Con stima e affetto
Gino

ACCADEMIA NAZIONALE DELLE SCIENZE
detta dei XL

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A BRIEF HISTORY OF ITALIAN BIOCHEMISTRY

from its origins up to the Second World War

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A NUMBER OF EXPLANATORY NOTES SERVING AS A PREFACE

What follows is not history in the true sense, at least not in the sense alluded to by the poet Heinrich Heine, who considered the writing of a history of one or more events to represent a sort of reverse prophesy, meaning a prophesy of what had already come to pass. Indeed, if the writing of history entails demonstrating that what came to pass was destined to come to pass, then the paragraphs that follow belong to a different category, given that they describe not circumstances, but only facts (or, better yet, only a small number of the available facts), most of which, for that matter, are unconnected. Indeed, there are many gaps that could have been filled through more thorough research (impossible given the small amount of time available) or with the "work of honest imagination, remaining as faithful as possible to information gleaned from unimpeachable sources" (as suggested by the French scholar of medieval studies George Duby). The latter method was avoided, however, in the conviction that it is not possible to construct an historic rationalization of biochemistry on a strictly national basis, given that scientific progress is inherently based on international and world-wide exchanges, borrowings and influences.

Another explanatory note is due to the reader, inasmuch as "to historians is granted a talent that even the gods are denied: to alter what has already happened". This scornful adage has been kept in mind throughout the present effort. Obviously, there has been no willful attempt to distort anything, the purpose of this document not being the singing of anyone's praises within the context of tribal lore. For that matter, as early as the first century of our epoch, Plutarch was already heaping scorn on those who held that the moon over Athens was more beautiful than that over Corinth. As such, in order to avoid involuntary errors (not omissions, of which there are naturally a good many) most of the facts referred to, the events narrated and the citations presented have been verified in the original documents and texts.

There is one last point to be made. Limits of space do not allow me to list all those who have contributed directly or indirectly to the preparation of this document. Nonetheless, I must acknowledge the assistance of Professor Alessandro Rossi Fanelli, a fond acquaintance of long date; I must also thank Professor Francesco M. Chiancone, who has so generously shared his advice with me, together with Dr. Marina Giannetto, who kindly allowed me to consult the materials stored in the Central State Archives. Special thanks go to Professor Alessandro Finazzi-Agrò, who suggested the subject of this research effort and graciously offered me invaluable information. I would also like to mention Mr. Mario Sanchioni, who unfailingly brought his masterful skills to bear on the often formidable technical difficulties presented by the need to photograph iconographic material. I should also state my indebtedness for revision of English to a friend of mine who chooses to remain anonymous. Last, but not least, sincere appreciation and thanks go to the Accademia Nazionale delle Scienze, detta dei XL (National Academy of Sciences, called of the Forties), for having made possible to include this monograph in her publications on the history of sciences.

THE RECOGNITION OF BIOCHEMISTRY AS AN AUTONOMOUS DISCIPLINE IN ITALY

> Quando dismento nostra vanitate
> Trattando l'ombre come cosa salda.
>
> [When I forget we are empty semblances
> And take shadows to be substances.]
>
> DANTE ALIGHIERI, *La Divina Commedia*
> Purgatory, XXI, 135-136

In the middle of the last century, the medical faculties of a good many Italian universities maintained laboratories of physiological and pathological chemistry that served primarily to provide technical support in the gathering of data potentially useful to the formulation of clinical and forensic diagnoses: in addition, they also functioned as research centers for the study of "animal chemistry" (primarily biological liquids). In practice, when applied to living organisms, chemistry became the handmaiden of clinical disciplines (the expression used at the time).

An important step towards official recognition of biochemistry as an autonomous discipline in the framework of the Italian university system can be traced back to 1870. In that year, Italy's Ministry of Public Education assigned the twenty-seven year-old Giorgio Roster of Florence to visit the universities of Germany, Austria and Switzerland and draw up a report on the teaching of the experimental sciences, with particular emphasis on chemistry. The full report was published in 1872 under the auspices of the aforementioned ministry, taking the form of a large volume with no less than 400 pages, 30 tables and 13 illustrations, printed in Milan by Civelli. Through this formal act, those responsible for determining Italian university policy let it be known that their model was the university system in German-language countries, where the chemical approach to the study of the structural and functional properties of living matter had already been firmly established. Beginning in 1866, two years after taking his degree in medicine, Roster became an assistant in the laboratory of physiological and pathological chemistry in the department of medicine and surgery at the Royal Institute of Applied and Advanced Studies (today's University of Florence). In light of his ability, the instruction he had received and his skill, this young physician was eminently qualified to grasp the innovations in science and education present in the universities of central Europe, ultimately drawing conclusions that proved useful in a subsequent restructuring of the courses of study leading to degrees in Italy. Roster must also have been a very enterprising individual endowed with the prudence of a fox, given that he managed to obtain what Stanislao Cannizzaro (the man praised by the London Chemical Society as the potential equal of Galilei, Torricelli, Volta and Galvani) had failed to achieve. It so happened that, in 1872, Cannizzaro, who had become a senator, alerted the Minister of Public Education to the benefits of establishing a professorship in physiological chemistry. This new discipline appeared so important to Cannizzaro that he actually modified the course of study in organic chemistry during his tenure at the University of Palermo's faculty of science, adding subjects typical of what is today known as biochemistry (Fig. 1). In the same spirit, Cannizzaro chose a young graduate in medicine, who, after a year's apprenticeship in a Rome chemical laboratory, was sent abroad for two years of further study. By the time this candidate for the establishment of the new discipline returned, however, the situation had changed, and though Cannizzaro pressed the Minister to maintain his tacit pledge, there was nothing to be done. Roster, on the other hand, was chosen in 1878 as the first professor responsible for teaching a subject then new to Italy: physiological and pathological chemistry, a title that can be considered the name originally given to the discipline now known as biological chemistry.

The time was fast approaching when it would seem appropriate for this discipline to take on a structure of its own. In the event, just a few years later, two other teaching posts in physiological chemistry were officially granted to temporary lecturers: in 1881 Giuseppe Colasanti (Fig. 2) was appointed in Rome, and in 1883 Antonio Pasquale Malerba was given the same position in Naples. Despite these developments, the prestige of the classic disciplines taught in the faculty of medicine was still so predominant that Roster took the first opportunity presented him for a transfer, becoming a full professor of hygiene in 1890. Likewise, and in the same year, Colasanti transferred to *materia medica* and experimental pharmacology. At this stage, however, physiological chemistry had assumed a fundamental, autonomous role in the study of medicine in Italy, to the point where the Superior Council of Public Education recognized the importance of the subject by exempting it from a measure eliminating all assignments for the teaching of other specialized subjects. It was at the University of Naples that the clarity of thought and purpose needed to elevate the discipline to an automonous field of study were first given expression in Italy: in 1892, the faculty of medicine, acting on a proposal by Giuseppe Albini, a professor of physiology, voted to establish a chair of physiological chemistry (Fig. 3). This meant that the designated faculty member, Malerba, after a period spent as an associate professor (from 1883 to 1887) was able to become the first full professor of physiological chemistry in Italy (1898), a position for which he was paid an annual salary of 5,000 lira.

It is important to note that at the beginning of the study of physiological (and pathological) chemistry the subject received significant attention from hygienists, pharmacologists, pathologists, clinicians and physiologists: the latter were the very people who attempted to give the discipline a well defined structure at the beginning of the 20th century, clearly separating it from the study of clinical chemistry and forensic chemistry (the two other branches of applied chemistry then known in the field of medicine). The result was the creation of a second chair of physiological chemistry, this time at the University of Rome, which was housed in the facilities of the Institute of Physiology and taught, beginning in 1903, by a temporary professor named Domenico Lo Monaco — who became a full professor in 1910. During the first decade of the 1900's no new chairs of physiological chemistry were established, but various universities did offer opportunities for the official teaching of the subject, assigning the task to full professors of physiology (Valentino Grandis at the University of Genoa, Aristide Stefani at the University of Padua and Arturo Marcacci at the University of Pavia). The years 1910 to 1920 witnessed a significant expansion in the field of physiological chemistry, both in terms of teaching and organization. For the first time, positions were awarded to scholars not engaged in the teaching of other subjects (at the universities of Catania, Padua, Palermo, Parma, Pavia and Turin), and the first Italian Society of Biological Chemistry was founded (1913) under the leadership of its president, Eugenio Centanni, a general pathologist (i.e. a physiologist of pathological states) at the University of Modena. The Society's official publication (Fig. 4) was a monthly review entitled: Biochimica e Terapia Sperimentale (Biochemistry and Experimental Therapy).

This was the situation in the faculty of medicine. Beginning in the early years of this century, however, biochemistry (which made its first appearance as the official title of the subject at the time, replacing physiological chemistry) was also taught in the faculty of mathematical, physical and natural sciences, being assigned to Giacomo Ciamician, a full professor of general chemistry at the University of Bologna. In all likelihood, the importance of this discipline and the need to establish it as an independent field of study first entered Ciamician's mind in 1897, when he was called upon to participate in the ministerial commission responsible for deciding whether or not to promote Malerba from temporary to full professor of physiological chemistry at the University of Naples.

In the two decades between 1920 and 1940, there were four chairs of physiological chemistry in Italy. In addition to those that already existed at the Universities of Naples and Rome, the faculties of medicine at the Universities of Padua and Turin raised the status of the discipline to the chair level. Following the death of Malerba in 1917, the teaching of the subject at the University of Naples was first assigned on a temporary basis to the physiologist Filippo Bottazzi, and then to Gaetano Quagliariello, until 1926, when Quagliariello was made a full professor. In Rome, the position was taken by Giuseppe Amantea following the death of Lo Monaco in 1930. Achille Roncato arrived in Padua in 1931, having been a full professor of physiology and an instructor of physiological chemistry at the University of Ferrara. In 1937, Francesco Paolo Mazza, a pupil of Quagliariello and the first chemistry graduate allowed to teach the new discipline in a faculty of medicine, was brought to the University of Turin. In practice, however, lessons in physiological chemistry were taught by an official instructor, or by a full professor of physiology or general pathology, and this was the case at all Italian universities in the period between the two world wars. Gaetano Quagliariello, Giuseppe Amantea, Achille Roncato and Francesco Paolo Mazza had all initially taken their chairs after passing competitive examinations in physiology, and only later were they given their definitive assignments in physiological chemistry.

Seen in this light, the 1942 announcement of a competition for a specific chair in biochemistry (which from that point on was no longer referred to as physiological chemistry, the title it had retained in educational parlance) represented an historic event for Italian biochemistry. The winners of the competition were Alessandro Rossi Fanelli, Francesco Cedrangolo and Giovanni Moruzzi, assigned respectively to the Universities of Pavia, Perugia and Bologna (the first two scholars had been pupils of Quagliariello). In the event, Rossi Fanelli was unable to take his chair in Pavia until 1945 on account of the war, and in 1949 he was called on to fill the chair of biochemistry at the University of Rome, following Giuseppe Amantea's transfer to the chair of physiology.

Despite the healthy growth in the number of chairs, biochemistry remained an elective subject for Italian students for a number of years. As early as 1919, the Superior Council of Public Education had included in its proposal for the reform of the university system a measure introducing into the medical school program compulsory "instruction in biochemistry, to be assigned on a temporary basis to a professor of chemistry who also holds a degree in biology or in medicine, or *vice versa*". For his part, Centanni, then president of the Italian Biochemical Society, expressed the hope that study of the subject would become compulsory not only in medicine, but also in veterinary, pharmaceutical and agricultural studies. The list of compulsory subjects, however, was set by law, and there was no easy way to change it. In 1922, the new president of the Italian Biochemical Society, Amedeo Herlitzka, sought to overcome this obstacle by writing a letter to the Minister of Public Education suggesting that the examination in biochemistry be made obligatory and be given together with the physiology exam (thus leaving the total number of examinations for the medical degree unchanged). No other official steps were taken in this direction for the next twenty years, in part because the Italian Biochemical Society had been sliding towards a state of torpor for a number of years, to the point where one of its founders, Alberto Ascoli, had to make an official plea in favor of its revival. The end of the organization was near, however. Indeed, if one wanted to set an official date, it would have to be 1943, when the review Biochemistry and Experimental Therapy, the Society's official publication, ceased to exist. It was not until 1954 that biochemistry became a compulsory subject in medical schools, and even then the step was not taken for cultural reasons or because of the positions held by the Italian Biochemical Society, the new Society founded in Rome in 1951 on the initiative of Gaetano Quagliariello, Alessandro Rossi Fanelli, Silvestro Silvestri and Giuseppe Amantea. Instead, the ministerial decision was made in response to outside pressure: the United States of America had threatened not to grant legal recognition to Italian medical degrees, because of the fact that two areas of study held to be of fundamental importance did not exist in the Italian *curriculum studiorum*: biochemistry and microbiology.

In the meantime, the number of chairs in biochemistry had multiplied. In 1950 Vincenzo Baccari was awarded the chair in Florence, Arturo Bonsignore in Genoa and Vittorio Zambotti in Pavia. In 1954 positions went to Camillo Lenti in Turin and Alfredo Ruffo in Perugia. And the rest is the story of our own times.

GROWTH AND CONTRIBUTIONS OF BIOCHEMICAL RESEARCH IN ITALY

> For there is no remembrance of the wise more than of the fool for ever; seeing that wich now is in the days to come shall all be forgotten. And how dieth the wise man? as the fool.
>
> *Ecclesiastes*, II, 16
> (KING JAMES version of the Bible)
>
> But what is there to do? what is left to be done?
> Is there no enduring crown to be won?
>
> THOMAS S. ELIOT, *Murder in the Cathedral*, 561-562

It is said that every generation contains four righteous men who, unbeknownst to the rest of mankind, uphold the world, justifying it before God. This historical account has been divided by centuries rather than generations in order to simplify the task of the writer, and for each century a handful of scientists has been found (chosen?) of whom it can be said that they upheld their age, and who perhaps existed for a larger purpose than simply to justify the present essay. Inasmuch as this separation of time into century-long units is nothing more than a convenient device, it is hoped that the reader will not object to passages which stray slightly from the rule.

The 18th century: organic material is subdivided into its different components

In general, the dawn of Italian biochemistry, understood in the modern sense of the term, is identified in two works by Lazzaro Spallanzani (1729-1799), one of which is posthumous: Dissertations on Animal and Vegetable Physics appeared in Modena in 1780, while Notes on Respiration was published in Milan in 1803. In the first effort, Spallanzani illustrated the digestive action of the gastric juices, apart from any mechanical action by the walls of the digestive tract, demonstrating the difference between the digestive processes and those of fermentation and putrefaction. In addition, he described a method for simulating digestion in a test-tube, a procedure that represented an invaluable tool for analyzing the chemical aspect of the digestive function. In the second work, Spallanzani completed the hypothesis proposed by Antoine Laurent de Lavoisier (1743-1794), who had discovered the chemical justification for the brilliant observation made in an earlier age by Leonardo da Vinci (1452-1519), who said that "animals can only live where the flame can live". Spallanzani's contribution was to locate the site of the biological oxidation that takes place deep inside animal tissues (marking the definitive introduction of the concept of cell respiration). Through an ingenious set of experiments performed on snails, he proved that the emission of carbon dioxide did not depend on the absorption of oxygen, inasmuch as it occurred to more or less the same degree even when these testaceans were enclosed in an environment lacking any gas, or filled with nothing but nitrogen (simultaneously he demonstrated that the nitrogen in the atmosphere does not participate in the exchange of gases).

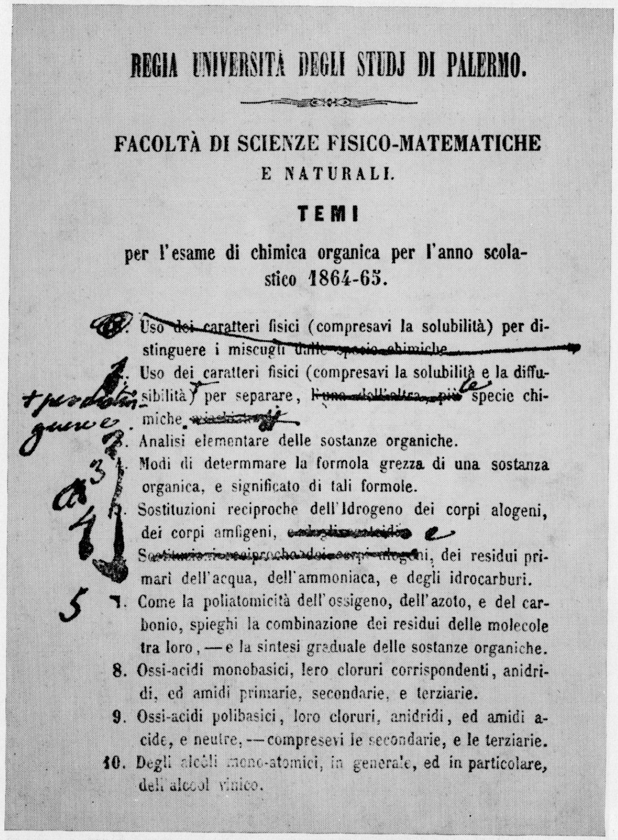
One may have to reach back to the scientific work of Jacopo Bartolomeo Beccari (1682-1766), however, to recognize the true founder of Italian biochemistry. The paper he presented to Bologna's Accademia degli Inquieti (Academy of the Curious) in 1728 — but which was published only in 1745 — presents the discovery of gluten derived from wheat flour, providing the chemical demonstration for the fact that this component of the flour is similar to the substances that characterize foods from animal sources. A surprisingly simple research method was used to separate the starch from the gluten (the name of the latter substance, a term still used today, was created by Beccari). He mixed the wheat flour with water and produced a paste which he then squeezed through a linen sieve in order to remove the water, which also carried away the starch. A durable fibrous substance was left inside the linen sack, explaining the term gluten, which means glue in Latin. When left exposed to the air, this substance underwent the same alterations that result from the putrefaction of meat. When subjected to chemical processes of distillation, the substance gave off alkaline vapors and liquids, exactly what happens in the case of animal meat. The starch portion, on the other hand, did not putrefy, and no alkaline substances were distilled off. Instead, it underwent fermentation, producing acid, "wine-like" substances (alcohols).

These results immediately received a significant amount of attention, and were widely cited in the years that followed (as in Kesselmeyer's fundamental text, Elementa physiologiae corporis humani, volume VI, Bernae, 1764, page 192 on). Eventually, however, they were forgotten (the last citation would seem to have been made by Gmelin in 1797). Equally worthy of mention is the connection Beccari drew in 1766 between gluten and *caseum* (coagulated milk), which confirmed his conjecture that the substance he had separated from the flour appeared to be a material that could only be derived from the meat of animals ("ab animantium corporibus"). But Beccari was also the first (or at least one of the first) to have discovered among the different components of a variety of foodstuffs, both animal and vegetable in origin, a common substance characterized by its soft, gelatine-like form and its lack of taste and odor, properties that made it seem identical to egg white (in effect, proteins) and which he identified from the fact that it coagulated when subject to heat or the addition of spirits of wine (meaning ethanol). The discovery of the fact that substances similar to those held to be typical of animals were to be found, and in significant quantities, in vegetables, overturned what had been held to be one of the fundamental differences between the two realms of nature, meaning the animal and the vegetable, at the beginning of the 18th century.

In actual fact, the gluten discovered by Beccari was not composed of a single substance, but rather a mixture of two proteins. It was Giovanni Taddei (1792-1860) who distinguished the two different substances present in wheat gluten, doing so in 1818: one was soluble in ethanol, corresponding to gliadin (Taddei called it gloiodina), while the other, which did not dissolve in ethanol, was called zimoma.

There is no mention of Beccari's discovery of gluten in the otherwise excellent History of Biochemistry by Marcel Florkin (in Comprehensive Biochemistry, M.G. Florkin and E.H. Stotz editors, Elsevier, Amsterdam, 1972). Nor is there any reference to the discovery of iron in the blood erythrocytes by Vincenzo Menghini (1705-1759), made in the 18th century and published in the minutes of the Institute of Bologna (volume II, part II) in 1746 under the title (Fig. 5): De ferrearum particularum sede in sanguine (On the Site of the Iron Particles in the Blood). Menghini drew blood from a dog and turned it to ash (thus transforming the ferrous ion bound to the haem into ferric oxide). He then held a magnetized knife near the ashes. Surprised at the significant amount of iron contained in the blood, he initially suspected that the metal might have been present in the clay jar used to incinerate the blood. He also wondered if the humidity in the air might not have moistened the knife, explaining the fact that the ashes stuck to the blade. In order to be certain of his result, he repeated the experiment, frequently changing the magnetized knifes and performing the procedure both alone and in the presence of friends ("mutatis saepe cultris, nunc solus, nunc cum amicis"), but the result remained unchanged. Having removed all possible doubts and convinced himself of the presence of iron in the blood, he extended the scope of his experiments to a variety of different animals (four-legged animals, birds, amphibious creatures and fish), publishing his paper, in which he concluded that the iron present in man and animals was not to be found in their flesh, nor in their bones or their fat, but in their blood, where, for that matter, it was not distributed homogeneously, being present only in the corpuscular portion ("non in carnis, non in ossibus, non in pinguedine, non in universo sanguine, sed in sola huius parte globulari"). Obviously, Menghini's method was not very accurate. Indeed, the iron attracted by the magnetized knife carried with it a portion of the ashes that had no magnetic properties whatsoever, meaning that the calculations for the amount of iron found in human blood were inaccurate by a significant degree of error, being 15 times higher than the actual concentration.

The importance of Menghini's observation was quickly understood by his colleagues, who went on to extend the scope of his experiments. In truth, Menghini himself had done nothing more than provide proof for the suppositions already raised by the experiments of Domenico Maria Gusmano Galeazzi (1686-1775). There exists a document by Galeazzi from 1746, also contained in the Minutes of the Institute of Bologna, which describes how a method similar to Menghini's was used by him to detect iron in the blood and urin of individuals



REGIA UNIVERSITÀ DEGLI STUDJ DI PALERMO.

FACOLTÀ DI SCIENZE FISICO-MATEMATICHE
E NATURALI.

TEMI

per l'esame di chimica organica per l'anno scolastico 1864-65.

~~Uso dei caratteri fisici (compresavi la solubilità) per distinguere i miscugli dalle specie chimiche~~

1. Uso dei caratteri fisici (compresavi la solubilità e la diffusibilità) per separare, ~~l'una dall'altra, più~~ le specie chimiche ~~[illegible]~~ + per distinguere.

2. Analisi elementare delle sostanze organiche.

3. Modi di determinare la formola grezza di una sostanza organica, e significato di tali formole.

4. Sostituzioni reciproche dell'Idrogeno dei corpi alogeni, dei corpi amfigeni, ~~[illegible]~~ e ~~Sostituzioni reciproche dei corpi alogeni~~, dei residui primari dell'acqua, dell'ammoniaca, e degli idrocarburi.

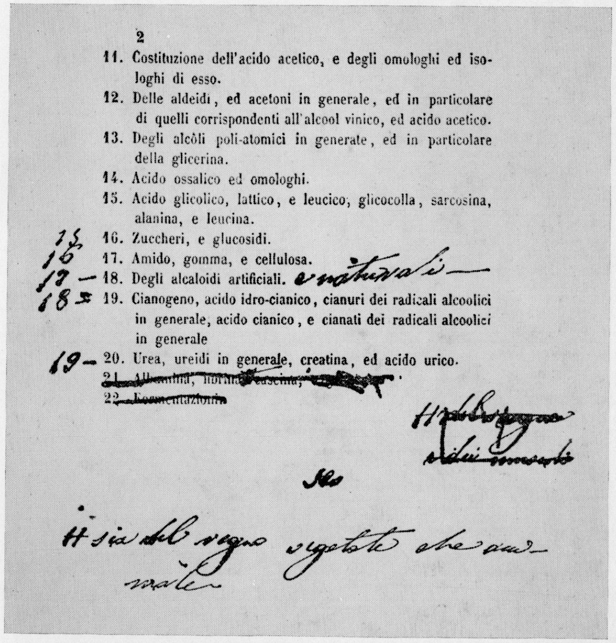
5. Come la poliatomicità dell'ossigeno, dell'azoto, e del carbonio, spieghi la combinazione dei residui delle molecole tra loro, — e la sintesi graduale delle sostanze organiche.

8. Ossi-acidi monobasici, loro cloruri corrispondenti, anidridi, ed amidi primarie, secondarie, e terziarie.

9. Ossi-acidi polibasici, loro cloruri, anidridi, ed amidi acide, e neutre, — compresevi le secondarie, e le terziarie.

10. Degli alcôli mono-atomici, in generale, ed in particolare, dell'alcool vinico.

Fig. 1a.



2

11. Costituzione dell'acido acetico, e degli omologhi ed isologhi di esso.

12. Delle aldeidi, ed acetoni in generale, ed in particolare di quelli corrispondenti all'alcool vinico, ed acido acetico.

13. Degli alcôli poli-atomici in generale, ed in particolare della glicerina.

14. Acido ossalico ed omologhi.

15. Acido glicolico, lattico, e leucico; glicocolla, sarcosina, alanina, e leucina.

15 — 16. Zuccheri, e glucosidi.

16 — 17. Amido, gomma, e cellulosa.

17 — 18. Degli alcaloidi artificiali. e naturali —

18 — 19. Cianogeno, acido idro-cianico, cianuri dei radicali alcoolici in generale, acido cianico, e cianati dei radicali alcoolici in generale

19 — 20. Urea, ureidi in generale, creatina, ed acido urico.

~~21 Albumina, fibrina, caseina, [illegible]~~

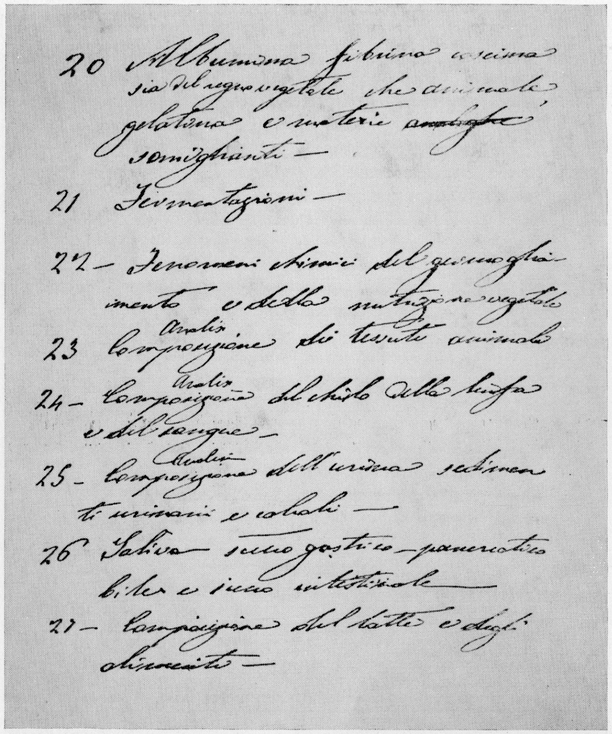
~~22 Fermentazioni~~

~~[illegible]~~

~~[illegible]~~

Il sia del regno vegetale che animale

Fig. 1b.



20 Albumina fibrina caseina
sia del regno vegetale che animale
gelatina e materie ~~analoghe~~
somiglianti —

21 Fermentazioni —

22 — Fenomeni chimici del germogliamento e della nutrizione vegetale

Analisi
23 Composizione dei tessuti animali

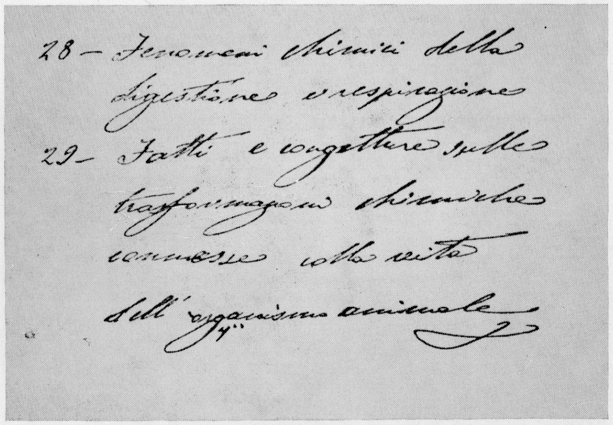
Analisi
24 — Composizione del chilo della linfa
e del sangue —

Analisi
25 — Composizione dell'urina sedimenti
urinari e calcoli —

26 Saliva — succo gastrico — pancreatico
bile e succo intestinale —

27 — Composizione del latte e degli
alimenti —

Fig. 1c.

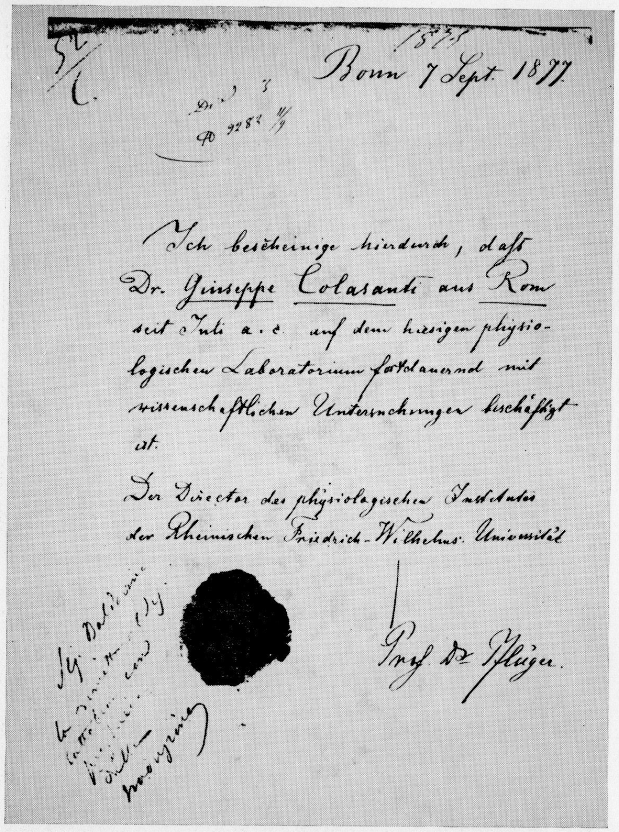


28 — Fenomeni chimici della
digestione e respirazione

29 — Fatti e congetture sulle
trasformazioni chimiche
connesse colla vita
dell'organismo animale
4''

Fig. 1d.

Fig. 1 - Contents of the examination in organic chemistry (four pages in all) at the faculty of science of the University of Palermo. The handwritten corrections were made by Stanislao Cannizzaro, who inserted subjects typical of biochemistry, such as: 23. Composition of animal tissues; 28. Chemical phenomena involving digestion and respiration: 29. Facts and hypotheses on the chemical transformations connected with the life of animal organism.



1575

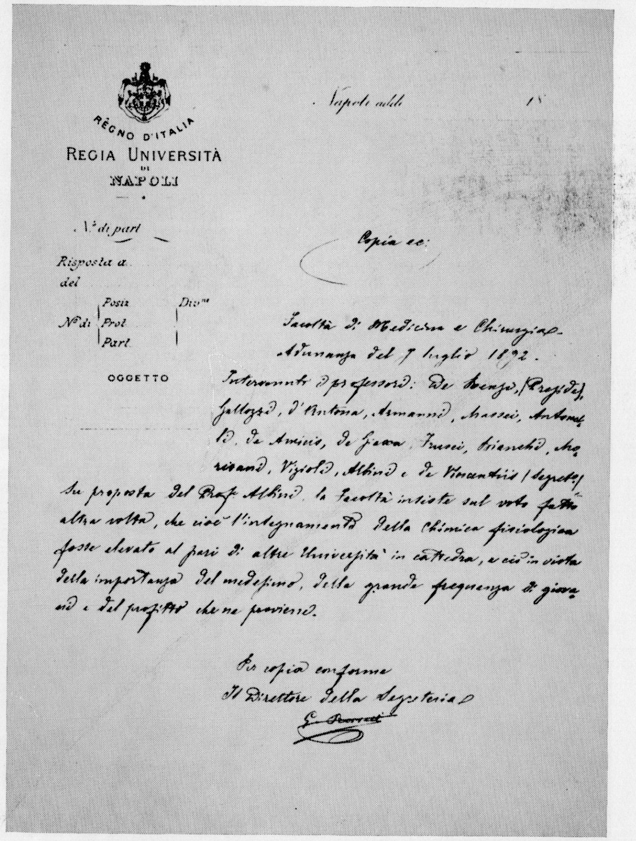
Bonn 7 Sept. 1877

Ich bescheinige hierdurch, daß
Dr. Giuseppe Colasanti aus Rom
seit Juli a. c. auf dem hiesigen physio-
logischen Laboratorium fortdauernd mit
wissenschaftlichen Untersuchungen beschäftigt
ist.

Der Director des physiologischen Instituts
der Rheinischen Friedrich-Wilhelms-Universität

Prof. Dr. Pflüger

Fig. 2 - Attendance certificate from the Physiology Institute at the University of Bonn, issued by Eduard Pflueger in 1877 to Giuseppe Colasanti.



REGNO D'ITALIA
REGIA UNIVERSITÀ
DI
NAPOLI

Napoli addì 18

N.° di part.

Risposta a
del

N° di Posiz. Prot. Part.
Div.ne

OGGETTO

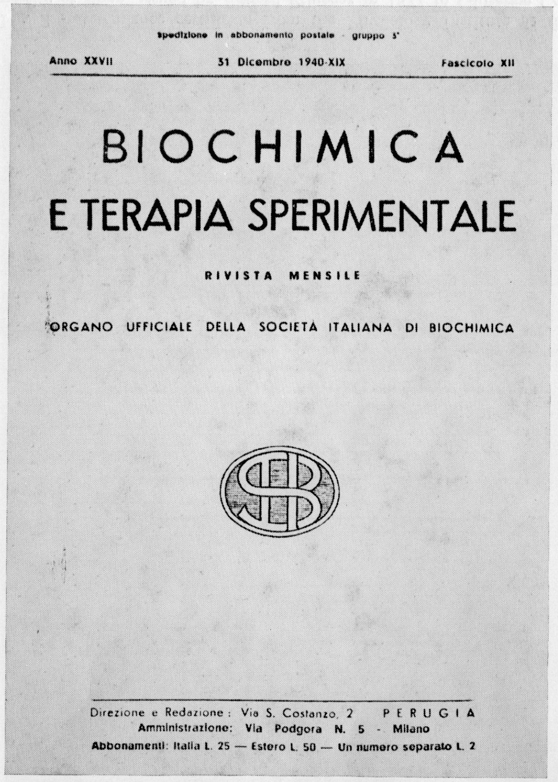
Copia ec.

Facoltà di Medicina e Chirurgia.
Adunanza del 7 luglio 1882.
Intervenuti i professori: De Renzi (Preside), Gallozzi, d'Antona, Armanni, Massei, Antonelli, De Amicis, de Giaxa, Fusco, Bianchi, Morisani, Vizioli, Albini e De Vincentiis (deputato)

Su proposta del Prof. Albini, la Facoltà insiste sul voto fatto altra volta, che cioè l'insegnamento della Chimica fisiologica fosse elevato al pari di altre Università in cattedra, e ciò in vista della importanza del medesimo, della grande frequenza di giovani e del profitto che ne proviene.

Per copia conforme
Il Direttore della Segreteria
G.

Fig. 3 - Official copy of the July 7, 1882 resolution with which the Council of the Faculty of Medicine and Surgery at the University of Naples expressed the hope that a chair would soon be establish for the teaching of physiological chemistry.



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BIOCHIMICA
E TERAPIA SPERIMENTALE

RIVISTA MENSILE

ORGANO UFFICIALE DELLA SOCIETÀ ITALIANA DI BIOCHIMICA

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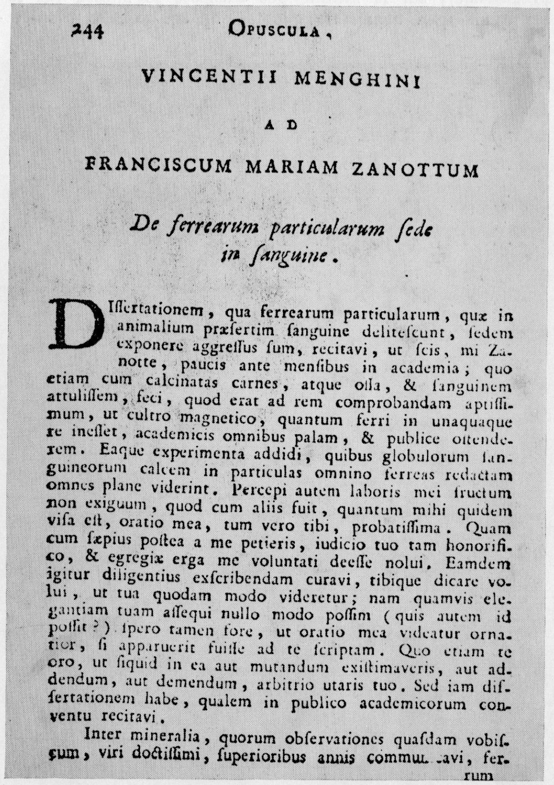
Fig. 4 - Title page of the review entitled Biochimica e Terapia Sperimentale, official publication of the first Italian Biochemical Society.



244   Opuscula,

VINCENTII MENGHINI

AD

FRANCISCUM MARIAM ZANOTTUM

De ferrearum particularum ſede in ſanguine.

DIſſertationem, qua ferrearum particularum, quæ in animalium præſertim ſanguine deliteſcunt, ſedem exponere aggreſſus ſum, recitavi, ut ſcis, mi Zanotte, paucis ante menſibus in academia; quo etiam cum calcinatas carnes, atque oſſa, & ſanguinem attuliſſem, feci, quod erat ad rem comprobandam aptiſſimum, ut cultro magnetico, quantum ferri in unaquaque re ineſſet, academicis omnibus palam, & publice oſtenderem. Eaque experimenta addidi, quibus globulorum ſanguineorum calcem in particulas omnino ferreas redactam omnes plane viderint. Percepi autem laboris mei fructum non exiguum, quod cum aliis fuit, quantum mihi quidem viſa eſt, oratio mea, tum vero tibi, probatiſſima. Quam cum ſæpius poſtea a me petieris, iudicio tuo tam honorifico, & egregiæ erga me voluntati deeſſe nolui. Eamdem igitur diligentius exſcribendam curavi, tibique dicare volui, ut tua quodam modo videretur; nam quamvis elegantiam tuam aſſequi nullo modo poſſim (quis autem id poſſit?) ſpero tamen fore, ut oratio mea videatur ornatior, ſi apparuerit fuiſſe ad te ſcriptam. Quo etiam te oro, ut ſiquid in ea aut mutandum exiſtimaveris, aut addendum, aut demendum, arbitrio utaris tuo. Sed iam diſſertationem habe, qualem in publico academicorum conventu recitavi.

Inter mineralia, quorum obſervationes quaſdam vobiſcum, viri doctiſſimi, ſuperioribus annis communicavi, fer-

rum

Fig. 5 - Opening page of the report by Vincenzo Menghini (1705-1759) on the discovery of iron in red blood cells.

living near iron mines and others far removed from these sites. Though Galeazzi failed to demonstrate a significant difference between these two groups, he did find high levels of iron in the urine ("ferri particulae plurimae in urinis inventae") of two women who lived far away from the mines, but had been treated with preparations containing large amounts of the metal. In this way he demonstrated that iron is eliminated through the urine.

A large number of other scientists in 18th century Italy devoted their efforts to research that could be considered biochemical in nature, and though their results were not as outstanding as those of Beccari and Menghini, some of these individuals deserve mention all the same. Without a doubt, the most original thinker of the group was Felice Fontana (1730-1805), who obtained experimental results that make his name part of the history of biochemistry, despite the fact that his chief interest was the pharmacology of drugs and poisons. Having been inspired by the experiments of Antoine Laurent de Lavoisier (1743-1794), whom he and Joseph Priestley (1733-1804) had both assisted, he analyzed the air using a eudiometer he had invented himself. After taking experimental data in London, Paris and other European cities, he concluded that the composition of the air is identical everywhere and constant over time. Fontana sent Priestley the data from this research in a letter published in 1799. He used what was also an ingenious method for that day and age to demonstrate that Mead was wrong in claiming that snake venom was acid at the moment of emission: he let the reptile bite a ball of string wrapped up in litmus paper, which demonstrated that the venom was neither acid not alkaline.

Other Italian scientists limited themselves to systematically applying known analytical techniques to a wide variety of entities. As is explained by Antoine François Fourcroy (1755-1809) in his *Système des connaissances chimiques et de leurs applications aux phénomènes de la nature et de l'art*, the chemical analysis of those years was based on distillation, combustion and the extraction of chemical components through the use of solvents, such as water, acids, alkalis and alcohols. By using these techniques, Carl Wilhelm Scheele (1742-1786) and Fourcroy (to cite just two names) isolated a large number of compounds between 1770 and 1800, including uric acid from urine, glycerol from various oils, hydrocyanic acid from almonds, benzoic acid from horse urine, gallic acid from gall nuts and calcium oxalate from rhubarb (the list could go on at length). At about the same time in Italy, Luigi Brugnatelli (1761-1818) was isolating suberic acid by treating cork with nitric acid, while other scientists made the first attempts at technological applications. Indeed, efforts were made to extract sugars from vegetables in order to substitute the cane sugar that Napoleon's continental blocade had eliminated from the Italian market. Working along these lines, Gioannetti successfully obtained sugar from zea corn, as did Cavezzali with grapes and Guerrazzi with chestnuts.

The 19th century: bio-organic molecules and their transformations

In 1803 John Dalton (1766-1844) introduced the concept of the atom to chemistry, and in 1811 Amedeo Avogadro (1776-1856) did the same for the molecule. This led to Michel Eugène Chevreul's (1786-1889) formulation of the two different approaches of chemical analysis as applied to the components of different organisms: one is geared towards separating (purifying and characterizing) the substances that make up the organic material, while the other aims at determining the nature and the proportions of the elements present in the individual substances. All the conceptual tools aided in efforts to characterize the compounds present in organisms, making it possible to study changes taking place at a molecular level involving the addition or substraction of one or more atoms.

During the 19th century, a large number of very methodical scientists devoted their efforts to biochemical research. Three of these individuals (who were connected by their scientific interests) deserve special mention: Carlo Matteucci (1811-1868), Cesare Bertagnini (1827-1857) and Raffaele Piria (1813-1865); the last of the three had studied medicine, while the first had earned a degree in mathematics and the second in chemistry.

After obtaining his degree, Carlo Matteucci went to Paris, where he became acquainted with the group of scientists that had formed around Jean François Dominique Arago (1786-1853). Having returned to Italy, he published *Il discorso sul metodo razionale scientifico* (An Examination of the Rational Scientific Method) in 1835. The work was not understood by his contemporaries, but it provided a clear illustration of the ties existing between physical chemistry and physiology. In 1841, in response to a proposal by Alexander von Humboldt, the Grand Duke of Tuscany offered Matteucci the chair in physics at the university of Pisa. Matteucci quickly arranged for the chemistry chair at the university to be awarded to Raffaele Piria, an esteemed colleague with whom he had already collaborated in his scientific work. Two years earlier, in 1839, the twenty-nine year-old Piria had published the results of his work on salicin, which he had carried out in the Paris laboratory of Jean-Baptiste Dumas (1800-1884). Salicin, which had been discovered by Leroux, was a substance used in therapeutic care. Joens Jacob Berzelius (1779-1848) and Justus von Liebig (1803-1873) had attempted to study a similar compound, amygdalin, but they had abandonned the effort before completion. Piria demonstrated that the breakdown of the salacin produces two components, one of which is glucose: this marked the beginning of work into glycosides. Studies involving the other component led Piria to discover salicylic alcohol, salicylic acid and a large number of other derivatives from the salicylic series. Raffaele Piria returned to Italy in hopes of forming a school of Italian chemistry that would be the equal of the French school. At Pisa he studied other glycosides, breaking down their glycosidic bonds with almond homogenates that contained an enzyme with glycosidase activity called synaptacia or emulside (which was later used to characterize other glycosides). During this same period, a follower of Piria, Cesare Bertagnini, inverted the terms of the problem, using the salicin to discover the glycosidases present in plants. The results were published anonymously (in 1847) in a Pisa-based review under the title *Sulla sinaptasia dei semi* (On the Synaptacia of Seeds), in what represented the first Italian work in the field of enzymology. Piria and Bertagnini continued to search for and study glycosides, two of which were characterized in a particularly thorough manner: popoline and phyllirine. This research attracted attention throughout Europe. Dumas stated that, "all of Piria's contemporaries agree that his discoveries rank among the most important modern developments in chemistry". For his part, Liebig, attending a reception at the English embassy on his way through Turin, spoke of the school of Piria as the true school of Italian chemistry.

One very important perception on the part of Piria was that many of the more complex substances dealt with in organic chemistry are generated by the condensation of simpler molecules that occurs when water is eliminated. Using this approach, he took up the challenge of studying proteins. Though the research effort might appear out of proportion with the modest scientific conditions of the time, Piria nonetheless managed to make a significant contribution in this area, producing indications for a possible structure of tyrosine in 1852. As was the case with the salicylic acid he had worked on, tyrosine produced a reddish violet color when treated with a solution of ferrous chloride, and so Piria suggested that the two molecules might contain a similar chemical group in their structures (as also mentioned in: Chemistry of the Amino Acids, vol. 3, page 2349 by J.P. Greenstein and M. Winitz, Academic Press, 1961). Significant research was also carried out on aspartic acid, which Piria was able to transform into malic acid through the action of nitric acid, thus providing a general method for moving from amino acids to hydroxyacids.

Together with Matteucci (who may have been the first to apply physical chemistry to physiology) Piria studied the effect of various compounds on the muscular currents of frogs, drawing his inspiration from the experiments of Galvani and Volta. Using batteries composed of numerous muscle elements (halves of thighs from frogs) placed in contact with each other, and employing a galvanometer, the two scientists observed that certain substances (such as hydrocyanic acid) did not modify the current to a significant extent, while other compounds (such as hydrogen sulphide) practically reduced the signal from the galvanometer to zero. In 1859, Matteucci became involved in a scientific dispute with D.L. Hermann regarding the issue of gas exchange in isolated muscle tissue. He had observed that the volume of oxygen absorbed was always higher than that of the carbon dioxide eliminated, and that the phenomenon did not vary significantly, even if the air was replaced with pure oxygen. What made the strongest impression on Matteucci (and established his fame among his colleagues) was that, during the muscular contractions, the absorption of oxygen and the elimination of carbon dioxide rose simultaneously. He considered this phenomenon to be related to the energy used during the muscular activity. Hermann, on the other hand, interpreted the exchange of gases in the isolated tissues as an indicator of incipient decomposition, saying that the phenomenon observed by Matteucci was traceable to the fact that, when the induced contractions occurred, the surface area exposed to the air grew, meaning that it was necessary for the phenomena of decomposition to increase as well.

Another nineteenth-century chemist, Francesco Selmi (1817-1881) made a name for himself with studies on organic material, and particularly with research on the changes that take place in proteins of animal origin following putrefaction. In 1872, Selmi discovered the existence of a fair number of nitrogen compounds that presented all the reactions of the alkaloids, and to which he gave the generic name of ptomaines. The importance of this discovery becomes apparent when one realizes that, up until 1872, every substance extracted with the classic procedures during a forensic medical examination that met with reactions typical of the alkaloids was thought to be a substance introduced by criminal means into the body while alive. Selmi was also responsible for the first Italian Chemical Encyclopedia, a significant volume from our point of view in that it contained information concerning "pharmaceuticals, medical pratice, animal and vegetable physiology and pathology, anatomy, toxicology and hygiene" (as is written on the title page of the first edition, published in 1868).

A number of physiologists followed in the footsteps of Selmi.

Among those who worked in Italy, Angelo Mosso (1846-1910) deserves special mention for having discovered and isolated trimetylamine in putrefied brain matter.

On occasion, it comes to pass in human affairs that the official representatives of a given discipline are not among the leading researchers in their field of scientific interest. This was the case with the teachers of physiological chemistry, perhaps because they dedicated the major portion of their energies to other medical disciplines. Giorgio Roster, who was really a hygienist, worked without great fanfare for a certain period of time on gall stones and stones in the urinary tract, while Giuseppe Colasanti, whose main interest was pharmacology, carried out a number of studies on uric acid, allantoine and pyrocatechin. Antonio Pasquale Malerba, on the other hand, who was the first Italian professor to hold a chair in physiological chemistry, devoted himself more exclusively to strictly biochemical research, though he was not in the forefront of the field: he investigated the presence of proteins in figs, demonstrated the existence of a number of fats in chestnuts and performed research on the metabolic course of protein sulphur.

Gleanings from the first decades of the 20th century

If one stops to look at the work accomplished in Italian biochemistry during the first decades of the 20th century, it becomes apparent that many of the efforts were published in the Italian language by the numerous journals founded over the years by university professors. Only one of these publications has the word biochemistry in its title, this being Biochimica e Terapia Sperimentale (Biochemistry and Experimental Therapy), the review of the first Italian Biochemical Society. The others present a wide variety of names, in part because biochemistry, a discipline that had struggled to take on a form of its own and receive autonomous recognition in Italy, was not their main field of interest: Archivio di Farmacologia Sperimentale e Scienze Affini (Archives of Experimental

Pharmacology and Related Sciences), founded in 1902; Archivio di Fisiologia (Archives of Physiology), founded in 1904; Rivista di biologia (Biological Review), founded in 1919; Archivio di Scienze Biologiche (Archives of Biological Sciences), founded in 1920; Archivio di Biologia (Biological Annals), founded in 1924; Bollettino della Società Italiana di Biologia Sperimentale (Bulletin of the Italian Society of Experimental Biology), founded in 1926; Fisiologia e Medicina (Physiology and Medicine), founded in 1929; Quaderni della Nutrizione (Notes on Nutrition), founded in 1934; and many others, including the minutes of the various academies, which were extremely important. It should also be remembered that, around the turn of the century, an Italian journal written entirely in French was published, one of whose secondary topics of interest was biochemistry: Archives Italiennes de Biologie (Archives of Italian Biology), founded by Angelo Mosso in 1882.

Obviously, one also had to publish work in foreign journals in order to participate in the international scientific forum, and, initially, the German-language publications were favored over the rest. The two most prestigious reviews were given the most attention: Hoppe Seyler's Zeitschrift fuer Physiologische Chemie and Biochemische Zeitschrift. The first article written by an Italian to appear in Hoppe-Seyler's Zeitschrift fuer Physiologische Chemie was published in volume 3 in 1879 and consisted of a study on the fermentation of oxyvalerianic acid by P. Giacosa. The first work by an Italian to appear in the Biochemische Zeitschrift was also published in the review's third volume, though in the year 1907. The work in question was an article by A. Primavera on a new method for the quantitative determination of fatty substances in human milk. A survey of all the volumes of these two reviews published through 1910 turns up a total of approximately one hundred articles written by roughly fifty Italian scientists. Not only was Italian biochemistry a known quantity in Germany, but it must also have been fairly well regarded, at least in terms of a number of its leading figures, given that three Italians sat on the editorial board of Biochemische Zeitschrift at the beginning of the century: F. Bottazzi of Naples, G. Galeotti of Naples and A. Bonanni of Rome. It was not until the end of the First World War that Italian articles appeared in other prestigious foreign magazines. Aldo Castellani, a noted tropicalist who in 1928 was made a Baronet by the Crown of England, was the first Italian to publish in the Biochemical Journal, doing so in 1922 with an article describing an original method for identifying inulin that appeared in volume 16 of the journal. In 1923, volume 5 of the Bulletin de la Société de Chimie Biologique presented the first two articles written by Italians ever to appear in that review (works by Ciamician and Ravenna on plant alkaloids, and by Artom on lipids in dog livers). Volume 70 of the Journal of Biological Chemistry, published in 1926, contains the first article written by an Italian to appear in that review: a work describing a new method for determining levels of cholesterol and lecithin by G.M. De Toni. Finally, articles written in Italian by F. Cedrangolo, and G. Scoz and L. De Caro were published in the very first volume of the highly specialized scientific journal known as Enzymologia. Indeed, Enzymologia continued to present articles in the Italian language up through the end of the Second World War (a detail that appears fairly significant in light of the move towards a united Europe, though it was not mentioned in the otherwise accurate, and very interesting, book by E.C. Slater entitled Biochimica et Biophysica Acta: The Story of a Biochemical Journal, Elsevier, Amsterdam, 1986).

These were the reviews, or at least the main reviews, that published the observations and discoveries of a wide range of researchers in biochemistry. It is more difficult, if not impossible, to give a brief summary of the research subjects dealt with by Italian biochemists during the first decades of the 20th century. In the event, we will limit ourselves to an initial overview, providing details for a limited number of studies, which are not necessarily the most important, but simply those that — for completely fortuitous reasons — happen to have made the deepest impression on the mind, or at least the taste, of this writer.

During the preparations for the first scientific conference organized by the Italian Biochemical Society, an event held in 1913, a list was drawn up categorizing the issues felt to be fundamental and typical of this still developing field. Two criteria were used: the experiences of various scientists during their visits to foreign laboratories and a review of the materials published in the "Zeitschrift, Zentralblatt, Jahresbericht and Handbuch with the word biochemistry as a reference". Table I presents the agenda of the aforementioned meeting, together with the names of the speakers, in chart form. It turns out that, although papers were presented for all the chapters (except that on secretions), there was a decisive numerical predominance of subjects involving bacteriology and immunology.

These were the predominant trends in Italian biochemical research around 1913. In reality, all areas of biochemical interest were touched upon by the curiosity of Italian scientists during the first decades of this century, and some very noteworthy results were produced, especially from the 1930s on, with some coming even earlier. One need merely mention Giuseppe Amantea, who back in 1923 used a method of this own to observe that the crystals of hemoglobin obtained from the blood of newborn children differed from those produced by the blood of adults. One can also point to the landmark work published in 1910 by Joseph Barcroft on the shape of the curve for the equilibrium of hemoglobin with oxygen, whose co-author was Mario Camis, a physiologist from Parma who had gone to England to work at Cambridge. As is well known, this curve was expressed by Hill's equation

$$y/100 = K x^n / (1 + K x^n)$$

where, y represents the percentage of oxygen saturation, and x the partial pressure of the oxygen, with K being the equilibrium constant and n a non-integral constant with a value close to 2.5. The explanation given at the time for the physical interpretation of n was that hemoglobin in solution existed as a mixture of aggregates, with n = 1, 2, 3, 4 etc., and that the observed value of n in the

TABLE I - *Subjects and speakers at the first scientific meeting of the Italian Biochemical Society, held in 1913.*

SUBJECT CATEGORIES	NAMES OF SPEAKERS
Physical chemistry of colloids	Brunacci, Mellis, C. Foà
Analytical methods	A. Ascoli, Micheli, Izar
Physiological Pathological Histological Microchemical } compounds	Centanni
The cell	Satta and Fasani, Filia
General processes: inflammation, degeneration, fever, tumors	Centanni, Moreschi
Blood, lymph, membranes, effusions into cavities	N.G. Bernabei
Metabolism and nutrition	Albertoni, Segale, Preti, Pari, Ferrarini, Zoia
Internal and external secretions	———
Plant physiological chemistry	Ciamician and Ravenna, Herlitzka, Inghilleri, Marcacci
Ferments	Sebastiani, Preti, Izar, Lombroso
Biochemistry of micro-organisms	Centanni, Belfanti, Viganò, Valenti
Antigens and antibodies	Belfanti, Moreschi, A. Ascoli, Stazzi, Micheli, Izar, Ciuffo, Sebastiani, Guerra
Toxicology and chemotherapy	Guerra, Mei-Gentilucci, Almagià
Special applications: forensic medicine, hygiene, obstetrics and gynaecology, etc.	Volpino

above equation was a statistical average of all the forms present in solution. After returning to Italy, Camis continued his research on hemoglobin. In an attempt to provide an experimental foundation for the theory of the state of aggregation of hemoglobin, he studied the variations produced by lactate on the surface tension of hemoglobin solutions. In 1921, he discovered that, at a constant temperature, the molecular surface energy (i.e. the product of the surface tension multiplied by the molecular surface area) fell with the rise in the lactate concentration. Camis interpreted these findings in terms of a molecular aggregation of hemoglobin. During the same year, Gaetano Quagliariello repeated Camis' experiments in the presence of various salts and acids, but he arrived at the conclusion that there was no connection between the decrease in surface tension and the molecular aggregation. Giulio Pupilli, a student of Camis', entered into the debate as well, performing a series of highly accurate refractometric measurements in 1923. In an approach worthy of Solomon, he worked along two separate lines, one supporting Camis' thesis and the other based on Quagliariello's assertion. As the reader can doubtless imagine, this precise, painstaking effort came to an end in 1925 when G.S. Adair, having determined the molecular weight of the hemoglobin, established once and for all that this protein was not a system composed of aggregates, but a single, well-defined molecule. Why do we harken back these facts? The point is simply to give an idea of the approaches and instruments brought to bear upon biochemical problems in Italy during the 1920s. Studies on hemoglobin began in Italy in 1892, with the appearance of an article on the multiple presence of hemoglobin in the blood written by Giovanni Gallerani of the University of Camerino — the same scientist who had done so much to popularize spectrophotometry in Italy with an invaluable booklet written in 1903. In the years that followed (between 1909 and 1913), E. D'Agostino of Naples measured the spectrum variation of ferric hemoglobin during the transition from an acid to an alkaline environment (a phenomenon he traced to the oxygenated hemoglobin), while F. Bottazzi devoted his attention to the conductivity of hemoglobin solutions that had undergone dialysis for long periods of time. By drawing up a thorough list of the articles and scientists involved in research on hemoglobin, one could illustrate the process through which techniques and tools were continually up-dated in the main centers of Italian biochemical research from the end of the 19th century on.

While on the subject of hemoproteins, it is impossible to ignore the contribution of Rodolfo Margaria, who spent a long period of time in England during the early 1930's, on a grant from the Rockefeller Foundation, studying the physiological effects of carbon anhydride with J. Barcroft, R. Brinkman and R.J.W. Roughton. Among other results, he obtained a large amount of experimental data pointing to a possible effect exercized by carbon dioxide on hemoglobin through direct combination with the protein, above and beyond the well known indirect effect stemming from its acidic properties. Though extremely interesting, these results were not suited to an accurate quantitative treatment. Margaria later went to Boston (U.S.A.) to work under A.A. Green (Harvard University), with whom he published an important paper in the Journal of Biological Chemistry demonstrating quantitatively that the presence of carbon dioxide shifted the curve for the equilibrium of hemoglobin with oxygen to the right, regardless of pH.

There is one last note to be made before leaving the subject of hemoproteins. In the decade that followed, Alessandro Rossi Fanelli produced the first experimental evidence demonstrating that hemoglobin and myoglobin both had the same prosthetic group, meaning that the physico-chemical and functional differences between the two molecules has to be traced to differences in the globins.

One could choose any one of a number of subjects in order to continue exploring the study of biochemistry in this century. I will opt for the metabolism of tryptophan. To be scrupulously honest, it must be mentioned that, as early as 1897, A. Capaldi of Naples had published in the Hoppe Seyler's review an original method for the quantitative determination of a catabolite of tryptophan, namely kynurenic acid. Forty years later, L. Musajo discovered xanthurenic acid and together with F.M. Chiancone demonstrated that it was derived from tryptophan through kynurenine. In 1942, when S. Lepkowsky and E.J. Nielsen discovered significant quantities of xanthurenic acid in the urin of rats with pyridoxine insufficiencies, Chiancone proposed a test based on a dose of trypthophan *per os* in order to diagnose pyridoxine insufficiencies in humans. The World Health Organization recognized this technique as a method for performing mass research on population groups suffering from malnutrition.

Having arrived at this point in the story, the noblest course would be to reach a conclusion, given that there is certainly no need for long lists of discoveries that would serve only to distract or astound those reading them out of curiosity. I would add just a brief mention of the metabolism of fats, inasmuch as the editor of the Annual Review of Biochemistry invited Camillo Artom to write an article on the subject in 1935. Thanks to an ingenious experimental technique (iodized fatty substances were administered intravenously, following which data were taken at various intervals of time to determine the quantities of iodine present in the soluble and insoluble fractions of the organs in acetone, and in the soluble fractions in chloroform), this physiologist from Cagliari was fairly successful in studying the distribution of the circulating lipids in various tissues, a number of intermediate products of the metabolism of fats and the excretion of lipids from the intestinal wall, all of which gave Artom an international reputation as a solid biochemist. During the 30's and 40's other Italian scientists took an interest in lipids as well, and fairly significant results were obtained by G. Quagliariello, F.P. Mazza, L. Califano, G. Perretti and G. Monasterio.

At this point it is easy to imagine that a good many other Italian biochemists, some brilliantly talented and others simply mediocre, were throwing out ideas during the first decades of the twentieth century. In some cases, they managed to bring these ideas under control, while in others they never even came close. None of them, however, received official international recognition.

THERE ARE MORE THINGS

Manche liegen immer mit schweren Gliedern
Bei den Wurzeln des verworrenen Lebens,
Andern sind die Stuehle gerichtet
Bei den Sibyllen, den Koeniginnen

[Many lie with leaden limbs
By the roots of life so grim
While others sit on stools serene
By the sides of sybils and queens]

Hugo von Hofmannsthal, *Gedichte*

Forgive me if today you are forgotten

William Shand, *Ferment*

Paul Valéry once wrote that no one knows the weaknesses of a work as well as its author. As for this small essay... On page 77 of his work El Aleph, Jorge Luis Borges wrote that St. Thomas Aquinus states in his *Summa Theologica* that God can not make the past disappear, and yet nothing is said about the intricate chain of cause and effect that remains so vast and secret that, perhaps, not a single event can be cancelled, no matter how remote or obscure it may be, without damaging the present. Many aspects of the past history of Italian biochemistry have not been recorded here: not because they have been cancelled, but merely because I have no knowledge of them at the moment. Nonetheless, even the events and figures not mentioned have undoubtedly led to consequences which appear in this brief survey, whose specific purpose was the following: to present our fellow biochemists from all over the world in attendance at the 19th meeting of the Federation of European Biochemical Societies with a general, but by no means inaccurate, history of Italian biochemistry up to the Second World War.

NOTES ON THE PRINCIPAL BIBLIOGRAPHIC SOURCES

The initial clues that made it possible to follow the laborious trail to the origins of the recognition of biochemistry as an autonomous discipline in Italy were found in the work by Francesco Cedrangolo, Scienza Metodo Umanità, Editoriale Scientifica, Naples, 1982.

Without a doubt, however, the most authoritative sources, which also prove to be the most surprising and intriguing, are the personal papers of the first biochemical professors (on file at the Archivio Centrale dello Stato, Piazza degli Archivi, Rome).

In the Archives and in the Library of the Accademia Nazionale delle Scienze detta dei XL are deposited correspondence, documents and also publications of Lazzaro Spallanzani, Felice Fontana, Raffaele Piria, Carlo Matteucci and Luigi Brugnatelli, who were all members of the Academy.

See, Guida all'Archivio Storico dell'Accademia Nazionale delle Scienze detta dei XL, by G. Paoloni and M. Tosti-Croce, Roma 1984 and Accademia Nazionale delle Scienze detta dei XL, Annuario, Roma 1987. Memorie di Matematica e Scienze Fisiche e Naturali dell'Accademia Nazionale delle Scienze detta dei XL: Indici 1782-1982, Roma 1982; id., *VI*, 1-2 (1982).

As regards names, academic titles, teachings and university positions, reference was made to a number of directories, both Italian and international, including: Annuario degli Istituti Scientifici Italiani, Athenaeum, Rome, 1918 and Zanichelli, Bologna, 1920; Index generalis, Annuaire Général des Universités, Gauthier-Villars, Paris, 1921; Minerva, Jahrbuch der gelehrten Welt, K.J. Truebner Verlag, Strassburg, 1908.

Stanislao Cannizzaro's failed attempt to establish the first university chair in physiological chemistry is described in: Stanislao Cannizzaro, Scritti vari e lettere inedite nel centenario della nascita (published by the Associazione Italiana di Chimica), Rome, 1926.

The official positions of the first Italian Biochemical Society regarding the establishment of a university chair in biological chemistry were published in the Society's periodical, Biochimica e Terapia Sperimentale.

The memories of Jacopo Bartolomeo Beccari, Vincenzo Menghini and Domenico Maria Gusmano Galeazzi can be found in: De Bononiensi Scientiarium et Artium Instituto Atque Academia Commentarii, Ex Typographia Laelii e Vulpe, Bononiae, MDCCXLV and MDCCXLVI.

Much information concerning Raffaele Piria, Cesare Bertagnini and Carlo Matteucci was drawn from: Raffaele Piria, Lavori scientifici e scritti vari (edited by D. Marotta), Tipografia Editrice Italiana, Rome, 1932.

Antonio Pasquale Malerba published a portion of his works in: Lavori eseguiti nell'Istituto Fisiologico di Napoli, fascicolo I, Tipografia dell'Accademia Reale delle Scienze, Naples, 1886.

Reference was also made to collections of abstracts from the scientific works of Angelo Mosso, Aristide Stefani and Giuseppe Colasanti.

Most of the information on 20th century developments was gathered by referring directly to the Italian and foreign periodicals cited in the text.

For earlier eras, additional information was drawn from the Enciclopedia Medica Italiana, Vallardi, 1909, and from the Enciclopedia di Chimica, UTET, 1868, as well as the invaluable supplements made by Rinaldo Pitoni to the Italian edition of E. Thorpe's Storia della Chimica, S.T.E.N., Turin, 1911.

With regard to more recent times, information was also obtained during pleasant conversations with Professor Alessandro Rossi Fanelli and Professor Francesco M. Chiancone.

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