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Notes and Comments

Louis Agassiz and the Discovery of the Coelenterate Nervous System

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In a communication to the American Academy in May 1849 Louis Agassiz presented an account of his observations on the structure and natural history of medusae.[1] Sea-shore biology was a field which had only recently engaged his attention. He was entranced with jellyfishes, their insubstantiality, transparency and luminescence. His account of *Sarsia tubulosa* and *Hippocrene* (now called *Bougainvillea*) *superciliaris* is the work of an enthusiastic and careful observer, but it contains several major errors of interpretation, particularly in the sections dealing with the muscular system. In spite of this, the paper is of unusual interest because it contains the first attempt at a detailed description of the hydromedusan nervous system. Coelenterates are the lowest organisms to possess a nervous system and at the time Agassiz wrote, nerves had not been discovered in any member of the phylum.[2]

Agassiz does not generally receive credit for discovering nerves in coelenterates. His findings were treated with considerable scepticism, as he himself appears to have anticipated. 'I do not wonder', he wrote, 'that the very existence of a nervous system in the Medusae should have been denied, and shall not at all be surprised if it were even now further questioned'.

Amongst the questioners was Agassiz himself who came to doubt the validity of his original findings and unobtrusively retracted them in 1862.[3]

[1] Agassiz, L. (1850), 'Contributions to the natural history of the acalephae of North America, Part I: on the naked-eyed Medusae of the shores of Massachusetts, in their perfect state of development', *Mem. Amer. Acad. Arts and Sci.*, Vol. 4, Pt. 2, 221-316.

[2] The term *Coelenterata*, introduced by R. Leuckart in 1847, is used here to cover not only Agassiz's 'acalephs' (medusoid coelenterates and ctenophores) but also the Anthozoa (corals, sea anemones and their relatives). As the ctenophores should probably be placed in their own, separate phylum, many zoologists restrict 'coelenterate' to the remaining groups, known also as Cnidaria, following Hatschek.

[3] Agassiz, L. (1862), 'Contributions to the Natural History of the United States of America', Vol. 4, *Hydroidae*. Little, Brown & Co., Boston.

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A few years later however, E. Haeckel[4] accurately described nerves in *Geryonia* and by 1878 the main features of the nervous system in a variety of medusae had been convincingly set out by Oskar and Richard Hertwig.[5]

My main purpose in this article is to assess the validity of Agassiz's account of nerves in medusae. I have concluded that in spite of his own retraction, he was the first person to give a substantially correct account of a major component of the nervous system in any coelenterate.

Methods of Observation

For preserving medusae as specimens for reference purposes, Agassiz used Goadby's method, which, as described by Forbes,[6] was essentially a way of pickling the animals in saline mixtures of increasing strength, alum being added during the early stages. For his histological studies however, Agassiz did not use chemical fixatives at all, but relied on observation of living tissues or of tissues in the process of death and decomposition. The way in which the tissues changed upon death was found to be instructive. Thin layers of more or less intact epithelial cells could be lifted from medusan cadavers; fibrous component were found to separate, becoming more visible, during decay. The macerating fluids used by later workers such as the Hertwigs permitted a more controlled process of dissociation, but the principle was the same.

Agassiz used ether and chloroform to immobilize his animals, noting that the effects of these anaesthetics were reversible.

He deliberately placed medusae in reagents which caused swelling and shrinkage (fresh water, saline solution, alcohol) in order to observe the changes they brought about on living tissues.

The observations on the nervous system were made with an Oberhäuser compound microscope. Agassiz used a low power lens combination for scanning and changed to a 'high dry' for detailed observations. The No. 8 lens referred to in the passage quoted on page 4 was Oberhäuser's most powerful objective. A surviving example of this lens has a focal length of 2.5 mm, a numerical aperture of 0.45, an initial magnification of 42.5 and a working distance of less than 1.0 mm.[7] A modern lens of this numerical

[4] Haeckel, E. (1865), *Die Familie der Rüsselquallen (Geryonida)*, Engelmann, Leipzig.

[5] Hertwig, O. and Hertwig, R. (1878), *Das Nervensystem und die Sinnesorgane der Medusen*, Vogel, Leipzig.

[6] Forbes, E. (1848), *A Monograph of the British Naked-Eyed Medusae*, Ray Society, London.

[7] Otto, L. (1970), 'Microscopes of Georges Oberhäuser (1798-1868) from the Collection of the Optical Museum in Jena', *Jena Rev.*, 2 (supp.), 7 pp.

aperture would easily resolve 0.5 microns, but it is doubtful if the best lenses in the 1840's could go below 1.0 microns[8] and we know that some of Oberhäuser's lenses showed considerable distortion.[9] In some Oberhäuser instruments of the period, a substage illuminating lens was used to focus the light on the specimen from below. We do not know if Agassiz's instrument had this feature, or whether he relied on the light-concentrating effect of the concave mirror. Agassiz boldly immersed his objective lens in the water covering the specimen when looking at living tissue. Objectives designed for immersion were not available until about 1860 and one can only speculate on the benefits which this practice would have yielded.

There can be no doubt that the microscopes available to the Hertwigs thirty years later were greatly superior to Agassiz's Oberhäuser, but assuming that the specimen was thin, transparent and well illuminated, there is no reason to doubt that he could have seen hydromedusan marginal nerve rings, which are thick bundles about 10 to 20 microns in cross section, and he might just have been able to see the thicker composite strands in the subumbrellar nerve net, which are about 1 micron thick. The finer strands and single nerve processes in the net could not possibly have been resolved.

The Basic Observations

In the verbatim quotations which appear below, notes in square brackets are my own interpolations, and omissions are shown by dots except in the case of references to figures not reproduced here, which are simply left out.

Regarding the species in which nerves were observed, Agassiz cites *Hippocrene*, *Tiaropsis*, *Staurophora* and *Sarsia* (where the first observations were made). The illustrations of *Hippocrene* are most informative, and the figures reproduced here are all for this species.

a) *Marginal Nerves* – The following extract refers to findings in *Hippocrene*:

> The nervous cord, following closely the course of the circular chymiferous tube [radial canal], is placed along the inner margin of the tube. It can easily be seen, either from above or from below, whenever a perfect view of the whole circular tube

[8] Bradbury, S. (1967), *The Evolution of the Microscope*, Pergamon Press, Oxford.

[9] Otto (footnote 7).

is obtained, and is actually drawn as a thread with double outlines in the figures above quoted... Under a low magnifying power, this cord appears simply as a thread following the chymiferous tube... When I first noticed it, it appeared to me as a small thread; and though its structure was not fully recognized then, its connection with the sensitive bulbs led at once to the appreciation of its real nature as the main cord of the nervous system. The difficulty of distinguishing between the tissues in this part of the body where so heterogeneous organs meet together, has rendered it for a long time difficult for me to ascertain the real nature of this cord. For here we have also circular muscles, or contractile fibres, which move the transverse partition [velum] of the lower part of the disk; we have an outer and an inner epithelium; and finally, the walls of the chymiferous tubes, which, at times, present themselves with so strongly defined outlines, that when the tube is not in its natural position, but more or less twisted, the sensitive cord does not appear on its margin as a distinct thread with peculiar outlines. But all the conditions for correct investigation of the facts having been assumed, I have repeatedly satisfied myself and others, that there is, along the inner margin of the chymiferous tube, a cord differing in its microscopic structure from all the contractile fibres and from all the epithelial cells around it, which follows the whole course of this circular tube, and enters into the lateral corners of the sensitive bulbs, where it forms part of their mass.

The last sentence in this passage is perhaps the most exact and careful statement concerning the marginal nervous system provided by Agassiz and it is factually correct. As subsequent workers have found there is indeed a ring of nerves in the precise location referred to. The nerves are distributed on either side of the velum adjacent to the circular canal. They form a distinct cord which can be seen under a dissecting microscope at about 50 × magnification.

Agassiz's Plate II, Fig. 14 (Fig. 1) showing the nerves (*f*) entering the base of the tentacular bulb in *Hippocrene* may be compared with drawings of the same region in *Sarsia*[10]. The nerve cord is also shown in Plate II, Fig. 17 (*b*), and Plate III, Fig. 15 (*b*) (Fig. 2). The latter is interesting as an indication of the sort of picture Agassiz obtained with the higher powers of his microscope. The resolution is obviously poor by modern standards. The account continues:

This cord, examined under high magnifying powers, such as Ocular 3, Objective 8, of Oberhäuser's microscope, appears as a string of several rows of nucleated cells, ovate in their form and placed with their longer diameter in irregularly continuous lines (Plate III. Fig. 13); that is to say, the cells are not strictly placed in juxtaposition by their ends, but alternate more or less, so as to form a cord-like mass, the elements of which are ovate cells placed side by side, their tips interposed between each other. This arrangement and the form of the cells make it easy, after the organ has once

[10] Mackie, G. O. (1971), *Neurological complexity in medusae: a report of central nervous organization in 'Sarsia'*, Actas del I Simposio Internacional de Zoofilogenia, University of Salamanca Press, Salamanca (Figs. 2 and 3).

been seen, to recognize it again in whatever position it may be observed, and of late I have frequently been able to trace it upon the circular tube, passing obliguely across it, or following it in an oblique direction, whenever the parts had been twisted. Tracing this cord for the whole course of the circular tube, we see it penetrate

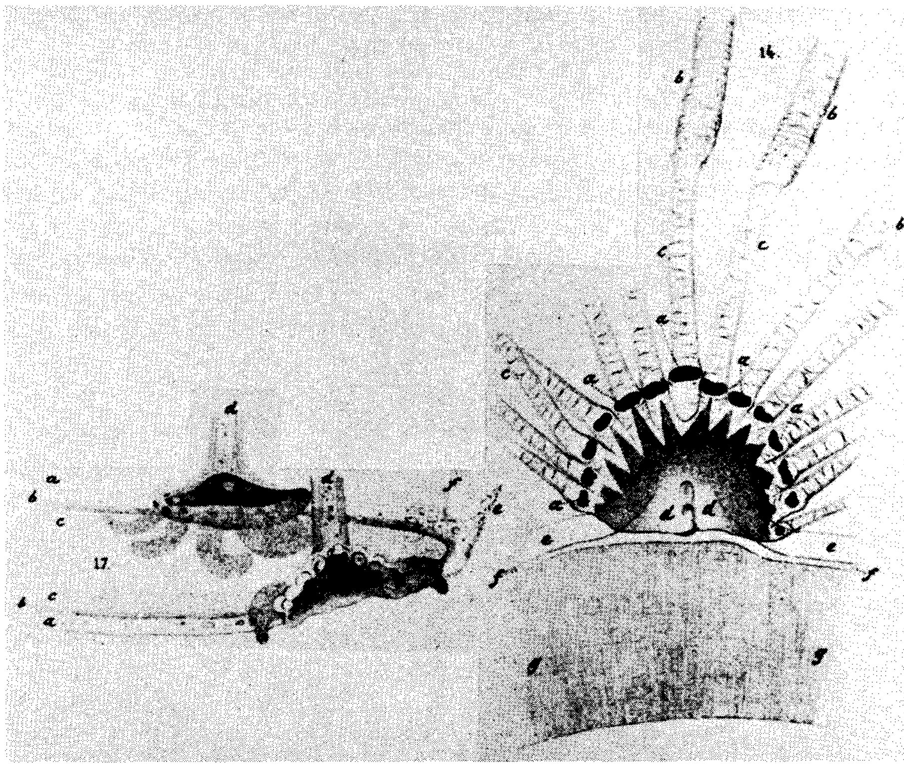

FIG. 1 – Figures of *Hippocrene* (*Bougainvillea*) from (Agassiz, 1850), Plate II.

Fig. 14: Tentacle bulb viewed from below, the tentacles stretching:

a. ocellus
b. distal part of tentacle
c. proximal part of tentacle
d. ganglion
e. ring canal
f. nerve ring
g. velum

Fig. 17: Margin seen from the side and slightly from above with two tentacle bulbs, the one on the right seen from outside and the one on the left seen from inside through the transparent body wall:

a. ring canal
b. nerve ring
c. velum
d. radial canal
e. exumbrella
f. subumbrellar muscle layer

into the angles of the sensitive bulbs (Plate II. Fig. 14, *f*) in which its cells mingle with colored pigment-cells in such a manner as to form a compact ganglion of heterogeneous elements, rather than a nervous bulb.

The reference to 'ovate cells' recurs elsewhere in the paper, although the figure reproduced here (Plate III, Fig. 13; present Fig. 2) is the only one showing the shapes of individual cells. Agassiz saw no nerve fibres in *Sarsia*, only:

> ...a cord of cells of a peculiar ovate form, arranged in six or seven rows, forming a sort of string, or rather similar to a chain of ovate beads placed side by side and point to point, but in such a manner that the individual cells would overlap each other for one half, one third, or a quarter of their length, being from five to seven side by side at any given point upon a transverse section of the row...

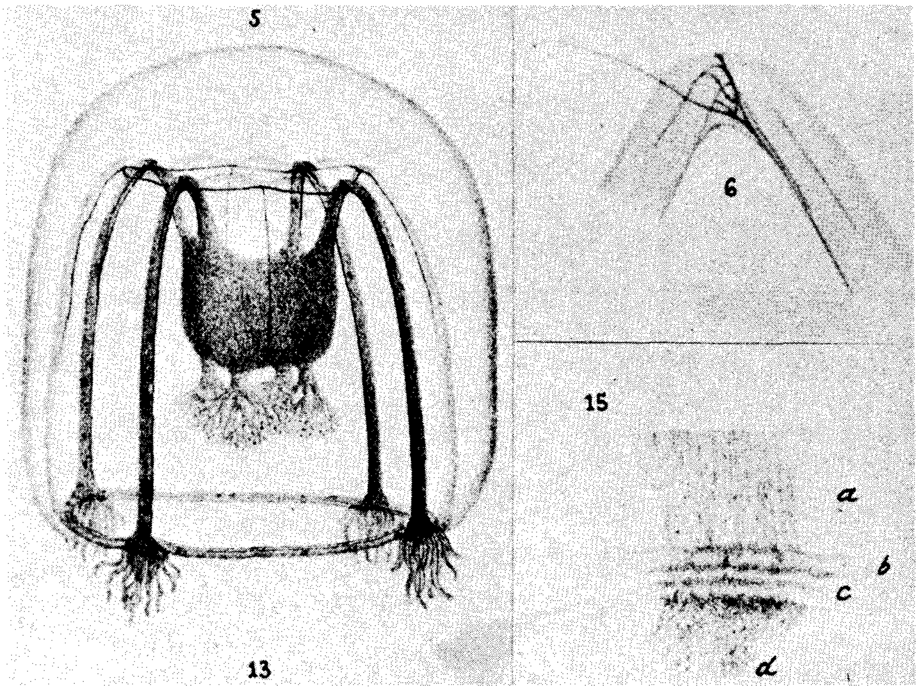

FIG. 2 - Figures of *Hippocrene* (*Bougainvillea*) from (Agassiz, 1850), Plate III.

Fig. 5: The whole medusa from the side. The marginal nerve ring is faintly shown running around beside the ring canal. Radial nerves run up under the radial canals. The upper nerve ring is shown spanning the interradial gaps between the arches of the radial canals. Descending threads run down in each quadrant midway between the radial canals.

Fig. 6: Enlargement of the arch of a radial canal with nerve plexus.

Fig. 13: The cells of the marginal nerve ring.

Fig. 15: Part of the margin seen from below:

a. velum — b. nerve ring
c. circular canal — d. outer wall of bell

The conclusion drawn by a contemporary reader would presumably have been that coelenterate neurones were fundamentally different from those described in other animals, where nerves were always found to have long delicate processes. The reluctance of later workers to accept Agassiz's findings probably stems more from this difficulty than from any other single factor.

And yet it is not hard to accept that Agassiz's observations were essentially accurate. The fibrous processes of hydrozoan neurons range from a few microns down to a few hundred millimicrons in diameter. They are hard to see even with well corrected lenses and with the aid of selective staining methods. As late as 1961, it was found necessary to hold a discussion entitled 'Is there a nervous system in Hydra?'.[11] Presumably what Agassiz saw and described as 'ovate cells' were the cell somata of the neurons. Some of the Hertwig's drawings (e.g. Tafel II, Fig. 3 for *Cunina*) where the nerve cord is drawn seen from the surface without maceration, have a similar appearance.

b) *Ganglia* – On entering the bases of the tentacular bulbs, the nerve cord 'forms part of their mass' according to Agassiz in the passage quoted earlier. Elsewhere he refers to the region as a 'ganglion' (*d*, in Plate II, Fig. 14). In *Sarsia*, where there is only one tentacle at each of the four radii, the reader is asked to trace the chain of nerve cells 'to the base of the eye speck [the ocellus which lies on the outside of the tentacle base], where these cells accumulate in a larger heap, with intervening coloured pigment forming a sort of ganglion'.

Both Haeckel and the Hertwigs subsequently found thickenings of the nerve rings at the tentacle bases. Haeckel called them 'ganglia', but the Hertwigs thought the structures insufficiently differentiated to merit the title.

The concept of marginal ganglia disappears from the hydromedusan literature after the Hertwigs until 1971, when they were redescribed. Under the electron microscope they can be seen to consist of a peripheral layer of cell somata surrounding a central mass of fibres in a neuropil-like array.

The structures now referred to as ganglia are more precisely delimited than the ganglia described by Agassiz. Agassiz evidently considered the greater part of the tentacle bulb in *Sarsia* to be composed of nervous tissue whereas in reality it is composed chiefly of cnidogenic tissue. Nerves are concentrated in the region of the ocellus and nerve tracts run from there, through the cnidogenic mass, to the tentacular ganglion which lies

[11] Lennoff, H.M. and Loomis, W.F. (eds.) (1961), *The Biology of Hydra*. University of Miami Press.

on the inside of the tentacle. Agassiz may have seen the true tentacular ganglion but failed to distinguish it from adjacent non-nervous tissue.

Haeckel was probably the first person to give an accurate account of the ganglia. Hardly had they been discovered than they were forgotten again for nearly a century.

c) *Subumbrellar Nerve Tracts* – Agassiz completed his description of the nervous system in *Hippocrene* with an account of nerves running up beside the radial canals from the tentacular bulbs and forming a second nerve ring around the apex of the subumbrellar cavity.

> On examining minutely the walls of the vertical tubes [radial canals], which are so uniform in their homogeneous structure, it is easy to discover on their inner surface one or two threads (Plate III. Fig. 5), following along the whole length of these tubes. Below the curve where the tubes bend to form the loop which is connected with the central digestive cavity, these threads combine into a plexus (Plate III. Fig. 6) of intricate fibres, from each of which arises another thread extending horizontally from one plexus to another (Plate III. Fig. 5), so that there is a circle of such threads all round the upper part of the chymiferous system, or below the centre of the gelatinous disk. This circular thread, considered in itself, may therefore be viewed as a ring encircling the upper part of the chymiferous system, forming a plexus of similar threads under the curve of each radiating tube, from which identical threads may be traced downwards to the sensitive bulbs, in which they also merge. From the middle of each upper horizontal thread, there arises a vertical thread extending downwards, and following the main course of the large inner vertical bundles of muscles.

This part of Agassiz's account is in some ways the most interesting and problematical. The fact is that nerves do run up the four radii, but not as 'one or two threads'. They form a plexus interspersed within the radial muscle bands, and are quite hard to see. It seems very likely that what Agassiz actually saw were the radial muscle fibres. He was in some doubt about the nature of the structures himself.

> I am not fully satisfied – he wrote – of the real nature of this apparatus, on account of the great difference there is between these threads and the sensitive cord of the lower margin. Far from consisting exclusively of short ovate cells connected together in several rows, we have here very thin threads, in which the cellular appearance is almost entirely gone, excepting where they combine to form a plexus, in which some of the threads have the appearance of long caudate cells. For a time I mistook these threads for muscular fibres...;

The remainder of this passage, too long to quote verbatim, explains in detail the reasons why he finally decided to call the fibres nerves rather than muscles.

It is worth noting that coelenterate histologists have continued to be bedevilled by the problem of distinguishing nerves from muscles. As late as 1898, T. Schaeppi[12] was confidently misinterpreting nerves as muscles in siphonophore swimming bells. Suspicions arise about the correctness of Hyde's identification of nerves in *Gonionomus* on the same grounds.[13]

Until recently I would have affirmed (had I known of it) that Agassiz's second nerve ring, which runs around the apex of the subumbrella, was probably an artefact, perhaps a crease caused by shrinkage of the bell. No such encircling strand or plexus has been seen by later workers. Recently, however, I studied a medusa (originally discovered and named by Agassiz) from the west coast, *Stomotoca atra*, and found that it has a nerve plexus in the very region where the encircling strand is figured in *Hippocrene*. It is not a well-developed circular cord with interradial branches as Agassiz depicts it, but a diffuse net running out from the radial nerve plexuses and bridging the interradial gap between them and the manubrial base. Whether or not the subumbrellar nerve pattern in *Hippocrene* and *Sarsia* is as Agassiz describes cannot be settled without a careful reinvestigation of these species. I am inclined to believe that Agassiz did not really see nerves in this region but mistook either muscles or creases for nerve cords. I doubt that with the optics available he could have seen these fine neurites. If so, the picture of nerve distribution in medusae which he arrived at is closer to reality than it has any right to be.

To sum up, I believe that Agassiz saw the marginal rings. I cannot give him the benefit of the doubt on the ganglia. Ganglia are present but not as he described them. The radial nerves, I firmly believe, he could not have seen although they too are there. The upper circular nerve likewise, although I hesitate to state that he was in error on this point when I myself have not examined the exact region in the species he worked on.

Agassiz's Retraction

The following statement constitutes a retraction of the previous account of nerves in *Sarsia*:

> As to a nervous system, it has not been possible to detect the least signs of a structure indicating its presence. When the innermost wall is seen in profile, along the radiating tubes and at the four intermediate points, its thickness resembles a thin cord, which might be easily mistaken for a nervous thread. The most intimate structure, the cells of the innermost wall, along the radiating tubes, do not differ from

[12] Schaeppi, T. (1898), 'Untersuchungen über das Nervensystem der Siphonophoren', *Jenaische Zeit. Naturw*, 32: 483-550.

[13] Hyde, I.H. (1902), 'The nervous system in *Gonionema murbachii*', *Biol. Bull. Woods Hole*, 4: 40-45.

those on each side; all are alike excessively transparent, and roud. When the animal is contracted in the manner described above, the innermost wall, at its eight points of adherence, comes strongly into profile, and, on this account, the nerve-like appearance of its thickness is more apparent than at any other part; but when the disk is uncontracted, and the innermost wall presses uniformly against the whole surface of the middle one, it is possible to observe this same appearance anywhere between these eight points. Looking at the disk from above, the innermost wall, where it bends downwards to become the outer wall of the proboscis, resembles, in profile, a quadrangularly-disposed cord, surrounding the inner wall of the proboscis like a nervous ring. At the junction of the transverse partition with the edge of the disk, the innermost wall bends upon itself at right angles, and there, again, when looking across the edge of this angle, its thickness appears like a nervous ring, running along the inner edge of the circular tube. The statement, in my paper on *Sarsia*, Mem. Amer. Acad. of Sc. and Arts, Vol. IV, pp. 246 and 247, that these Acalephs have a specialized nervous system, was based upon these appearances.[14]

While Agassiz never retracted his account of nerves in *Hippocrene*, we must assume that he meant to withdraw all his previous claims.

Subsequent History

Why did Agassiz withdraw his claims? The simplest explanation is probably the best. He looked again, and changed his mind. He was not the man to change his views just because they were adversely received. He may, however, have been induced to look again because of the inner doubts occasioned by the failure of his views to find acceptance. Clues to this may lie in private letters or other source material.

It is very clear that his claims met with profound scepticism. As late as 1876, Romanes expressed extreme reservations about 'the well known statements of Prof. L. Agassiz regarding the nature and distribution of the nervous system which he describes as occurring in the Medusae'.[15] After reviewing these statements Romanes continues:

...I may be permitted to remark, with reference to the passage just quoted, that the conclusion so positively enunciated concerning the function of the structures described has always appeared to me, as it has appeared to biologists in general, a conclusion that is certainly unwarranted by the facts. As the learned Professor himself insists, the cells to which he so confidently attributes a nervous character represent 'a peculiar type of the nervous system, a type different from all those types which have yet been recognized in the animal kingdom'; and this fact alone, one would think,

[14] Agassiz (footnote 3, pp. 199-200).

[15] Romanes, G.J. (1867), 'Preliminary Observations on the Locomotor System of Medusae', *Phil. Trans. Roy. Soc.*, 166: 269-313.

ought to have inspired extreme caution in founding deductions upon such a basis regarding a question of such high importance as is that concerning the presence of a nervous system in the class Hydrozoa.

Haeckel[16] categorically denied that the objects described by Agassiz as nerves corresponded to the nerves which he himself found in *Geryonia*. The only prior claim allowed by Haeckel is that of R. Leuckart with respect to nerves in *Eucope* (*Phialella*). (Leuckart's paper, published in 1864, is not available to me at the time of writing).

It was left to the Hertwigs, the appearance of whose great monograph in 1878 established that year forever as the *anno domini* of coelenterate neurohistology, to put the matter in reasonable perspective:

> Dem gegenüber müssen wir hervorheben, dass der von Agassiz entdeckte Zellstrang am Rande der Schirmglocke mit unserem Nervenring und dem ihn bedeckenden Sinnesepithel wohl identisch ist, dass dagegen die von ihm gemachten Beobachtungen bei der mangelhaften Erkenntniss der histologischen Zusammensetzung der Theile zu der Deutung eines Nervensystems nicht berechtigen.[17]

In conclusion, whatever the errors of interpretation contained in his account Agassiz is surely entitled to the credit for discovering medusan marginal nerve rings. Although he himself subsequently came to doubt his own findings, his claim that coelenterates possessed a nervous system proved to be correct, and can now be seen to have rested on a valid observational basis.

[16] Haeckel (footnote 4).
[17] Hertwig (footnote 5).