Hist. Ophthal. intern. 3, 213 – 260 (1984)

THE DISCOVERY OF THE LAMINA BASALIS CHOROIDEAE BY CARL WILHELM LUDWIG BRUCH (1819 — 1884)

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Table of contents

Introduction

In the middle of the 19th c., the arrangement of the several retinal layers was still subject of considerable confusion and controversy. **BRUCH** (1844b, p. 9) speaks of "the mysterious, much-discussed ***tunica Jacobi***" described by the irish anatomist and ophthalmologist **ARTHUR JACOB** (1819) in his article "*An account of a membrane in the eye now first described*"; JACOB's membrane was indeed associated with a variety of retinal structures; **FRIEDRICH ARNOLD** (1832) assigns it to a *pigmented* layer, calling it "***stratum cinereum pigmenti s. membrana Jacobi***". On the other hand, **JACOB HENLE** (1841), following the terminology "***Membrana Jacobiana s. Stratum bacillosum***" of **EMIL HUSCHKE** (1835, p. 238), identified JACOB's discovery with the rod-layer and mentioned that it was often mistaken for the pigmented layer of the choroid: "*Da weder JACOB noch die Anatomen, welche sich nach ihm mit diesem Gegenstande beschäftigten, die Charactere dieser Haut erkennbar genug angaben*" (**HENLE**, 1841, p. 738). ("Since neither JACOB nor the anatomists who studied this object described the characteristics of the membrane clearly enough".)[1]

In 1844, the year of BRUCH's discovery, there seems to have been no evidence for an *additional* layer between the choroid and the pigmented epithelium. **HUSCHKE** (1844, pp. 713—714) writes: "*Die Stäbchenschicht oder Jacob'sche Haut (. . .) liegt unmittelbar unter der Aderhaut, ohne jedoch mit ihr verwachsen zu sein*". ("The layer of rods or JACOB's membrane lies immediately beneath the choroid, without being conjoined in man".) Apparently in 1844, even recognized anatomists still confused pigment epithelium and rod layer. In this light, BRUCH's achievement, his technical acumen and his inductive thinking which enabled him to render visible a membrane ten to fifty times thinner than either the pigment epithelium cells or the rods' outer segment seem all the more marvelous.

The following paper shall describe **BRUCH**'s life and career as a scientist, his scientific goals, achievements and struggles which shed light on the general conditions of research and on academic life in the middle of the 19th century; besides discussing the circumstances and antecedants of BRUCH's discovery of the *Lamina basalis choroideae*, this paper presents the wide range of his inter-

[1] A careful reading of ARTHUR JACOB's original article (1819) does not provide a final answer to the question whether or not JACOB discovered what is called today "BRUCH's membrane". Many elements of his description of "a new membrane in the eye" could indeed apply to BRUCH's membrane; however his mention of "turning the membrane over the black choroid coat" (JACOB, 1819, p. 303) implies that he had removed BRUCH's membrane and the pigment epithelium together with the choroid and was in fact dealing with the receptor layer of the retina. This conclusion is supported by JACOB's remark that his membrane "in the bird presents a rich yellow brown tint" (JACOB, 1819, loc. cit.), nowadays explained by colored oil droplets in the bird's receptor layers.

ests as they are reflected in his publications and summarizes achievements in the subsequent search for the ultimate structure, physiological functions and clinical importance of BRUCH's membrane.

A. BRUCH's life and career as a scientist

Family background and education

CARL WILHELM LUDWIG BRUCH, son of the Hassian notary public CARL FRIEDRICH BRUCH (1789—1857), was born in Mainz on May 1st, 1819. BRUCH's parents were both natives of Saarbrücken, a small town in the Saarland, but had moved to Mainz as a result of its occupation by Napoleon's troops. BRUCH's father, an enthusiastic ornithologist, owned a remarkable collection of preparations of European birds. His collector's instinct and his interest in biology undoubtedly stimulated his son's intellectual development from a very early age on. (**BRUCH**, 1862a, p. 182; see footnote 25a for quotation).

In the year 1837, the young BRUCH began to study medicine in Giessen. In the Fall of 1840, he travelled to Berlin to attend lectures by **JOHANNES MÜLLER** (1801—1858), the most distinguished German physiologist of that time. In Berlin he became acquainted with a young assistant of MÜLLER's, **JACOB HENLE** (1809—1885), who was to influence his scientific career and sponsor his "Habilitation"[2] at the university of Heidelberg in 1845. In July of 1842, BRUCH received his doctoral degree from Giessen as "***doctor medicinae, chirurgiae et obstetricae***".

— Postdoctoral work and first academic appointments in Heidelberg and Basel

Subsequently **BRUCH** spent ten months in Vienna and eight months at the university of Zürich for postdoctoral training, as he writes in his letter to the Dean of the medical faculty in Heidelberg in January 1845. Vienna was especially attractive to anatomists, not only because of the Medical School's fascinating collection of anatomical wax models out of **PAOLO MASCAGNI**'s (1752—1815) workshop, bus also because of its renowned medical faculty. In the 1840's, the celebrities included such teachers as **JOSEPH BERRES** (1796—1844), professor of anatomy (1831—1844), who concentrated on microscopical anatomy, and **KARL von ROKITANSKY** (1804—1878), professor of pathological anatomy (1834—1875), whose revolutionary "*Handbuch der pathologischen Anatomie*" had just been published. Finally, the improved, multiple-lens microscope constructed by the Viennese optician **SIMON PLÖSSL** (1794—1875) was a critical instrument for histological investigations; it had only recently become available to the public and opened new horizons in

[2] i.e. the thesis that in German-speaking countries serves as a qualification for a faculty-chair.

microscopical anatomy (Fig. 1). **BRUCH** mentions using PLÖSSL's microscope in the preparitions leading to his discovery of the Lamina choroideae basilaris in 1844, later named after him "*BRUCH's membrane*" (detailed discussion below).

In January of 1845, BRUCH applied to the Dean of the medical faculty in Heidelberg for permission to present himself for examination as "*Privatdozent*"[3]. In his Habilitation-thesis, "*Nonnulla de rigore mortis*" (BRUCH, 1845a), BRUCH presented arguments against **EMIL DU BOIS-REYMOND**'s theory of *rigor mortis*, based on animal electricity; he convincingly characterized the process in terms of physics and chemistry, coming quite close to present-day views of this phenomenon (see below). BRUCH's "Habilitation" was rated excellent "*summa cum laude*". From the winter of 1845 to the summer of 1850 he lectured on anatomy in Heidelberg in the old institute of anatomy, which in BRUCH's times was housed in a former Dominican cloister (Fig. 2).

In the year 1850, **BRUCH** was offered the chair of anatomy and physiology in Basel, in succession to **C. G. Jung** (1794—1864). The portrait (Fig. 3) showing BRUCH in his early thirties was taken during this time. The anatomy institute in Basel where BRUCH taught from 1850 to 1855 is the subject of the etching in Fig. 4.

In 1851, **BRUCH** married his mother's younger step-sister MARIA MAGDALENA RETTIG of Schwetzingen, who bore him four children (see family tree in the appendix). Various members of the BRUCH family as well as colleagues from the medical faculty in Basel were chosen as god-parents, according to the State Archive of the canton of Basel (Staatsarchiv des Kantons Basel-Stadt). **E. BONJOUR** describes BRUCH's activity in Basel in the following terms[4]. "*Um einen tüchtigen neuen Dozenten zu gewinnen, begab man sich*

[3] The academic title reserved to a faculty member who has qualified himself through the "Habilitation" (see above) for — but does not yet hold — a faculty chair.

[4] "In order to engage an industrious new teacher, (a delegation was sent) to Heidelberg to interview potential candidates; the choice fell upon the 28 year-old Privatdozent KARL BRUCH of Mainz, previously assistant professor at the institute of physiology and anatomy. With the (financial) support of the Freiwillige Akademische Gesellschaft, BRUCH was offered a full professorship; the same year, he began to lecture on 'Normal Anatomy and Physiology', subjects which were taught only in increasingly rare places by a single man. Through his indefatigable labors BRUCH contributed greatly to the felicitous conditions which prevailed in the medical faculty with an enrollment of eighteen to twenty students. One would find him from morning until night in the institute, teaching or independently conducting research. In his person, students had an invaluable teacher, regarding particularly the most important and the most difficult subjects, on account of his marked talent as a scientist. BRUCH, however, was unable to support his family on an exceedingly low salary of SwFr. 1500 and the meagre income from tuition fees without having to bring yearly financial sacrifices. The modest additional benefits granted to this deserving teacher were unable to attach him to Basel when he was called in 1855 to a similar post in Giessen." (E. BONJOUR, 1960, p. 580)

nach Heidelberg, besprach sich dort mit möglichen Kandidaten und entschied sich für den achtundzwanzigjährigen Privatdozenten Karl Bruch aus Mainz, bisher Assistent des Physiologisch-Anatomischen Instituts. Mit Hilfe der Freiwilligen Akademischen Gesellschaft wurde er zum o. Prof. berufen und begann noch im gleichen Jahr über 'Normale Anatomie und Physiologie' zu lesen, die anderswo immer seltener in einer einzigen Hand vereinigt waren. Durch seinen unermüdlichen Eifer trug er viel zu dem erfreulichen Zustande bei, in welchem sich damals die Medizinische Fakultät mit einer Zuhörerschaft von achtzehn bis zwanzig Studierenden befand. Man traf ihn den ganzen Tag teils dozierend, teils für sich arbeitend im Institut an. An ihm besaßen die Studierenden einen Lehrer, der ihnen gerade in den wichtigsten und schwierigsten Fächern durch sein entschiedenes Forschertalent von unschätzbarem Werte war. Aber Bruch konnte, als Familienvater, mit dem überaus niedrigen Gehalt von Fr. 1500 und den spärlich fallenden Kollegiengeldern in Basel nicht wirtschaften, ohne daß er jährlich pekuniäre Opfer brachte. Die kleinen Gehaltszulagen, die man dem verdienstvollen Dozenten bewilligte, vermochten nicht, ihn hier festzuhalten, als ihn 1855 ein Ruf nach Giessen erreichte'' (**E. BONJOUR**, *1960, p. 580).*

So far, no students have been discovered whose doctoral thesis **BRUCH** might have sponsored in Basel. However, the Staatsarchiv Basel communicated the following piece of information:

''*Gemäss (Fakultäts)protokoll examinierte BRUCH unter anderen den später berühmt gewordenen Anatomen* **WILHELM HIS** *(1831—1904) im September 1854 in Anatomie (Milz und Endigungen der Nerven).*''[5]

According to HIS' memoirs, **BRUCH** had no influence on his thesis: ''*Die Dissertation sollte nachgeliefert werden, und so setzte ich mich in der nachfolgenden Zeit an deren Bearbeitung. (. . .) Ich mikroskopierte in einem kleinen auf der Rheinmauer des Kollegiumgebäudes aufgesetzten Häuschen im Arbeitszimmer meines Schwagers* **MIESCHER** *und hatte als Zimmernachbar* **C. BRUCH**, *in dessen Verhalten indessen schon damals Eigentümlichkeiten hervortraten, die mit seiner späteren Krankheit in Verbindung stehen mochten'' (quoted after LUDWIG, 1965, p. 48).*[6]

On the other hand, the fact that **BRUCH** was elected Dean of medical faculty in 1852 (KOLB, 1951, p. 116) does not lend support to **HIS'** retrospect assessment of BRUCH.

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[5] According to the faculty records, BRUCH examined the later famous anatomist WILHELM HIS (1831—1904) in September 1854 in anatomy (spleen and nerve endings).''

[6] ''The dissertation was to be handed in at a later date, so I than began to revise it (. . .). I examined my preparations under a microscope in a tiny building set upon the Rhine-wall of the institute, in my brother-in-law MIESCHER's study; my next-door neighbour was C. BRUCH, whose behaviour already manifested pecularities which may have been connected to his later illness.'' (quoted after LUDWIG, 1965, p. 48)

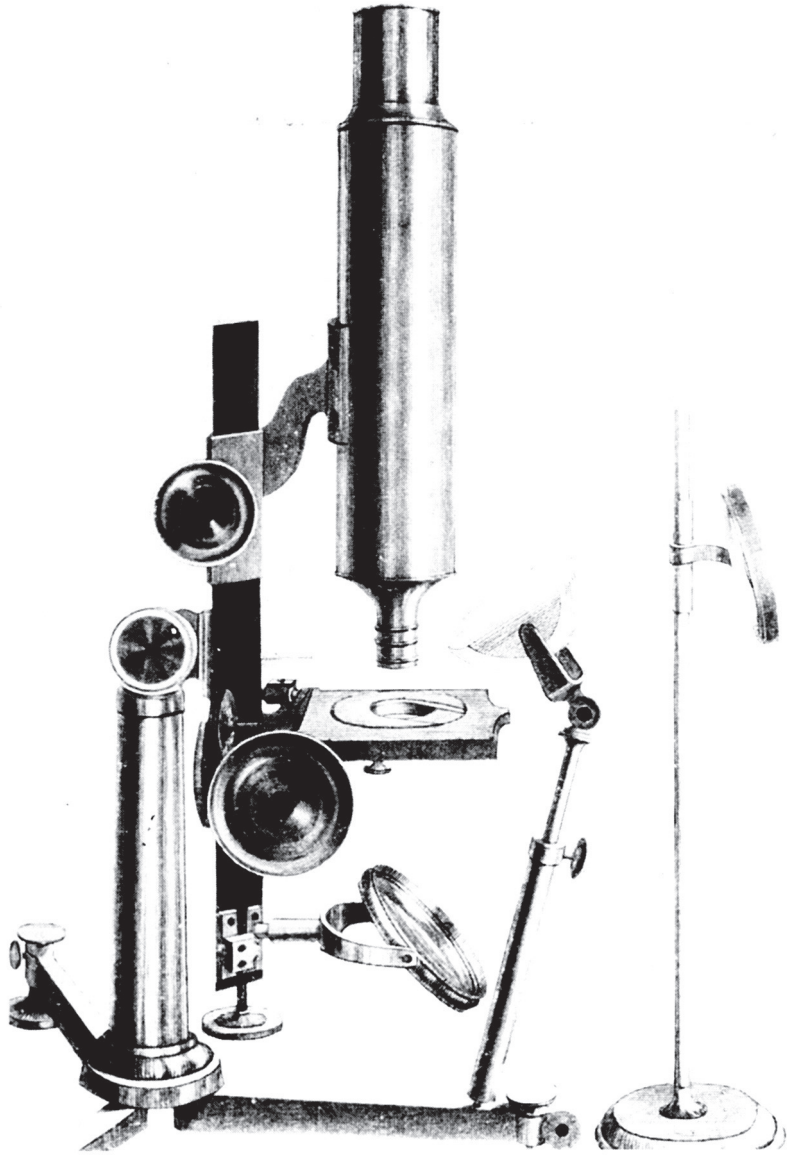

Fig. 1: PLÖSSL's microscope. Colored copper-engraving by HUMITSCH after a drawing by CARL VON NAGEL. Source: JOSEPH BERRES, Anatomie der mikroskopischen Gebilde des menschlichen Körpers, vol. I. Vienna (1836). According to V. PATZELT (1947, p. 6). PLÖSSL used (in addition to 3 – 6 oculars) objectives consisting of 7, later of 9 achromatic double-lenses, which, aligned in varying numbers, could be combined to 4 to 5 different systems with a 25- to 500-fold magnifying power.

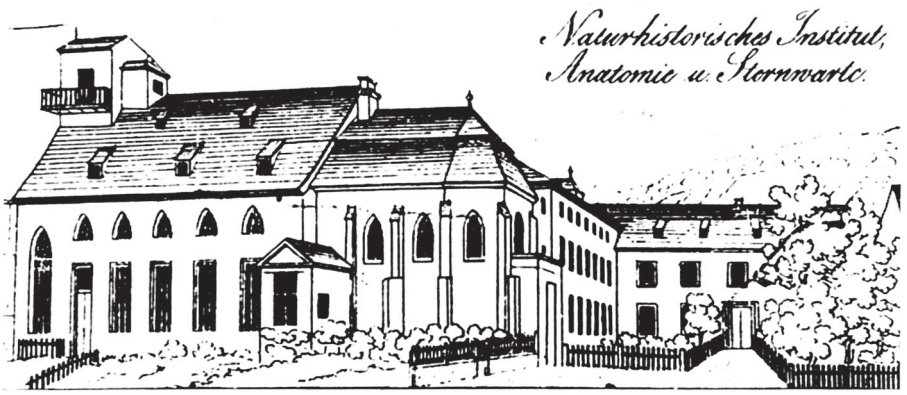

Fig. 2: The old anatomy institute of the university of Heidelberg, housed in a former Dominican Cloister until 1849. Drawing dated 1830, unsigned. Source: Archives of the Heidelberg University Library. By permission of the rector of the Ruprecht-Karls-University Heidelberg.

—BRUCH's appointment in Giessen and quarrels with colleagues

In the Fall of 1855, **BRUCH** transferred to Giessen to succeed **THEODOR L. W. BISCHOFF** (1807—1882) as professor of anatomy and physiology. He lectured on "General Anatomy or Histology", "Embryology", "Pathological Anatomy" and "Teratology". Fig. 5 offers a view the anatomy institute built according to plans by BISCHOFF in Giessen.

After eight semesters of teaching, **BRUCH** had to retire and yield up his post as Director of the Anatomy and Physiology Institutes. His successor, **CONRAD ECKHARD** (1822—1905), conjectured, "*daß schon in der Zeit seines Hierseins sich eine Geisteserkrankung zu entwickeln begann*".[7] **ECKHARD**, who had passed his Habilitation-exam in Giessen in 1849 and had been prosector under **TH. BISCHOFF** since that year, mentions: "*wiederholten und ernsten Beschwerden seitens der Zuhörer über (BRUCH's) Verfahren beim Unterricht, in Folge derer "eine Ministerialcommision erschien und während mehrerer Tage eine Prüfung vornahm", die "zur Enthebung seiner Ämter 1860 führte"*. He continues: "*Mit dem Weggang BISCHOFF's nach München traten für nur wenige Jahre kleine Veränderungen ein. An die Stelle von BISCHOff wurde BRUCH berufen und zum* ***Direktor beider Institute*** *ernannt. Die* ***Physiolo-***

[7] "that some sort of mental illness began developing in BRUCH's years at the University of Giessen."

Fig. 3: Portrait of CARL W.L. BRUCH, around 1851. By permission of the Basel University Library.

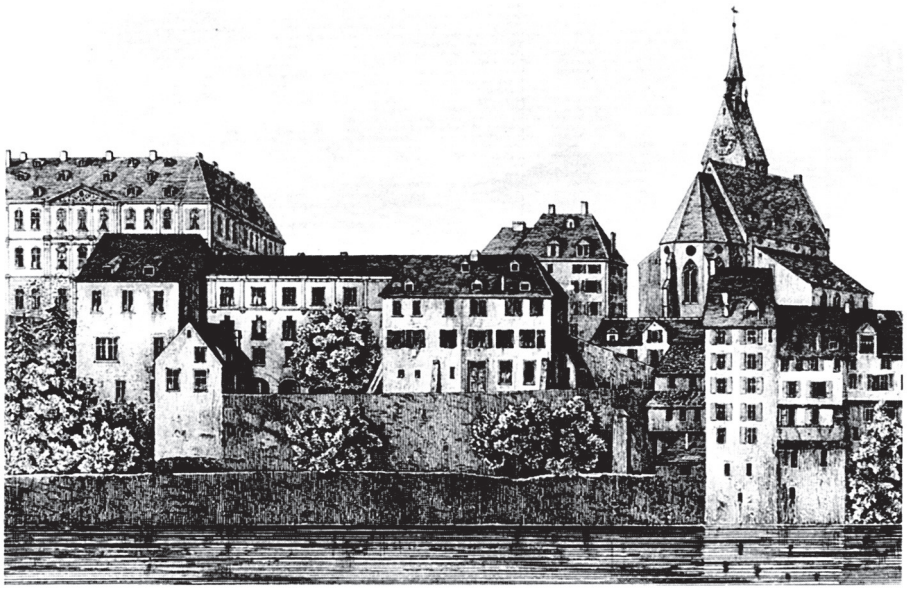

Fig. 4: The Lower College in Basel in 1850. Source: WILHELM HIS (1885, p. 36).

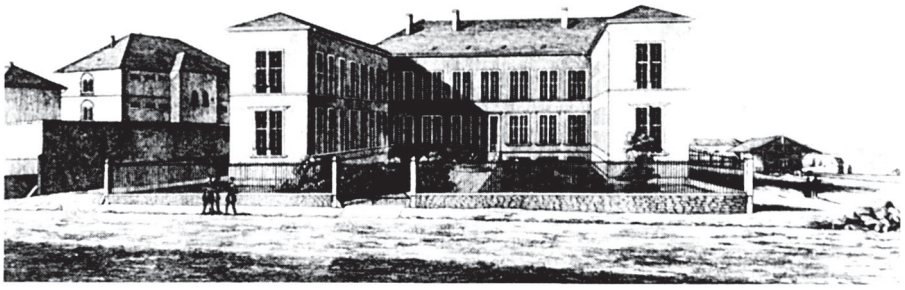

Fig. 5: The Anatomy-Institute in Giessen around 1850. Source: BISCHOFF (1852).

*gie hat er aber **nie gelehrt**. Ich, bis dahin Prosektor, wurde Extraordinarius in der med. Fac. mit der Verständigung, die Physiologie zu lehren. . . Kurze Zeit darauf, bei Gelegenheit einer Berufung nach Königsberg, wurde ich hier zum ord. Prof. in der med. Fac. ernannt mit dem Bedeuten jedoch, daß man BRUCH das Directorium des physiologischen Instituts nicht nehmen könne. . . Ich empfand es oft recht drückend, daß die Direction des physiologischen Instituts nicht in meinen Händen war. Ich unterließ aber jeden Antrag auf Änderung der Verhältnisse, als sich schon damals die Ereignisse anfingen vorzubereiten, die . . . zur Enthebung seiner Ämter 1860 führte, . . . Da der begabte Mann 1884 im Irrenhaus zu Heppenheim starb, so geht man wohl kaum in der Annahme fehl, daß schon in der Zeit seines Hierseins sich eine Geisteserkrankung zu entwickeln begann."*[8] It should be noted that no substantive evidence for the complaints about BRUCH's manner of proceeding in his lecture mentioned by **ECKHARD** have turned up so far, in spite of careful searches. Several unpublished letters from the Giessen university archives shed interesting light on the general working-conditions and special problems with which **BRUCH** and his colleagues on the medical faculty had to deal with.

For instance, it had been customary that corpses reaching the anatomical theatre during the ***summer*** term be transferred immediately to the professor of *surgery*, **ADOLPH CARL GUSTAV WERNHER** (1809—1883) who required them for demonstration purposes in his course on operative surgery. On the other hand, corpses available during the ***winter*** term were reserved for **BRUCH**'s section course, which was offered together with the anatomy-lecture. In a letter from the Ministry of the Interior dated May 11th, 1857 it says:

"In dem laufenden Semester hat dagegen die genannte Direction (des anatomischen Instituts) in der angegebenen Beziehung eine Änderung eintreten lassen, in Folge derer die Übergabe der Leichen an den Professor der Chirurgie

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[8] "repeated and serious complaints voiced by the audience regarding BRUCH's manner of proceeding in his lectures" which led to "the appearance of a ministerial commission charged with conducting an investigation lasting several days and resulting in BRUCH's dismissal in 1860." He continues: "When BISCHOFF transferred to Munich, negligible changes took place which lasted only for a few years. BRUCH was called to replace BISCHOFF and was nominated director of both institutes. However, he never taught physiology. I, up to then prosector, became Extraordinarius (i.e. full professor, but without a proper chair in the faculty. Author's note). With the understanding that I would teach physiology . . . shortly thereafter, at the occasion of an offer to join the medical faculty in Königsberg, I was granted a chair in the med. fac., accepting the fact that it would be impossible to relieve BRUCH of his position as director of the Physiological Institute . . . I found it often quite depressing, not to be in charge of the Physiol. Institute. I refrained, however, from proposing any change in the existing situation, when the very events which led to BRUCH's dismissal began to take place, . . . Since this talented man died 1844 in an asylum in Heppenheim, it is probable that during his years at Giessen a mental disease had already begun to develop." (ECKHARD, 1907, pp. 16—18).

unterblieben und diesem sonach das erforderliche Unterrichtsmaterial für die Operationschirurgie entzogen worden ist''.[9] BRUCH's actions thus necessarily led to serious conflicts with his colleague **WERNHER** despite the fact that BRUCH and WERNHER were cousins, since WERNHER'S father had married one of BRUCH's aunts (see appendix for family tree).

During the same semester, **BRUCH** collided with another colleague, the anatomist **Hermann WELCKER** (1822—1897). Apparently. the latter had complained of the short supply of microscopes and of the fact that the assistent was not sufficiently available.[10] During his first term, **BRUCH** had conducted the course on anatomical section ***together*** with **WELCKER**; subsequently, he ostentatiously scheduled his course to coincide with WELCKER's. **BRUCH**'s financial distress and thus his dependence on tuition fees for a living may have been partly responsible for this overtly uncooperative behavior.

From the viewpoint of the historian of science it is most interesting to realize that in 1856 **WELCKER** had developed ***a new technique*** in microscopical preparations, the *microtome*, which — as **JOHANN EVANGELISTA PURKINJE** (1800—1877) had shown — was far more revealing than manually prepared sections (cf. J.-H. SCHARF, 1963, p. 487). **BRUCH**, who taught the traditional method of histological preparation, in its most sophisticated and difficult form, was certainly unable to ***elicit*** the same enthusiasm from students as his colleague **WELCKER**, who introduced a revolutionary, more manageable and exciting technique. As a representative of the older generation of anatomists, BRUCH probably despised the microtome as much as his colleague **ALFRED WILHELM VOLKMANN** (1800—1877) in Halle, who is said to have left his prosector's demonstration saying: ''*Lasst mich aus mit Eueren Tüfteleien, ich schneide mit freier Hand.*'' (''Leave me alone with your hair-splitting subtleties, I cut by hand!''). But, continues **J.-H.SCHARF** (1963, p. 487), ''*Der Siegeszug des Mikrotoms war trotzdem nicht aufzuhalten*'' (''the triumphal march of the microtome was not to be held up'').

It is an irony of history that the old-fashioned manual technique perfected by **BRUCH** had alone been capable of revealing these ultrafine structures which were not resolvable in serial sections by the microscopic techniques available in BRUCH's times. These fine membranes, by themselves invisible under these microscopes, could be made visible only by manipulating the various layers and watching the movements within the tissue, an observation impossible to make in serial sections.

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9 ''During the (summer-) term, the directorate of the anatomy-institute has introduced a change in this arrangement, to the effect that corpses have no longer been transferred to the professor of surgery, thus depriving the latter of the necessary teaching material.'' (Source: University Archives, Giessen)

10 These facts can be inferred from an unpublished letter written by BRUCH on May 25th, 1857. (Source: University Archives, Giessen)

— BRUCH's retirement and death

During the summer term of 1857, **BRUCH**'s lectures were attended only by a very small number of students; BRUCH began announcing private tutorials in his home instead of offering public lectures, a practice which led to a report of the university to the Ministry of the Interior in Darmstadt (August 12th, 1857, fig. 6), ultimately leading to BRUCH's dismissal. Whether an incipient illness was responsible or not can no more be ascertained, since no record of **BRUCH**'s life at Heppenheim have been preserved (by personal communication of the asylum's director).

Following his retirement from teaching, BRUCH moved to Frankfurt, closer to his friend, the anatomist **J. C. LUCAE** at the Senckenberg Institute of Anatomy. BRUCH, a corresponding member of the Senckenberg Society since 1853 became "an active contributor to the Society's publications and held well-frequented lectures"[11] After 1860 **BRUCH** concerned himself mainly with embryological problems. On January 4th 1884, BRUCH died in Heppenheim. He was buried in Offenbach on the Main, his last place of residence. His tombstone, however, no longer exists.

B. BRUCH's scientific achievements: A selection and a survey

I. BRUCH's topics of research

Starting in 1844, the year his now-famous monograph "*Untersuchungen zur Kenntniss des körnigen Pigments der Wirbelthiere in physiologischer und pathologischer Hinsicht*" (1844b) appeared, **BRUCH** published until 1873 nearly sixty articles, primarily in renowned scientific journals of the period such as **HENLE** and **PFEUFER**'s "*Zeitschrift für rationelle Medizin*", or **SIEBOLD** and **KÖLLIKER**'s "*Zeitschrift für wissenschaftliche Zoologie*", and a series of papers written with a broader audience in mind, in "*Abhandlungen der Senckenbergischen Naturforschenden Gesellschaft*", in "*Berichte über die Verhandlungen der naturforschenden Gesellschaft in Basel*" or in "*Neue Denkschriften der Allgemeinen Schweizerischen Gesellschaft für die Gesammten Naturwissenschaften*".

BRUCH focussed his analytical mind on a great number of important problems addressed by the scientific community in his day. Inspired by **FRIEDRICH TIEDEMANN** (1781—1861) and **LEOPOLD GMELIN** (1788—1853), **BRUCH** examined in a series of experiments the physical and chemical changes underlying the various colorations of blood.

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[11] cf. obituary notice in: Berichte der Senckenbergischen Naturforschenden Gesellschaft 7, (1883/84) p. 7.

In his paper on granular pigments (1844b) **BRUCH** not only investigates the different forms and the distribution of various pigments in several vertebrates (including humans), but describes his discovery of a separate membrane in the retina (see below).

A significant number of papers including a lengthy monograph are devoted to cancer research, its forms, growth and diagnosis (BRUCH 1846d—1849d) and its relation to embryology.

II. BRUCH's membrane

— BRUCH's discovery of the Lamina basalis choroideae

BRUCH's first major monograph (1844b) deals with vertebrate pigments, in particular with the structure and formation of normal pigments and of pigments resulting from pathological processes. **BRUCH** examined various animal and human eyes under the microscope (Fig. 7). He writes (1844b, p. 6):

„Jedem Untersucher muss, wenn er eine Partie Pigment von der Choroideae abstreift, die enorme Masse von Kernen auffallen, die mitten unter den abgestreiften Pigmentzellen umher liegen und oft das ganze Sehfeld bedecken. Zuerst beim Schweine fiel es mir auf, dass diese Kerne in grösseren Gruppen zusammenhalten, und beim Zugiessen von Flüssigkeit (Wasser, Essigsäure) unter dem Microscope sich in flächenartigen Ausbreitungen bewegen, so dass ich auf die Vermuthung kam, sie möchten durch irgend ein zähes Bindemittel vereinigt sein."[12-1]

Apparently, **BRUCH** initially assumed a colloid agent responsible for the cohesion of the cell nuclei he had observed under the microscope. It was only after a series of experiments with varying light-intensities and chemicals that he was able to convince himself that he was confronted with a separate membrane (BRUCH, 1844b, pp. 6—7): *„Es ergab sich dann auch nach genauerer Besichtigung bei gedämpftem Lichte, dass viele von ihnen auf einer sehr zarten, glashellen, structurlosen Membran aufsitzen, welche letztere durch Essigsäure noch durchsichtiger wird, zugleich aber ihre schmalen Fältchen deutlicher hervortreten lässt, die ihr stellenweise ein fasriges Aussehen geben. Dass keine wirkliche Faserung Statt hat, sah ich sehr gut, wenn ich die Membran flottiren*

[12-1] "Upon removing a bit of pigment from the choroid, every observer must have noticed the enormous mass of nuclei which lie scattered beneath the removed pigment cells and often cover the entire field of vision. (. . .) In the eye of pigs I first noticed that these nuclei are assembled in larger groups; when I added a liquid (water, acetic acid) to the preparation, these nuclei spread in what seemed to be a plane surface, so that I conceived the idea that they might be joined together by some resilient binding agent."

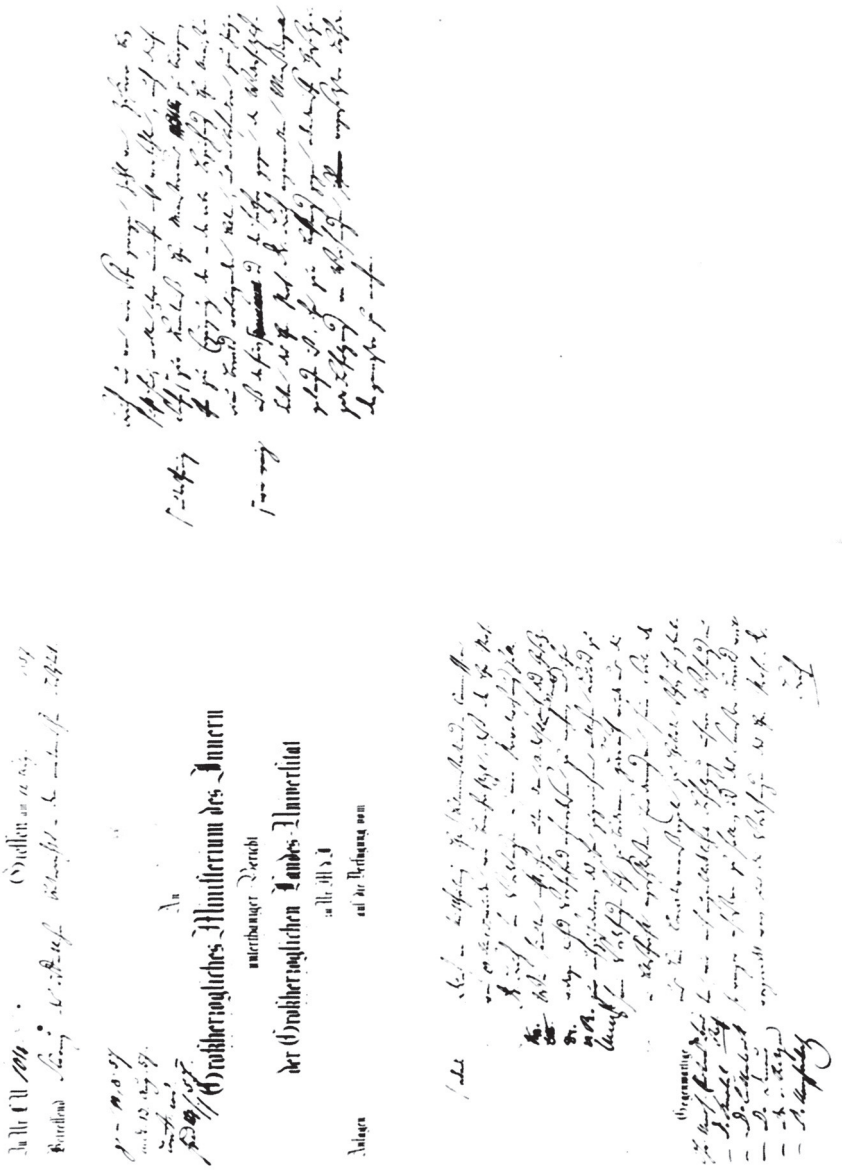

Fig. 6a/b: Photograph of the Letter of the University to the Ministry of the Interior dated August 12th, 1857, filing a complaint against Prof. Dr. BRUCH *"who is said to lecture in his private home, despite official admonitions informing him of the illegality of his manner of proceeding"*. By courtesy of the Archives of the Justus-Liebig-University Giessen.

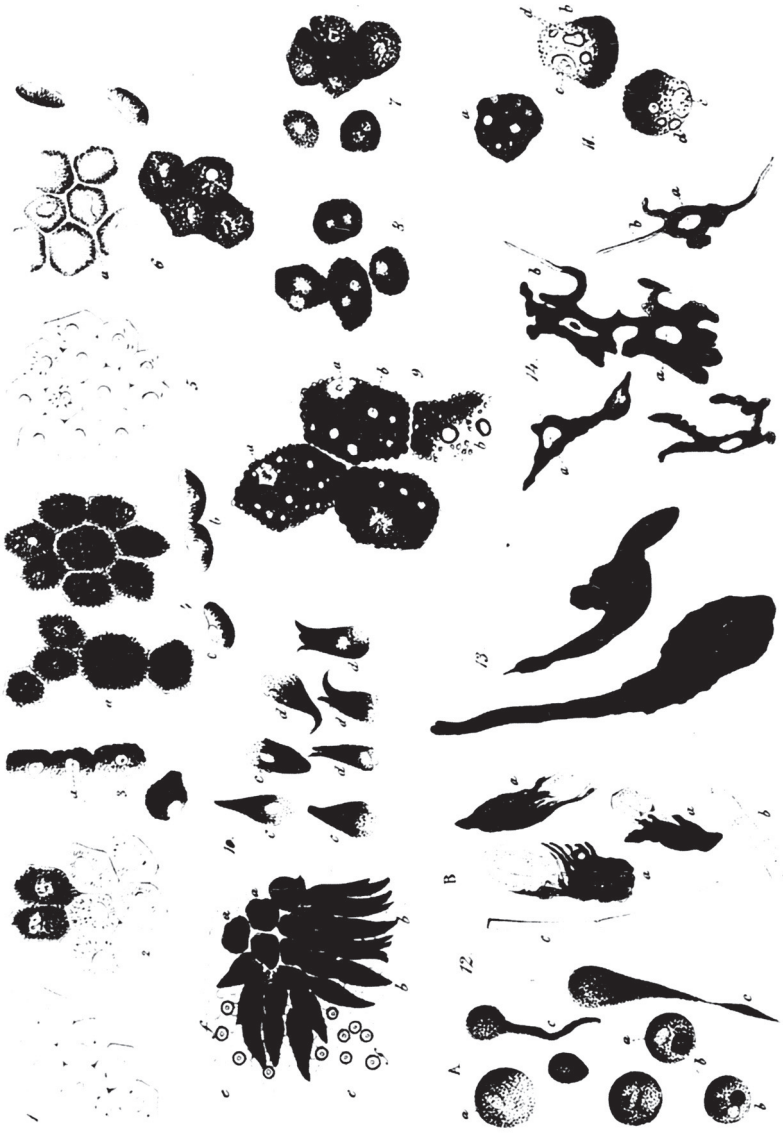

Fig. 7: Lithographed ink-drawings by C.W.L. BRUCH of pigment cells of the choroid in cow (Nr. 4), in pig (Nr. 6), in man (Nr. 7, 8) in rabbit (Nr. 9), in duck (Nr. 10), in frog (Nr. 11), in pike (Nr. 12), in carp (Nr. 13); pigmented cells of the Lamina fusca in man (Nr. 14). The magnification is 330x using PLÖSSL's microscope, ocular 1 and lenses 5, 6, and 7.

liess, oder nach Färbung mit Jod, das auch die Conturen deutlich macht. Feste Theile werden vom Jod immer gelber gefärbt, als die umgebende Flüssigkeit."[12-2]

He also made sure that he was not dealing with an artifact resulting from his preparation-technique (BRUCH 1844b, p. 7): *„Von geronnenem Zelleninhalte, der oft ähnliche Formen bildet, in welche Zellen und Zellkerne zufällig eingeschlossen werden können, unterscheidet man sie sehr leicht durch ihre gleichmäßige Dicke und Durchsichtigkeit, durch die Falten und die häufige Veränderung derselben; ferner dadurch, dass man sie in grössern Fetzen erhält, vor Allem aber durch die sehr regelmässige Anordnung der aufsitzenden Kerne . . . In keinem Falle aber kann ich die letztere für eine zufällige Bildung halten. — Oft sassen auch Pigmentzellen und freie Pigmentkörnchen darauf, die sich abspülen liessen; noch öfter sieht man diese Membran mit den aufsitzenden Zellkernen an der Peripherie eines Stückchens abgestreifter Pigmentschicht hervorragen.*"[12-3]

Having discovered the membrane, **BRUCH** (1844b, p. 8) systematically searched other parts of the eye for its presence: *„An der Iris geht das beschriebene Häutchen bis zum Pupillarand, d.i. so weit, als in allen Fällen die Pigmentschicht reicht; eine bestimmte Grenze dem Tapetum gegenüber konnte ich nicht wahrnehmen.*"[12-4]

He raises the question of its origin and function, and states that earlier controversies regarding the structure of the chorio-retinal layers (see Introduction) are solved (BRUCH 1844b, p. 9): *„Ganz zweifelhaft ist mir die Bedeutung und Funktion der beschriebenen Membran, abgesehen davon, dass das Vorkommen jener zahllosen Kerne zum Theil erklärt wird. Ob sie sich zum Pigment verhält, wie etwa die structurlose Membran der Schleimhäute zu ihrem Epithelium, ob sie selbst eine junge Pigmentschicht, oder ob sie nur einen Ueberzug*

[12-2] "A thorough examination under low intensities of light revealed that many of (these nuclei) rest upon a very delicate, clear and structureless membrane; acetic acid makes the latter even more transparent and renders its tiny folds more visible, which in places give the membrane its fibrous appearance.

[12-3] "Because of the membrane's even thickness and transparence, its wrinkles and their frequent changes, it is easily distinguishable from coagulated cell contents, which often assume similar forms, in which by accident cells and cell nuclei can become enclosed; typically, the membrane is obtained in larger pieces and above all, it is characterized by the highly regular arrangement of the adjacent cell nuclei (. . .). In no event can I take the membrane to be an adventitious formation. — Pigment cells and unattached pigment granula frequently rested upon the membrane from which they could be rinsed off; even more often can one observe this membrane supporting cell nuclei as it sticks out from beneath the periphery of a removed piece of pigmented layer."

[12-4] "At the iris, the described membrane extends all the way to the edge of the pupil, i.e., as far as in all events the pigmented layer reaches; I was unable to observe a definite boundary between the membrane and the tapetum."

für die Choroideae abgibt wie über die Plexus choroidei, überlasse ich competenteren Richtern. Jedenfalls aber halte ich die Frage über die mysteriöse, viel besprochene ***Tunica Jacobi*** und ***Membrana pigmenti*** *für spruchreif. Die Ansichten darüber und die Verwirrungen in der Wahl dieser Ausdrücke sind bei* HENLE *zusammen gestellt.''*[12-5]

Although the "meaning and function" of this membrane was unclear to **BRUCH** at the time, it was a great achievement in itself to have ***first*** made it visible by means of an extremely difficult microscopical preparation; thus ***definitely proving*** its existence, which hitherto had been the object of speculation.

The intricacy of BRUCH's method of preparation becomes evident in his own description (BRUCH 1844b, p. 7):

,,Um sie rein darzustellen, entfernte ich mittels eines zarten Haarpinsels die Pigmentschicht von der Choroideae, und erhielt sie dann durch Schaben der letzteren mit flach gehaltener Messerklinge, wenn auch nicht jedesmal, doch sehr häufig, aber nur in microscopischen Stückchen. Waren die Augen nicht sehr frisch, so war die Mühe in der Regel vergebens. Ich fand sie mit Bestimmtheit bei der Katze, beim Schweine, Kalbe (u.a. bei einem 13 Zoll langen Fötus), beim Schafe und beim Menschen, bei welchem ich sie über die ganze Choroideae, das Corpus ciliare und die hintere Fläche der Iris verfolgt habe.''[12-6]

BRUCH's preparations are taken from samples of normal and pathological tissues from a wide variety of animals: sheep, bovines, pigs, rabbits, ducks, frogs, pikes, salmon, horses, ravens, deer, cuttle-fish, dogs, cats and even from a whale (Fig. 7).

He examined under the microscope and drew pigment-cells from eyes, but also from other organs, such as the beaks of ravens and ducks, from the lung and bronchial glands of a man, from the ovaries of a cow, the nose of a calf-fetus. His examination (BRUCH 1844b, p. 41) of animal pigments led him to the con-

12-5 "The meaning and function of this membrane is quite unclear to me, except that it partially explains the incidence of that mass of nuclei. I leave it to more competent judges to decide whether it relates to the pigment in similar fashion as e.g. the structureless membrane of the mucous tissues to their epithelium, or whether it represents a young pigment-layer of, or only a lining for the choroid and the choroid plexus. In any event, however, I believe that the time has come to raise the problem of the mysterious, much-discussed Tunica Jacobi and Membrana pigmenti. HENLE (1841, p. 783 ff) lists the opinions concerning this matter and the confusions resulting from the choice of these expressions.

12-6 "In order to isolate the membrane, I removed the pigmented layer from the choroid with the hairs of a delicate brush and then obtained it by scraping the choroid by means of a knife-blade held flat, if not always, at least very often, but only in microscopic shreds. If the eyes were not very fresh, the effort was generally spent in vain. I found it with certainty in cat, pig, calf, (including a 13 inch long fetus) sheep and in man, where I followed it across the entire choroid, the ciliary zonule and the posterior surface of the iris."

viction: *„daß . . . das körnige Pigment im normalen und anormalen Zustande wesentlich ein und dasselbe sei, und daß es seine Entstehung . . . einer Veränderung des Blutfarbstoffs verdanke."*[12-7]

Subsequent achievements in the search for the structure, function and clinical importance of BRUCH's membrane

A whole series of further discoveries and technical developments was necessary to render the morphology of BRUCH's membrane transparent and to demonstrate its function as an electrically isolating layer of high resistance (Figs. 11—12).

Chronology of important ancillary developments and scientific achievements after 1844

1865: **ALARIK FRITHIOF HOLMGREN** (1831—1897) discovers that the electrical potential between the cornea und the fundus of the eye changes as light falls upon the retina, thus discovering the electroretinogram.

1908: **M. WOLFRUM**, in a light-microscopical study of the choroid described BRUCH's membrane as a five-layered structure.[13]

1932: **ERNST RUSKA** (b. 1906) together with **BODO VON BORRIES** (b. 1905) invented the electron microscope using magnetic lenses, attaining resolving powers beyond those possible with the light microscope.

1950: **TSUNEO TOMITA** first records electrical responses to illumination from ***within*** several layers of the retina with the help of a glass capillary microelectrode; he observes the phenomenon of a potential-reversal at depths between 70 and 120 μm from the inner surface.

1956: **GILES S. BRINDLEY**, in similar experiments, discovers a barrier of high electrical resistance in the zone of potential reversal described by **TOMITA**; he provisionally called it *"R membrane"* and tentatively identified it with the external limiting membrane and the surface membrane of the rods and cones.

1959: **KENNETH T. BROWN** AND **THORSTEN WIESEL**, on the basis of exact measurements of the reversal of electrical potential situate the *R membrane* in a more scleral direction, and identify the *R membrane* with *BRUCH's membrane*.

12-7 "that . . . granular pigment in the normal and the pathological state is basically one, and that its formation . . . is the result of a transformation of haemoglobin."

13 "these are vitreal to scleral: the basement membrane of the pigment epithelium, an inner collagenous layer, an elastic layer, an outer collagenous layer and the basement membrane of the choroid."
For a detailed study of BRUCH's membrane see Spitznas, 1974.

1963 — 1968: It was discovered that the *R membrane* is made up at least of two components. ***One*** layer consists of BRUCH's membrane, the other, more vitreal, consists of the ***inner*** bounding membrane of the pigment epithelium. This conclusion was confirmed in

1963: by **GILES S. BRINDLEY** and **D.I. HAMASAKI** by means of electrophysiological experiments (Fig. 11), supported in

1965: by **ADOLPH COHEN** by electromicroscopic studies, and confirmed in

1968: by **L.A. RODRIGUEZ-PERALTA**, who examined its permeability to dyes.

A detailed investigation of the fine structure of the five individual layers of BRUCH's membrane descending to the macro-molecular level and supported by many detailed electron micrographs was performed by **M. SPITZNAS** (1974). According to **SPITZNAS** (1974, p. 140): *"For a long time, BRUCH's membrane was thought to be a diffusion barrier between choroid and retina. This opinion was based on the experimental observation that silver nitrate entering BRUCH's membrane from the blood stream through the wall of the choriocapillaries is deposited there without reaching the pigment epithelium. New experiments with tracers of small molecular size like peroxidase show, however, that these substances pass through BRUCH's membrane without difficulty and enter the intercellular spaces of the pigment epithelium. The functional role of BRUCH's membrane could, therefore, be that of a filter that transforms the individual streams of fluid from the choriocapillaris into an even 'rain'. The connective tissue islands between the lacunae of the choriocapillaris are so large that, on the retinal side, they are neighbored by areas of 20—30* or more photoreceptors. As these areas are fed from the choroid, their metabolic situation could be expected to be worse than that of photoreceptors adjacent to the lumen of the choroidal capillaries. Therefore, it is likely that BRUCH's membrane with its fiber system and networks facilitates an even distribution of the nutritive substances to all sides, so that an uniform supply to photoreceptors is guaranteed."

Fig. 9 gives the position of BRUCH's membrane within the human retina. A schematic drawing of the membrane's infrastructure is found in Fig. 10.

Only fourteen years ago, the functional importance of BRUCH's membrane for normal vision was still unknown. According the **G.S. BRINDLEY** (1970, p. 66): "All that we know now is that it (the high electrical resistance of the R membrane) helps experimenters to know the position of electrodes." Meanwhile, clinical observations have revealed the importance of the intact R membrane for normal vision.

ISAAC MICHAELSON (1980) devotes an entire chapter to "*Disturbances of the Lamina of BRUCH.*" He distinguishes between normal and pathological changes which, sooner or later, lead to impaired vision. Degenerative

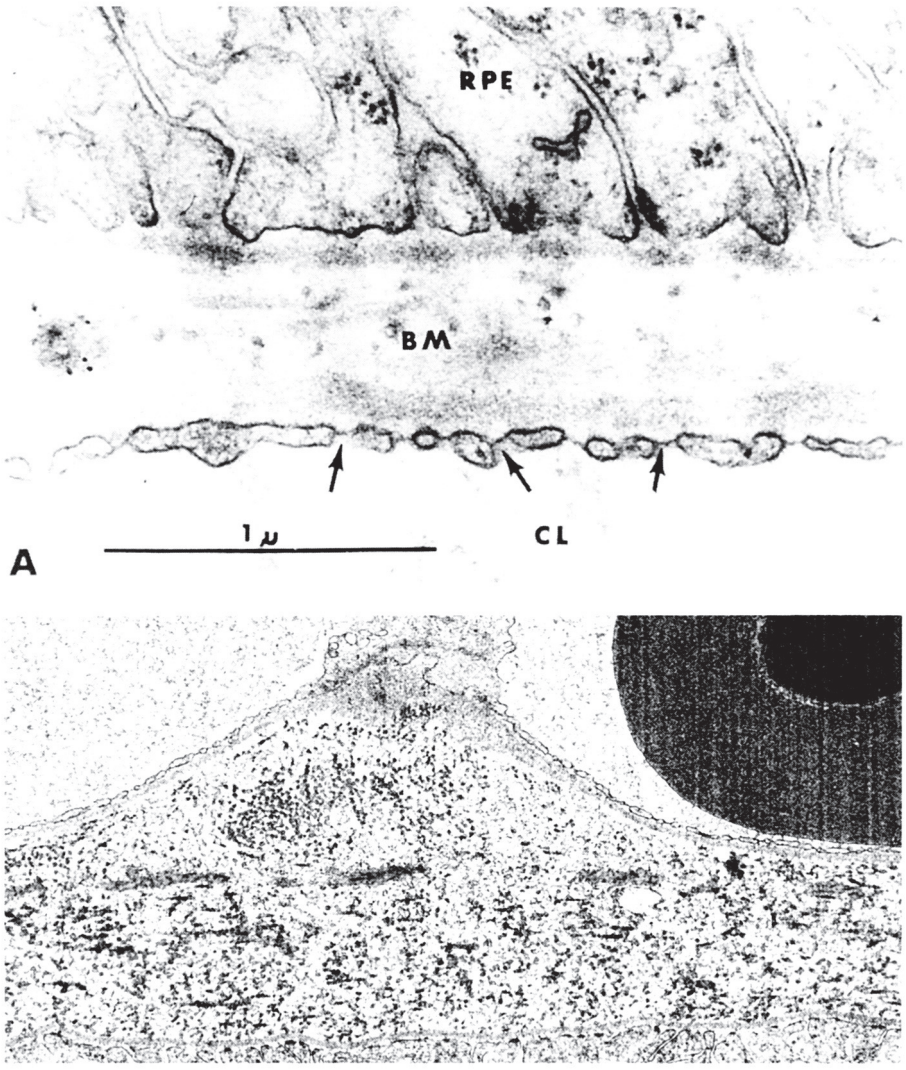

Fig. 8 *a:* Electron-micrograph of BRUCH's membrane by Dr. A. COHEN, Source: STRAATSMA, B.R. et al. eds. (1969), p. 6. By permission of the University of California Press.

b: Electron-micrograph of BRUCH's membrane of a young adult Rhesus monkey (Maccaca mulatta). The choriocapillaris is above and the edge of the retinal epithelium is below. The basal lamina of these two cell systems enclose layers of collagen and elastin fibers forming together BRUCH's membrane. The magnification is 24.000 x. Provided by the courtesy of PETER GOURAS and HILD KJELDBYE of the Department of Ophthalmology, Columbia University, College of Physicians and Surgeons, New York City.

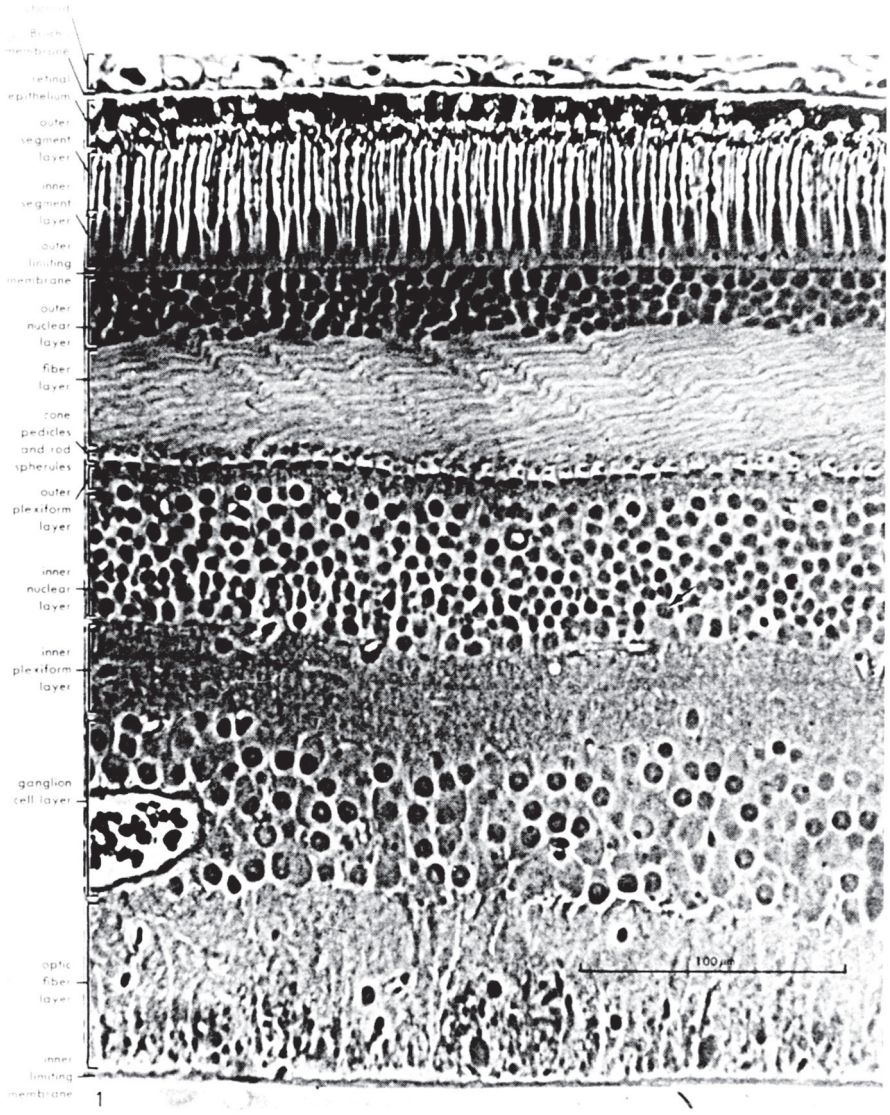

Fig. 9: Vertical section through a human retina, about 1,25 mm from the center of the fovea (where both rods and cones are found). Material fixed in osmium tetroxide, embedded in Araldite, cut about 2 to 3 μm thick and photographed by phase-contrast microscopy. From: BOYCOTT, B.B. and DOWLING, J.E. (1969), p. 116.
Source: RODIECK (1973), p. 4.

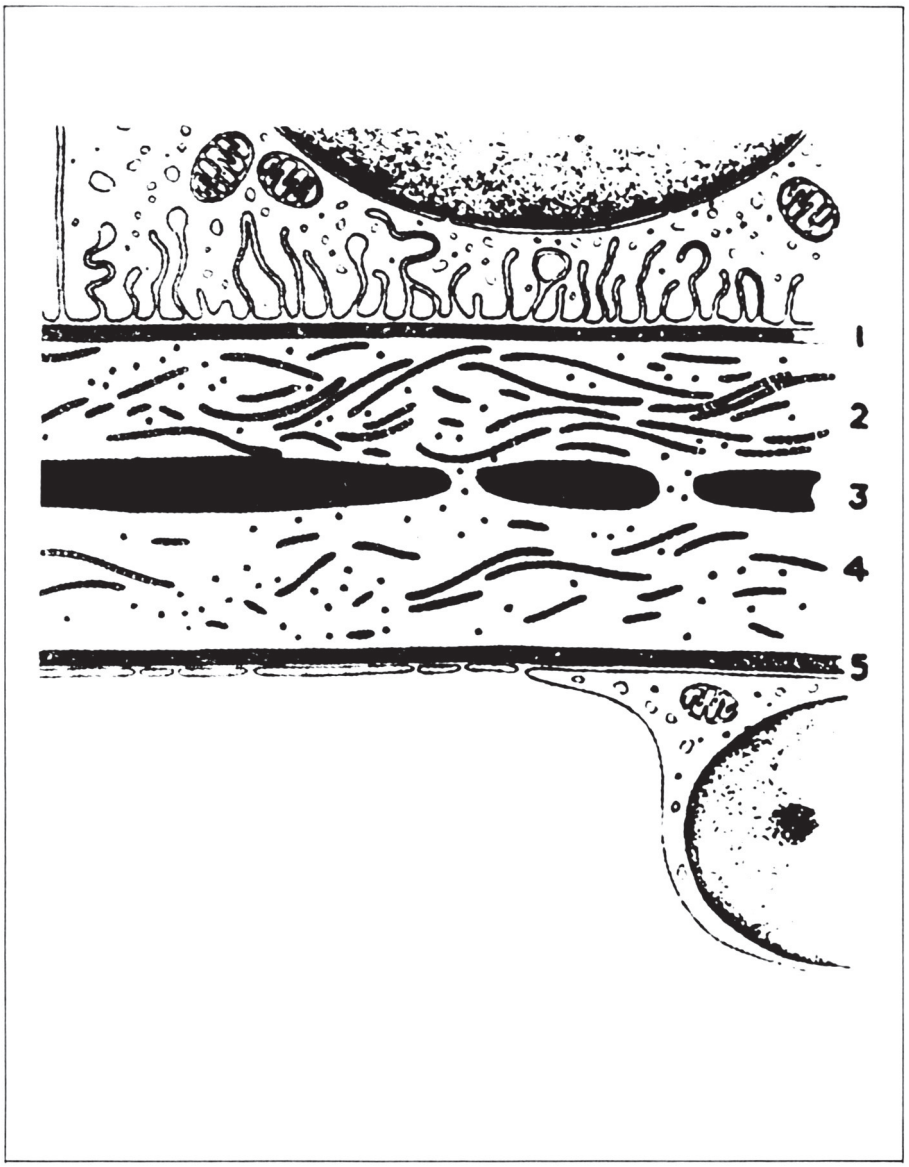

Fig. 10: Schematic representation of the five layers of BRUCH's membrane by Y. NAKAIZUMI (1964, there: Fig. 1, p. 380): 1) Basement membrane of pigment epithelium; 2) inner collagenous zone; 3) interrupted elastic tissue zone; 4) outer collagenous zone; 5) basement membrane of choriocapillary endothelium. Note the basal infoldings of the plasma membrane of the pigment epithelial cells and the fenestrations in the choriocapillary endothelium.

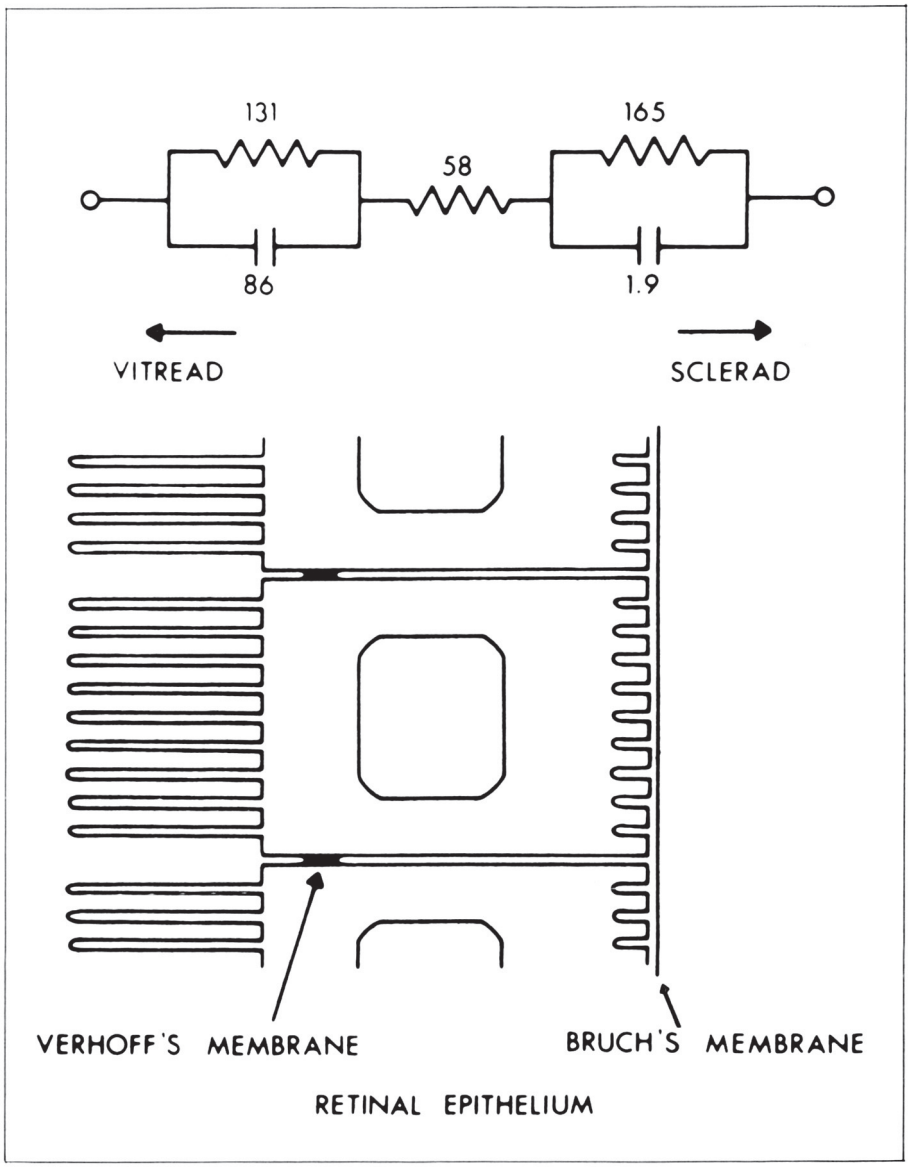

Fig. 11: Schematic diagram showing an electrical equivalent circuit of the frog R-membrane, together with the associated surfaces of the retinal epithelium that probably accounts for these electrical values. Resistances in Ω cm^2, capacitances in μF cm^{-2} (electrical values from BRINDLEY and HAMASAKI, 1963). From RODIECK (1973), Fig. XVIII-3, p. 529. The individual cells of the pigment epithelium are connected by small rims forming VERHOEFF's membrane.

thickening and tears of the Macula resulting from age are classified as normal changes. **DUKE-ELDER** (1967, pp. 522—523) writes:

"These (senile) changes in the pigmentary epithelium are reflected in degenerative and hyperplasic changes in its derivative, the hyaline portion of BRUCH's membrane (. . .). In the aged it becomes yellowish, less elastic so that it easily exfoliates or tears, leading to the occurrence of spontaneous breaks (. . .) and frequently contains irregular aggregations of lipids and calcareous granules."

In addition, traumatic lesions or high degrees of myopia (minus 6 diopters or more) can lead to localized changes (**MICHAELSON**, 1980, pp. 741 and 744).

In light of these facts, it is not surprising that within the last seven years more than sixty articles in five different languages appeared discussing anatomical, physiological and clinical aspects of **BRUCH**'s membrane (source: computer of the Medical Library, National Institutes of Health, Bethesda, Md.).

In summary, BRUCH's membrane may be described as ***a pentalaminar structure*** interposed between retina and choroid, formed on its lower border by the basal lamina of the retinal epithelium and on its upper border by the basal lamina of the choriocapillaris (Fig. 8b); in between are elastin and collagen fibers forming the inner three layers, i.e., the outer collagenous, elastic and inner collagenous layers; it serves at least three functions:

1) anatomically, of providing a mechanical support between retina and choroid;
2) physiologically, of providing an even flow of nutritive substances from the choroid to the retina;
3) electrophysiologically, as a part of BRINDLEY's *'R' membrane*, of ensuring that electrical signals are properly isolated.

Furthermore, **SPITZNAS** (1974) hypothesizes that **BRUCH**'s membrane serves as a mechanical barrier against intraocular pressure.

III. BRUCH's biochemical, pathological and osteological studies

On haemoglobin

Between 1844 and 1853, **BRUCH** conducted a series of haematological experiments to discover whether the appearance of arterial and venous blood depended more on a physical or a chemical change in the blood. **BRUCH** (1844, p. 447) argued: *„dass **beide** Erklärungsweisen . . . begründet, aber für bestimmte Fälle zu beschränken sind"* — — ("that **both** explanations are founded, but applicable to specific situations"). His experiments had led him to postulate with certainty three causes of haematological pigmentation (BRUCH, 1844, p. 447):

"1. Durch chemische Veränderung des Blutfarbstoffs; Sauerstoff, Kohlensäure.
2. Durch Anwesenheit oder Abwesenheit der Blutzellen oder anderer suspendirter, das Licht reflectirender Körper; stark gewässertes Blut.
3. Durch Veränderung der Gestalt und reflectirenden Oberfläche der Blutzellen; concentrirte Salzlösungen, schwach gewässertes Blut."[14]

It was only in the year 1852 that **BRUCH**'s experiments, *"welche die Einwirkung der Gase auf den freien Blutfarbstoff ausser Zweifel stellten"* ("which demonstrated beyond doubt the action of gases on unbound haemoglobin") were universally confirmed, not lastly by **JUSTUS VON LIEBIG** (1851, *Annalen der Chemie* III, p. 112). In the year 1857, **BRUCH** (1857, p. 168) succeeded in providing conclusive evidence „daß nur der Sauerstoff activ auf den Farbstoff einwirke, die Kohlensäure, der Wasserstoff, der leere Raum usw. nur durch Austreibung des absorbirten Sauerstoffs wirke und die dunkelste Farbe die natürliche des Farbstoffs sei."[15]

On rigor mortis

In his latin Habilitation-thesis, *"Nonulla de rigore mortis"* (1845), **BRUCH** discusses a phenomenon which, in his time, had not yet been fully explained, and presents arguments against **ERNST BRUECKE**'s hypothesis (1842), *"dass alle Erscheinungen der Todtenstarre unter der einfachen Voraussetzung erklärt werden können, dass in den Muskeln flüssiger Faserstoff zum Gerinnen komme"* ("that all manifestations of rigor mortis can be explained by the simple premise that liquid *fibrin* coagulates in the muscles." (**BRUCH**, 1850c, p. 329). **BRUCH** (1850c, p. 330) assigned rigor mortis to a contraction of muscles and found *„durch Messung der Breite der Querstreifen . . . daß die einzelnen Muskelprimitivbündel im todtenstarren Muskel sich verkürzen"* ("by measuring the width of the lateral striated muscles . . . that the individual muscle bundles shorten as a result of rigor mortis"); BRUCH's observation is closely matched by the theories of rigor mortis accepted nowadays; thus BRUCH clearly opposed **du BOIS-REYMOND**'s hypothesis of electrical activity producing muscle contraction observed in rigor mortis. The scientific battle between **du BOIS-REYMOND** and **CARL WILHELM LUDWIG BRUCH** is published in a brief declaration by **BRUCH** in HENLE and PFEUFER's *„Zeitschrift für rationelle Medizin"* (1850, vol. IX, pp. 329—331).

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[14] 1. A chemical alteration of haemoglobin; oxygen, carbon dioxyde;
2. the presence or absence of blood cells or other, light reflecting particles in suspension; strongly diluted blood;
3. a change in the configuration and light-reflecting surface of the blood cells; concentrated, saline solutions, weakly diluted blood."

[15] "that only oxygen actively influences the coloration of blood; carbon dioxyde, hydrogen, a vacuum etc. only acts by expulsing the absorbed oxygen and that the darkest hue is natural to the pigment."