, Bubanović also published a “*Laboratory manual of medical chemistry*” (original title “*Praktikum medicinske kemije*”), first printed in 1937. After this first edition, four more editions were published in: 1939, 1946, 1948 and 1952.^[27]

His laboratory manuals were printed on more than 450 pages, each edition in two issues: 1. Inorganic, organic and general part and 2. Biochemical part. Issue one covers the qualitative analysis of cations and anions, determination of pH values, density of liquids, melting point, instrumental methods such as polarimetry and colorimetry, volumetric methods (neutralization, redox and precipitation titrations) in addition to exercise regarding electrolysis and colloidal chemistry. Also, qualitative tests and specific reactions of mono-, di- and polysaccharides, fats, oils and cholesterol as well as proteins are described. Issue two covers reactions involving major groups of organic compounds in human body and food as well as the analysis of normal and pathological urine, blood, gastric juice, other body fluids (saliva, bile) and faeces analysis.

His vision and a great sense for teaching medical biochemistry and chemistry in general is best demonstrated by the fact that some of the exercises described in this laboratory manual are still performed today at School of Medicine, as well as some other faculties which teach chemistry classes at Croatian Universities. That only proves that Bubanović created an incredibly strong foundation for medical chemistry education in Croatia.

CONCLUSION

From all this, it is obvious that the impact that Fran Bubanović had on medical chemistry education in addition to science and science communication is unmeasurable. He had a major role in establishing a stimulating scientific

milieu for generations of scientists by organizing a modern and practical chemistry education not only for medical students, but much broader. His textbooks and laboratory manuals have a remarkable didactic value and eight of his textbooks have been cited a total of 20 times which clearly demonstrates their relevance. Furthermore, five of his younger colleagues and assistants later became university professors, including one academician (Mihovil Proštenik). It should also be kept in mind that his enormous contributions were made in very turbulent and uncertain time in history, between and during the world wars. That makes his legacy even greater when we examine it in a historical context.

Today, at the Department of Chemistry and Biochemistry, we honour Professor Fran Bubanović by celebrating his day in November each year (around his birthday) since 2013. That is also the year from which the lecture hall at the Department, which originates from his first days, bears his name. It is impossible to really depict his enormous contribution to medical chemistry and biochemistry education in just one paper. It is sure that without him medical education in basic sciences as well as science communication in Croatia would have been completely different. Bubanović in many occasions argued on the importance of acquiring knowledge in basic science for solid medical education. From today's perspective, Bubanović was a true visionary and a man well ahead of his time. In the age of molecular medicine, being a truly successful modern physician implies integrative understanding of basic (bio)chemical and molecular principles of life more than ever. For all his efforts, we can only sincerely thank Fran Bubanović and try to look up to him as a role model of truly fascinating and inspiring teacher.

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