# Wilhelm Roux (1850-1924) and blood vessel branching

**A Passariello***

*PhD candidate, Philosophy Department, Sapienza University of Rome

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Corresponding author: Dr. Alessandra Passariello, alessandra.passariello@uniroma1.it



**Abstract** The essay explores the work of the XIX century embryologist Wilhelm Roux (1850-1924) with particular focus on his research on the vascular system in the formation of his embryological theories.
The "Introduction" outlines an epistemological analysis regarding two of Roux's early works: his doctoral dissertation on blood vessel branching (1878) and his theoretical volume on functional adaptation (1881).
Section I, "Wilhelm Roux (1850-1924) and the prelude to *Entwicklungsmechanik*", delineates the epistemological background to Roux's academic formation: Darwinian revolution and biophysical research in physiology respectively shape the debates of the time that opposed historical to proximate causality and vitalistic causality to a physical-chemical one.
Section II, "Order in blood vessel branching: Roux's anatomical observations", introduces Roux's vascular observations: the identification of a regularity in vessel bifurcating angles and the verification that the whole vascular structure can be interpreted by the optimality principle of minimal physiological work.
Section III "Functional adaptation and blood vessel branching", introduces Roux's embryological concept of functional adaptation, which he intended to be a transposition of the Darwinian logic of variation and selection within the organism, and shows how Roux attempts to use this new concept to explain the developmental constraints on blood vessel direction.
Section IV, "A resourceful mechanistic explanation", stresses the epistemological ambiguity of the key concept of "mechanistic" causality and notes how this prevents giving a perfectly coherent picture of Roux's thought on development in the two texts examined.

**Keywords** Wilhelm Roux; Vascular System; Experimental Embryology; Hemodynamics; Functional adaptation; Internal selection

## Introduction

This essay explores the work of the XIX century scientist Wilhelm Roux with particular emphasis on the role played by the vascular system in the origin of his embryological theories.

In the late XIX century, physiology and comparative anatomy had already inspected the structure and the functioning of the vascular system in order to understand metabolism (C. F.W. Ludwig 1816-1895) and pathology (J. F. Cohnheim 1839-1884), and to find out taxonomical proximities between species (E. Geoffroy Saint Hilaire 1772-1844).

In this context Roux's questions concerning the developmental appearance of vascular structure were a complete novelty as were his attempts to get a deeper look into the theoretical principles which are used to explain the details of blood vessel branching.

Of Roux's explanatory principles, we separate his appeal to hemodynamical laws from his use of the concept of functional adaptation.

The theory of development by functional adaptation is extensively addressed in the work "Der Kampf der Theile im Organismus" (1881) which will be quoted here in the French translation "La lutte des parties dans l'organisme" (2013)[7] .

While the aim of Roux's work is highly theoretical, his writing is profusely annotated with empirical details about experiments and scientific observations, blood vessel branching playing the role of a paradigmatic case study.

Roux's interest in vascular morphogenesis had already started during his university period spent at the Jena Medicine Faculty (1873-1877) where, in 1877, he defended his doctoral thesis about liver blood vessel branching, published in 1878 under the title "*Ueber die Verzweigungen der Blutgefasse des Menchen*[8] " (tr. eng. "On the bifurcations of human blood vessels").

We know from this and further publications (Roux 1879)[9] that he personally performed most of the experiments he describes, thus assuring both observational amplitude and reliability of his conclusion.

However, the repeated appeal to vascular analyses in Roux's early research, firstly in his doctoral thesis (1878) and later in the nearly "philosophical" work on functional adaptation (1881), does not point to a common theoretical framework. Indeed different questions underlie the two texts:

- the former (1878) is mainly concerned with the relationship between form and function in the vascular architecture and inspects the vascular system with the clear aim of finding anatomical generalizations that correspond to an optimal physiological condition,

- the latter focuses on the embryological causes of vascular morphology, with particular emphasis on the explanation of morphological development traits that show a kind of adaptation to induced stimuli. In this latter case, the focus is on the relationship between form and function but in a clearly different sense: functionality is the capacity of a developing organism to react to internal-external stimuli and arrange its form accordingly, that is, in order to cope with them.

There are certainly some points of intersections between the two texts and their related questions: in his doctoral dissertation, apart from relating the vascular architecture to a principle of minimum physiological work, Roux also addressed the issue of embryological causes, though he was said to have done it naively (Kurz et al. 1997[10] ). This morphogenetic interest, described in the section III.1 of his thesis ("Gestaltende Wirkungen der hydraulischen Kräfte in Röhren bewegter Flüssigkeit") places this early text in closer contact with his following research on developmental causes.

As Churchill (*Dictionary of Scientific Biography*[11] ) noted, "even at this early stage in his career Roux did not confine his generalizations to a descriptive equation. […] By making an analogy between hydrodynamics and hemodynamics, Roux implied a search for a causal connection between function and form" (p. 571). Otherwise said, as early as 1878 Roux was looking for mechanisms underlying vascular formation[i] [12] . We will see that the term "mechanism" and the correlated notion of "mechanistic explanation" have a different meaning in the two texts (1878, 1881): a physical (hemodynamical) force in the former and a statistical (population) process in the latter.

In order to understand the difference between the two senses of "mechanistic explanation" employed in the two texts, we need to put Roux's embryological theory into what we call the appropriate epistemological context. In this essay, the term "epistemology" will be used to refer to the overall set of scientific (and sometimes extra-scientific) assumptions constraining and defining the space of possible valid questions to be posed in a certain discipline (Rheinberger 2010[13] ).

From this epistemological point of view, if we really want to understand what "explaining" means when it is used either with respect to the hemodynamical laws or to the concept of functional adaptation, we need to frame these terms in the broader history of their discipline.

Both those concepts fall within the field of Experimental Embryology, which is the English translation for *Entwicklungsmechanik* (literally, developmental mechanics). More accurately, the foundation of *Entwicklungsmechanik* dates back to the publication of Roux's *Einleitung* in 1895[14] , both a manifesto for a nascent discipline and an introduction for the new periodical Archiv fur Entiwicklungsmechanik (1895-1924). Roux's doctoral thesis on vessel branching (1878) and his work on functional adaptation Der Kampf der Theile im Organismus (1881) precede the 1895 manifesto. Nonetheless, the scientific questions at the basis of those works and their respective answers, that is the concepts of physical constraints and functional adaptation, obey the main tenets of *Entwicklungsmechanik* and can thus be considered a prelude to its future framing.

## Wilhelm Roux (1850-1924) and the prelude to Entwicklungsmechanik

Wilhelm Roux (1850-1924) lived during one of the most exciting period for his discipline: at the end of the XIX century, biology metabolized the Darwinian revolution, was experiencing a second experimental turn through the rise of embryology and was approaching, through the rise of genetics, the discovery of quantitative tools able to describe the regularities of heredity. Progress in the study of evolution, development and heredity was setting the stage for biology to become the queen of XX century sciences.

Wilhelm Roux, whose French surname recalls his belonging to a Huguenot family dating back to the XVIII century, was born in Jena in 1850 and there, after joining up the army during the 1870-1871 French Prussian War, he started his studies at the Medical Faculty. At the time, the study of medicine embraced broader phenomena than human physiology and pathology and Roux was soon fascinated by the lessons of the zoologist and anatomist Carl Gegenbaur, of his successor at the chair of anatomy, Gustav A. Schwalbe, of the physiologist Wilhelm Prayer and the Darwinian zoologist Ernst Haeckel (Churchill 1973[15] ).

Haeckel in particular left a strong mark on Roux's further reflections. In the aftermath of Darwin's publication of the Origin of Species, Ernst Haeckel was one of the main supporters of the Darwinian revolution that explained the diversity of species as the result of evolution from a common ancestor through a continuous process of change crossing geological times with patterns (especially morphological ones) that could be explained through the aid of random variation and natural selection.

One immediate effect of Darwin's evolutionary theory was on taxonomy or the science of classification. From the turn of the XVIII century, taxonomy classified living beings according to their similarities and dissimilarities. There were functional classifications such as the one proposed by the French scientist George Cuvier according to whom functional similarities among organs (analogies) were induced by common conditions of existence and were a reliable empirical basis for classification. Others, such as the anatomist and embryologist Etienne Geoffroy Saint-Hilaire built their taxa by comparing the anatomical structure of species, that is, by comparing the relative disposition of their internal (bony) parts (Russell 1982).

Unlike comparative anatomy, Darwin interpreted homologies among species as a tool for reconstructing the timing of their evolutionary divergence from a single common ancestor and used tree-branching as the most convincing representation of life's diversity: in a tree-like representation, species similarities were converted into species proximity and the flat classification of comparative anatomy was substituted with a time dependent phylogenetic one.

When Roux attended Haeckel's lessons in Jena he could appreciate one of the main source of phylogenetic classification. Not only did Haeckel suggest, following his predecessor Karl Ernst von Baer's interpretation that in order to build faithful phylogenetic trees embryological characters had to be taken into account together with anatomical ones. He went further in saying that evolution proceeds in every species by "recapitulating", during ontogeny, all the life cycle of its immediate ancestor and by adding one "terminal" character to it. Within the Darwinian framework these processes of "recapitulation" and "terminal addition" can be understood as two mechanisms respectively explaining "heredity" and "variation" (Gould, 1977[16] ).

From the point of view of Haeckel's theory of "Ontogeny" that "recapitulates phylogeny", no kind of explanation was needed in order to understand the specific succession of developmental stages in an organism's life cycle other than the past phylogenetic history of its species. He assumed that every organism, during its development, goes through all the phylogenetic steps which link the single common ancestor to its species-specific type. This meant that individual ontogeny was represented, and most importantly explained as a sort of rapid accumulation of phylogenetic steps.

This kind of developmental explanation is referred to as "historical" because it considers the causality underlying the succession of developmental stages in a single organism to be its past phylogenetic history, as if crystallized in heredity. No proximate embryological causes, amenable to experimental testing, are mentioned but only ultimate (phylogenetically based) descriptive ones.

It is exactly against this historical and descriptive explanation of ontogeny, represented by Haeckel's "biogenetic law" (Haeckel 1866[17] ), that Roux developed his *Entwicklungsmechanik* (mechanics of development) where the term "mechanics" argues in favor of a step-by-step analytical (vs historical) and experimental (vs descriptive) analysis of developmental events.

*Entwicklungsmechanik* is thus primarily concerned with an emancipation of developmental enquiry from the yoke of phylogenetic necessity and provides a clear and fruitful break between evolutionary and developmental explanations (Allen 1975[18] , 2005[19] ).

While Darwinism can help understanding the mechanisms accounting for biological diversity, developmental biology aims at discovering the immediate mechanisms accounting for embryological phenomena.

Therefore, Roux's interest in the law governing the formation process of the vascular system represented a break from the dominant Darwinian tradition: embryology started looking back to immediate causes of phenomena instead of using a historical (phylogenetic) notion of explanation.

However, how were those immediate causes to be conceived? At this point of the story, Experimental Embryology crosses the boundaries of another well-rooted epistemological debate. Not only do the characteristics of living beings have to be explained by making reference to immediate (and possibly experimentally corroborated) mechanisms but those mechanisms also have to be either distinguished from or eventually reduced to ones operating in non-living beings, in particular physical-chemical phenomena.

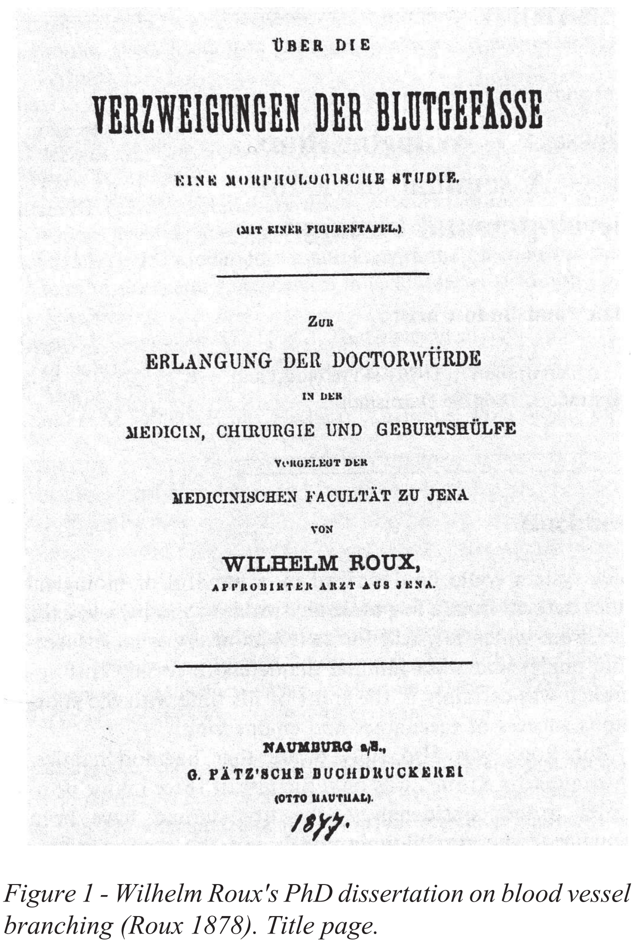
The mechanistic-vitalistic debate, between those who supported the existence of specific biological causality and those who equated it to physical-chemical principles, had a huge echo during the late XIX (C. Bernard, C. Ludwig, H. von Helmhotz) and early XX century (W. Roux, H. Driesch, J. Needham, J. Woodger) and Roux's epistemological concept of what must be considered as a scientific explanation for developmental phenomena lies fully within this important debate.

In *Einleitung*, Roux defines the new discipline as "the doctrine of the causes of organic forms" (Roux, 1895, p. 149) where the term "cause" has two different shades of meaning. Stricto sensu "in accordance with Spinoza's and Kant's definition of mechanism, every phenomenon underlying causality is designated as a mechanical phenomenon" (p. 150) where the term "mechanical" makes reference to the explanation of the phenomenon in terms of "movements of masses". Mechanical explanation is thus the only kind of explanation that grasps causality and in so doing constitutes an exact science. Accordingly, since the ultimate aim of physics and chemistry is to reduce "magnetic, electric, optical and chemical phenomena to movements of parts", the ultimate aim of embryology is to formulate its own explanation in mechanical terms, that is, to become "developmental mechanics". Besides this narrow sense of causality, which restricts scientific explanation to purely mechanical causes[ii] , there is a second carefully crafted path to formulate a causal explanation in embryology: lato sensu, a "causal explanation will always consist in tracing back a particular phenomenon to modi operandi of more general validity", that is, to (-non-mechanical- physical, chemical or biological) reliable generalizations, constantly valid under the same set of conditions[iii] [20] . According to this broader sense, causality is not restricted to mechanistic (that is mechanical) explanation and, though the ultimate aim of developmental mechanics is to attain such physical-chemical reducibility of embryological phenomena, in those early days of embryology it was more productive to engage in a higher level biological explanation. For this reason, Roux made a distinction between causal statements explaining embryological phenomena referring to constant relationships between "complex", that is, non-reducible, components, and causal statements ultimately formulated in terms of mechanistic relationships between "simple (physical-chemical) components".

As Roux himself wrote "the too simple mechanistic conception on the one hand and the metaphysical conception on the other, represent the Scylla and Charybdis, between which to sail is indeed difficult, and so far by few satisfactorily accomplished" (Roux, 1895). Concretely, embryologists should always aim at mechanistic generalizations but the empirical impossibility of attaining this deeper level of explanation should not lead them to metaphysical generalizations about immaterial, causal forces or entities.

This internal polarity between mechanistic and non-mechanistic causality within Developmental Mechanics does not reduce the discipline's radical novelty with respect to the former descriptive and evolutionary approach to development that was dominant in the second half of XIX century embryology (Allen 2007[21] ). Independently from whether it is a thoroughly mechanistic science or just a causal, yet not mechanistic one, Roux's *Entwicklungsmechanik* aimed at giving a proximate explanation instead of an historical one and, most of all, tackled the issue of ontogeny through experimental methods and techniques and not through comparative analysis of development in phylogenetically related taxa.

The next paragraphs will introduce Roux's vascular observations and try to frame the tone of his arguments concerning the vascular system within the confines of the first historical-mechanistic (proximate) and the other mechanistic (physical-chemical)-vitalistic debate.


ÜBER DIE

VERZWEIGUNGEN DER BLUTGEFÄSSE

EINE MORPHOLOGISCHE STUDIE.

(MIT EINER FIGURENTAFEL.)

ZUR

ERLANGUNG DER DOCTORWÜRDE

IN DER

MEDICIN, CHIRURGIE UND GEBURTSHÜLFE

VORGELEGT DER

MEDICINISCHEN FACULTÄT ZU JENA

VON

WILHELM ROUX,

APPROBIRTER ARZT AUS JENA.

NAUMBURG a/S.,

G. PÄTZ'SCHE BUCHDRUCKEREI

(OTTO HAUTHAL).

1877.

*Figure 1 - Wilhelm Roux's PhD dissertation on blood vessel branching (Roux 1878). Title page.*

## Order in blood vessel branching: Roux's anatomical observations

"*Già da studente, preparando la sua dissertazione di dottorato, egli ricercava le cause dei fatti esaminati,* *cioè della forma del lume delle diramazioni vasali, tema assegnatogli dallo Schwalbe, continuatore di Gegenbaur. Egli riconobbe così che i vasi sanguigni si diramano secondo le leggi idrodinamiche, adattandosi cioè da una parte alla forza idraulica della corrente, dall'altra agendovi lo stimolo ad accrescersi ed insieme la inibizione ad accrescersi della tunica interna". Così egli intravedeva quella che chiamò la "lotta tra le parti degli organi", e per la prima volta dimostrava come lo sviluppo e l'accrescimento di un organo influiscono in un determinato modo su un altro organo.*"

(Castaldi, 1925, p.98[22] )

Roux's empirical observations on the branched structure of the vascular system are extensively presented in his doctoral thesis "Ueber die Verzweigungen der Blutgefasse des Menchen" (1878, Figure 1) and further enriched in his "Ueber die Bedeutung der Ablenkung des Arterienstammes bei der Astabgabe" (1879). At the time those texts were written, Roux was ending his formal education in Jena (1878) and had just enrolled at the Hygienic Institute in Leipzig to do laboratory analysis. His work was strongly influenced by Schwalbe's interdisciplinary concern for the relationship between anatomical form and physiological function[iv] .

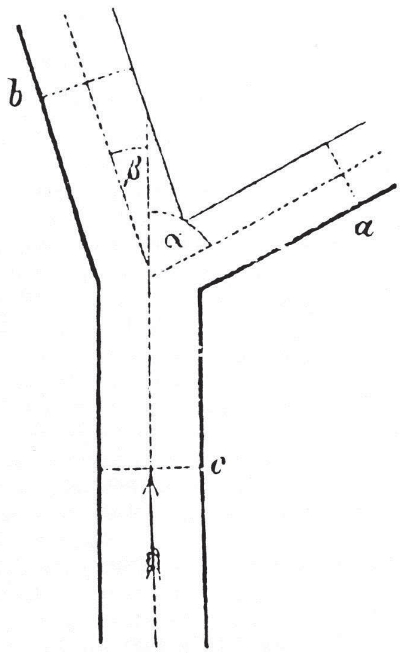



*Figure 2 - Schema of an idealized vascular bifurcation (Kurz et al. 1997). For explanations of symbols, see the text.*

Central to Roux's doctoral dissertation is the observation of the structure of blood vessels in the human liver and an attempt to correlate it to some laws for regularities.

In order to make the vascular architecture visible, Roux developed an advanced version of the ancient technique of wax injection, which consisted of "injecting wax into the vessels and, upon dissolving the surrounding tissues" being "left with only a naked casting of the branches" (Churchill 1973, 570)[v] [23] .

He focused on two parameters, the lumen of the vessel and its bifurcating angle and managed to find a set of structural regularities, which gained a special, functional meaning if linked to hemodynamical laws.

In other words, the regularities of vascular system's structure showed a sort of optimality when analyzed through the lens of metabolic and embryological functioning.

If we consider an idealized bifurcation of a stem trunk into two branches, such as the one depicted in Figure 2, the diameters a, b and c represent the lumen of the respective vessels while the angles $\alpha$ and $\beta$ represent the distance of the vessels from their stemming trunk, or their bifurcation angles.

A first observation emerging from Roux's work concerns the correlation between the lumen of the branches and their bifurcation angles, this correlation being the object of Roux's laws.

He isolates three kinds of possible bifurcations which differ with respect to the ratio a/b, a and b being respectively the diameters of the branch vessels (Figure 3)

In the first typology of bifurcation a/b=1, the bifurcating angles of the branches a and b from the main trunk c are equal (Figure 3a).

Differently, if the ratio a/b>1, the larger branch a will deviate from the main trunk of a angle $\alpha$ smaller than the bifurcating angle $\beta$ of the smaller branch (Figure 3b).

Finally for a/b>>1 , the smaller branch b being tiny, has a bifurcating angle $\beta$ between 70° and 90° (Figure 3c).

In a quotation of D'Arcy W. Thompson's "On growth and form", Roux's laws are generalized as follows:

- "if an artery bifurcate into two equal branches, these branches come off at equal angles to the main stem;

- if one of the two branches be smaller than the other, then the main branch, or continuation of the original artery, makes with the latter a smaller angle than does the smaller 'lateral' branch;

- all branches which are so small that they scarcely seem to weaken or diminish the main stem come off from it at a large angle from about 70° to 90°."

(D'Arcy W. Thompson, 1917, pp. 667-668[24] )

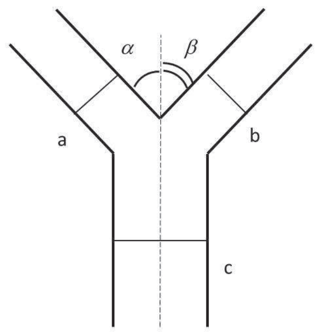



*Figure 3a*

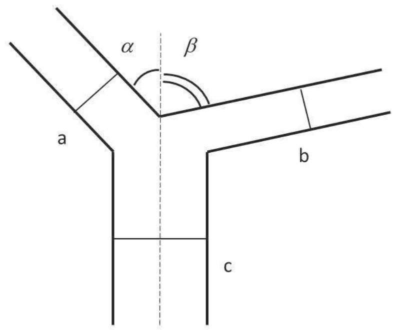



*Figure 3b*

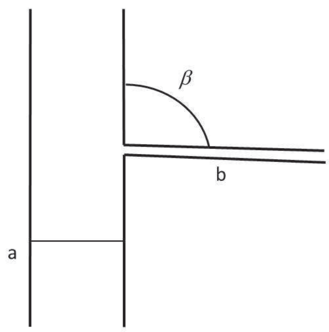



*Figure 3c - Visual representation of Roux's laws on bifurcating angles.*

Roux abstracted his laws from repeated empirical measurements, details of which are reported in his doctoral thesis (Table 1).

He used to take scrupulous note of the absolute values of the bifurcating angles and of the ratio a/b of the diameters of the two branches and his aim was to give a mathematical form to those correlations despite the numerous exceptions (Kurz et al. 1997).

However, what is constitutive about Roux's observations is the fact that the architecture of the branching pattern - at least with respect to the link between the ratio a/b and the bifurcating angles - could be explained by appealing to the constraints of hydrodynamic forces, that is, once we know the ratio a/b we can derive the bifurcating angles by applying to hemodynamical laws.

And we can do this precisely if we introduce a functional physiological criterion for minimum work: the whole branching structure of blood vessels is such as to accomplish circulation by exspending a minimum of energy. Given this physiological principle for optimality, the vascular system develops towards an optimal adult structure, this optimality being a sort of physiological end condition and not a properly morphogenetic one: what is physiologically optimal is the accomplished branched structure not the branching process.

Hemodynamical laws are a theoretical instrument for calculating (and eventually predicting) the relationships between the size of the branches and their bifurcating angles according to an optimality principle. They play the role of physical constraints on the (physiological) functionality of the system.

D'Arcy Thompson (1917) provides a clear explanation of this constraining role by underlining that energy loss is dependent on distance and lumen.

In Figure 4 the distance is the one between either C or D, the bifurcating points on the main trunk, and P, the external point to be reached by the vascular structure.

"If the large artery, AB, give off a comparatively narrow branch leading to P (such as CP or DP), the route ACP is evidently shorter than ADP but on the other hand, by the latter path, the blood has tarried longer in the wide vessel AB, and has had a shorter course in the narrow branch. The relative advantage of the two paths will depend on the loss of energy in the portion CD, as compared with that in the alternative portion CD', the latter being short and narrow, the former long and wide" (D'Arcy Thompson, 1917, p. 667).

**Tabelle I.**

| α | a/b | β |
|---|---|---|
| 18 | 0,83 | 14 |
| 18 | 0,88 | 17 |
| 23 | 0,43 | 8 |
| 23 | 0,72 | 14 |
| 23 | 0,80 | 18 |
| 22 | 0,88 | 19 |
| 22 | 0,95 | 21 |
| 24 | 0,66 | 11 |
| 24 | 0,85 | 18 |
| 25 | 0,57 | 16 |
| 25 | 0,77 | 18 |
| 27 | 0,71 | 11 |
| 27 | 0,91 | 20 |
| 27 | 0,91 | 21 |
| 36 | 0,40 | 15 |
| 37 | 0,71 | 22 |
| 39 | 0,85 | 30 |
| 40 | 0,68 | 9 |
| 40 | 0,83 | 25 |
| 42 | 0,81 | 28 |
| 42 | 0,83 | 32 |
| 43 | 0,77 | 29 |
| 43 | 0,81 | 33 |
| 49 | 0,71 | 10 |
| 48 | 0,88 | 11 |
| 46 | 0,69 | 14 |
| 44 | 0,88 | 22 |
| 50 | 0,58 | 17 |
| 51 | 0,86 | 29 |

| α | a/b | β |
|---|---|---|
| 55 | 0,33 | 7 |
| 54 | 0,61 | 10 |
| 55 | 0,83 | 17 |
| 60 | 0,45 | 15 |
| 60 | 0,55 | 27 |
| 57 | 0,87 | 39 |
| 66 | 0,75 | 27 |
| 68 | 0,83 | 48 |
| 83 | 0,38 | 4 |
| 86 | 0,44 | 9 |
| 76 | 0,86 | 32 |
| Vereinzelt: | | |
| 90 | 0,43 | 34 |
| 102 | 0,43 | 4 |
| Ausnahmen: | | |
| 26 | 0,71 | 6 |
| 46 | 0,83 | 6 |
| 48 | 0,91 | 6 |
| 60 | 0,50 | 12 |
| 17 | 0,83 | 19 |
| 44 | 0,74 | 0 |
| 15 | 0,80 | 28 |
| 23 | 0,98 | 14 |
| 16 | 0,83 | 20 |
| 27 | 0,87 | 33 |
| 20 | 0,83 | 33 |
| 16 | 0,94 | 23 |
| 62 | 0,91 | 39 |
| 67 | 1,00 | 30 |
| 76 | 1,00 | 18 |
| 32 | 0,87 | 8 |
| 15 | 0,73 | 13 |
| 27 | 0,91 | 36 |

**Tabelle II.**

| α | a/b | β |
|---|---|---|
| 38 | 0,23 | 16 |
| 38 | 0,76 | 27 |
| 45 | 0,37 | 14 |
| 45 | 0,66 | 19 |
| 45 | 0,43 | 21 |
| 46 | 0,59 | 35 |
| 46 | 0,87 | 37 |
| 50 | 0,18 | 6 |
| 49 | 0,90 | 23 |
| 51 | 0,37 | 6 |
| 51 | 0,41 | 8 |
| 60 | 0,26 | 19 |
| 60 | 0,41 | 37 |
| 63 | 0,25 | 16 |
| 64 | 0,31 | 20 |
| 66 | 0,47 | 32 |
| 70 | 0,33 | 8 |
| 71 | 0,66 | 22 |
| 75 | 0,31 | 10 |
| 74 | 0,33 | 14 |
| 77 | 0,20 | 20 |
| 78 | 0,88 | 25 |
| 76 | 0,83 | 30 |
| 80 | 0,50 | 18 |
| 81 | 0,52 | 20 |
| 80 | 0,59 | 27 |
| 80 | 0,77 | 39 |
| 88 | 0,36 | 20 |
| 82 | 0,50 | 42 |

| α | a/b | β |
|---|---|---|
| Vereinzelt: | | |
| 29 | 0,45 | 18 |
| 32 | 0,54 | 24 |
| 35 | 0,47 | 28 |
| 40 | 0,39 | 25 |
| Ausnahmen: | | |
| 49 | 0,43 | 22 |
| 53 | 0,59 | 13 |
| 54 | 0,51 | 19 |
| 62 | 0,34 | 6 |
| 62 | 0,34 | 8 |
| 62 | 0,26 | 15 |
| 62 | 0,23 | 16 |
| 63 | 0,45 | 16 |
| 64 | 0,47 | 20 |
| 65 | 0,43 | 45 |
| 66 | 0,50 | 32 |
| 74 | 0,37 | 11 |
| 75 | 0,29 | 10 |

*Table I - Absolute values of bifurcating angles, α and β, together with the ratio of the branch diameters a/b in the vascular architecture of human liver.*

Significantly, at the end of this quotation D'Arcy Thompson introduces Roux's laws.

As previously stated, the hemodynamical constraints are only related to the bifurcating angles of the branches while both their respective diameters and their destination (in Figure 4 the point P), at least in this first formulation, are considered as independent parameters of the system.

But, if the bifurcation angles of the branches can be calculated from their diameters, how can those diameters be calculated with respect to the size of the stem trunk?

Roux never explicitly addressed this issue but there is evidence in his doctoral thesis that he knew that his empirical observations on the relationships between branch and trunk diameters could be brought back to the same principle of optimality which had already proved fruitful in detecting the bifurcation order (Kurz et al. 1997).

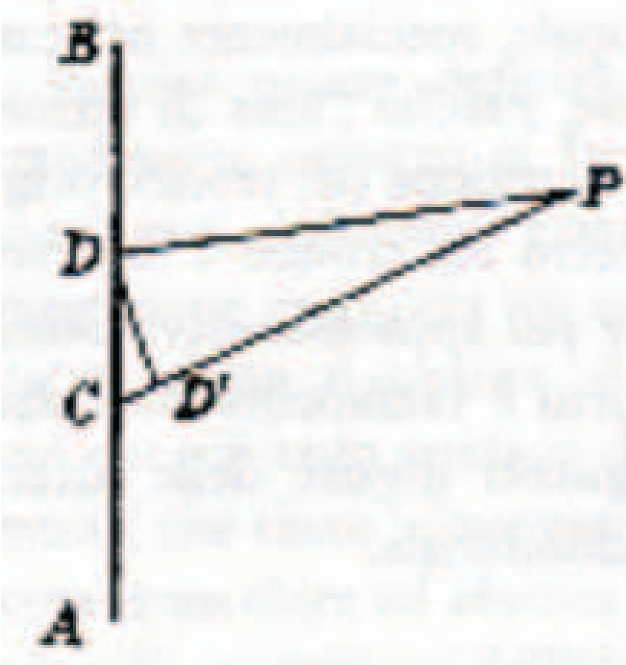



*Figure 4 - Path ACP is compared to path ADP in the light of the optimality principle of minimum work (D'Arcy Thompson 1917).*

In 1901[25] Thoma addressed one fundamental parameter describing the relationships between the trunk diameter c (Figure 2) and its branches a and b.

This relationship was defined by the equation:

$c^{\Delta} = a^{\Delta} + b^{\Delta}$

Δ being the diameter exponent parameter.

Following Thoma's identification of the diameter exponent, the story gets far richer since Thoma himself, D'Arcy Thompson (1917), Cecil Murray (1926[26] ) and more recent works (Kurz et al. 1997) all tried to calculate its optimal value and to corroborate it with empirical observations[vi] [27] .

However, this is another story, to which Roux, whose interests soon turned to the initial developmental phases of cellular differentiation, did not make any direct contribution.

Until now, our analysis has stressed Roux's emphasis on the close matching between the anatomical regularities underlying vascular architecture and a condition of physiological optimality: mathematically described vascular forms (Roux's laws) reflect the best hemodynamically described vascular function (principle of minimum work).

However, the relationship between form and function can be intended as a relationship between an explananda (the form) and its explanans (its function) with respect to two different questions:

- (1) why has the vascular system come to have such a regular branching structure?

- (2) how is this regular branching structure produced during development?

This duality corresponds to Mayr's (1961[28] ) difference between ultimate (why? How come? questions) and proximate (how? questions) causes: (1) by stressing the physiological optimality of human vascular architecture, Roux seems to advocate that, once we assume a principle of minimum work as the proper criterion for efficiency, either the present vascular architecture has been selected for its optimal efficiency or different vascular architectures have been excluded because of their scarce efficiency. In other words, vascular regularities are evolutionary adaptations i.e. characteristics being selected for because of their fitness value. In the context of this former question, hemodynamical laws play the role of physical constraints: fluid mechanics set the basis and the limits for an optimal physiological condition as it defines the adaptive value of the vascular structure and in this sense, it is said to ultimately explain its existence. However, what is most important is that in this former question hemodynamical laws do not explain the developmental origin of vascular regularities; they are not rules of construction, only physical constraints on vascular functionality[vii] [29] .

If we move to the second question (2), addressing the issue of which originating proximate causes are responsible for the development of vascular morphology, we get closer to the difficult intersection connecting Roux's 1878 dissertation and his 1881 work on Functional Adaptation.

What are the proximate causes of vascular morphology? Roux offers two different but not necessarily conflicting answers. In 1878 "by making a parallel between vessel branches and the shape and direction of flowing water" he hypothesized that "blood pressure had a bearing on the patterns of branching" (Churchill 1973, p. 570), which in other words means there is a direct mechanical (hemodynamical) effect of blood flow on the shape and direction of the vessels. This explanation is purely mechanical (or to be precise hemodynamical) and remarkably in line with the later tenets of *Entwicklungsmechanik*: morphological rules should be reducible to physical mechanisms (hemodynamical forces) directly shaping the organism's structure. However, in 1881, Roux' morphogenetic explanation of the vascular structure underwent a curious reformulation through the introduction of the concept of functional adaptation. While in 1878 physical forces were sufficient to account for vascular morphogenesis, in Der Kampf Roux once more tackled the problem of functionality: the finest details of vascular structure are the result of an adaptive reaction of the organism to relevant stimuli occurring during development. If ever hemodynamical forces can explain the overall branched structure they are not enough to explain the direction and the thickness of spreading vessels: some adaptive (regulatory) mechanisms coupling organisms to environmental demands are necessary to explain the finest morphological details.

## Functional adaptation and blood vessel branching

The concept of functional adaptation (funktionelle Anpassung) was introduced by Roux in his 1881 Der Kampft der Theile im Organismus and retrospectively used to explain, among other morphological phenomena, the developmental appearance of some seemingly "finalistic dispositions" of the vascular architecture. Blood irrigation of growing organs in normal development, of tumors in pathologies or of the fetus during pregnancy are, according to Roux, all examples of the capacity of the vascular system to react to developmental stimuli by rearranging its own structure. More generally, functional adaptation is the capacity of the system to change its form according to the requirements of a new function.

At the time Roux was writing, the concept of functional adaptation appeared to be a very close analogy to Lamarck's principle of the acquisition/loss and inheritance of morphological traits through the principle of use and disuse[viii] . However, before examining the relation between Roux's concept of functional adaptation and Lamarck's concept of acquisition and loss of characteristics, it is worth distinguishing between an original formulation of the "principle of use and disuse" by Lamarck himself and its fortune among his followers[ix] .

Lamarck believed that physical matter in living organisms was so organized as to functionally react to changes in the external environment (Lamarck 1802[30] ), the term "functionally" meaning nothing more than the induced agreement between the environmental perturbation and the direction of the external change. He believed that such a reactivity could be ultimately explained as a material property of living beings, and thus did not depend in any way from anthropomorphic notions such as the "will", "habits" or "action" (Gayon 2006[31] ).

However, the solid anchoring of Lamarck's theory in the material world of natural laws became a misleading point in its reception. According to the received view of Lamarck, best known as Lamarckism, the developmental matching of form to the newly required function could be explained through the aid of an inner disposition, not only a vital[x] but a finalistic cause directing the process of morphological change.

It is reasonable that Roux received Lamarck's ideas filtered through a Lamarckist reading. This would explain why he conceives his concept of functional adaptation as a denial of Lamarck's appeal to a finalistic cause, to which he opposes a Darwinian solution, but at the same time leaves the door open for what he considers to be Lamarck's inheritance of acquired characteristics (acquired, though, by non-finalistic processes).

In relation to the functional acquisition/loss of traits, the publication of Darwin's "Origin of Species" subverted the logic of the argument: species' acquisition of environmentally well adapted traits or loss of non-adapted ones during evolution, was the result of a process of natural selection acting on organisms showing random variation in their morphological traits. Traits acquired through a process of natural selection are called adaptations.

In the "Origin of Species" Darwin (1988[32] ) aimed at explaining the diversity of species[xi] [33] as a result of adaptation to different external environments. He assumed that:

- despite heredity, organisms show random variation

- provided the ecological resources are not infinite, natural selection acts on organisms by favouring the reproduction of the fittest or by eliminating the less fit.

Unlike the theory attributed to Lamarck, no finalistic stance is included in Darwin's theory of species evolution.

As Heams (2012[34] ) has cogently said, Roux saw the possibility to shift "from a teleological causality (the Lamarckist solution) to an historical one (the one aimed at through the reformulation of the Darwinian logic within the organism)", a shift which is also evident from the subtitle of Der Kampf "Contribution pour un perfectionnement d'une theorie de la finalité mechanique" where the term "finalité mechanique" makes reference to the possibility of identifying proper mechanisms causing apparently finalistic traits.

In the introduction of Der Kampf, Roux writes

"La finalité n'est pas une réalité volue mais devenue, pas une réalité téléologique mais historique, apparue de manière méchanique; car ce n'est pas ce qui correspondait à un objectif préétabli qui a sourvécu mais ce qui possedait les caractères nécessaires les plus à meme de permettre sa survie" (Roux, 2013, p. 30)

Though not formulated in physical-chemical terms (stricto sensu mechanistic), Darwin's natural selection could be understood as a lato sensu "mechanistic explanation" of evolutionary phenomena, opposing Lamarck's teleological (vitalistic) concept of an inner disposition.

However, Darwin's theory of natural selection on organisms was deemed unable to account for complex adaptations (e.g. the compound eye) that required the correlated variation of many functionally dependent traits. This objection, recognized by Darwin himself (1988) and further stressed by Mivart (1871[35] ), was probably one of the weakest spots of the newborn evolutionary theory. Roux's concept of functional adaptation aims at filling precisely this gap: if Darwinian variation of traits is random with respect to the organism's functionality (and thus not correlated), functional adaptation is the precise mechanism for understanding infra-organism correlated changes during development in response to hereditary or environmental variation.

Roux speaks about an improvement of Darwinian theory ("Contribution pour un perfectionnement […]"), which by itself is not sufficient to account for the origin of such "fine grained finalistic dispositions": no combination of blind variations could originate such a functional outcome as the perfectly adapted, all-encompassing vascular branching. As in the case of the eye, pointed out by Darwin himself, the functional complexity of the vascular architecture also seemed hardly to be evolvable by random variation and natural selection.

What was needed, according to Roux, was a mechanism allowing for the functional correlation of infra-organism parts during development: whatever (hereditary or environmental) random variation had occurred (e.g. an increase in the number of appendages), there should be a mechanism able to accommodate the variation through a process of developmental rearrangement (e.g. vascular irrigation, muscle formation for the new appendages). Whether the effects of such a process were inheritable or restricted to the individual life span is highly controversial in Roux's work. Their persistence through generations would explain the evolution of complex traits: once a random (inheritable) variation has occurred, functional adaptation drives the organism to rearrange its internal structure accordingly while its trans-generational effects simulate the occurrence of inherited functionally correlated variation[xii] [36 37] .

However, even if we are not so strict about the possibility of inheriting functionally adapted traits, functional adaptation is still a powerful concept for explaining developmental plasticity i.e. the capacity of the organism to react to internal or external variation to preserve a functional outcome.

In order to define "functional adaptation" mechanistically, Roux exploited Darwin's selectionist mechanism and tested its strength at the infra-organism level of molecules and cells.

That is the origin of the first[xiii] 38 39 transposition of the Darwinian logic made up of random variation and selection from the external environment to the internal one: the first theory of internal selection[xiv] .

The bulk of the argument is that as natural selection explains the origins of different well-adapted species, internal selection accounts for the origin of different well-adapted organism parts: evolution is mirrored by differentiation and growth.

This parallelism unavoidably reminds us of Haeckel's "biogenetic law" where the course of ontogeny is explained through phylogeny (the pattern of evolution). However, the huge difference between the two formulations is that Roux does not consider evolution to be an explanation of development but the explanatory mechanisms at stake in Darwinian theory to be coopted to explain development.

Initially, Roux states that variation exists at every level of the organisms: molecules vary with respect to their chemical duration, their assimilating capacity and their time of duplication. Variation in molecules and cells' assimilating capacities within a population trigger a selectionist process which allows, mechanistically, for the survival of the fittest.

Citing Weismann's interpretation of Roux' selectionist account of functional adaptation (1909, p. 247): "Just as in […] personal selection" (to be intended as natural selection) "variability and inheritance lead, in the struggle for existence, to the survival of the fittest, so in histonal differentiation" (to be intended internal selection) "the same three factors lead to the victory of what is best suited to the parts of the body in question". Further on Weismann points out "variability - in this case that of embryonic cells with different primary constituents - must be assumed; inheritance is implied by the multiplication of the cells by division; and the struggle for existence here assumes its frequent form of a competition for food and space" (ibidem).

When dealing with the law of dimensional hypertrophy of a muscle for example, selection of proliferating and/or growing cells can be accomplished through selection of those cells able to react to the external stimulus through the metabolic capacity of hyper-assimilation. This reactive capacity is itself a random variation affecting only a niche in the cellular population.

By postulating internal selection of responsive cells, Roux's theory explains how development can accommodate functional changes, with no need for inherited correlated variation to occur. In this way, he found a mechanistic (non-finalistic) solution to Lamarck's problem of ontogenetically acquired characteristics.

In order to understand the explanatory role of functional adaptation in the case of vascular structure, we should return to Roux's description of the vascular branching in terms of vessel angles, lumen, directions and wall thickness. As previously noted, in order for hemodynamical principles to play the role of constraints on functionality in Roux's laws, the point of arrival of the vessel (in Figure 4 point P) has to be already established.

Unless we make the hypothesis that the points to be irrigated are predetermined by the system, which means hereditary, we need a specific mechanism to identify areas requiring blood supply and this is precisely the role that Roux attributes to functional adaptation.

The boundary between hereditary and acquired traits, however, is not so easy to detect. Scientists tend, according to Roux, to mistake this difference between hereditary and acquired for the other well-known difference between congenital and post-embryological (after birth or hatching) (Roux 2013, p. 62). This amounts to mistaking a difference concerning the cause of the developmental origin of morphological characteristics for a difference concerning the ontogenetic time of their appearance.

Indeed, acquired traits (through the mechanisms of functional adaptation) cannot be relegated to the post-embryonic period because the interactions of the organism with the external environment start far earlier than its birth.

From this point of view, congenital blood vessel morphology - "la structure de leur paroi et la forme de leur lumière" (Roux 2013, p. 63) - may be the result of functional stimuli and all the more so because they already show metabolic activity at birth (unlike other organs such as those belonging to the respiratory system and the digestive tract).

Even if "we are not able to determine the extent to which traits are inherited or acquired by functional adaptation" ("nous ne sommes pas en mesure de determiner la part de ce qui est héreditaire et de ce qui est acquis par l'adaptation fonctionnelle") (Roux 2013, p. 63), the are some clues which can help us pointing to one or the opposite direction: hereditary traits for an organism, according to Roux, tend to show a fixed and defined development and they cannot be easily diverted from their path.

Roux considers regeneration of an adult snail eye as a perfect example of a hereditary characteristic. Once the experimenter has removed the snail's eye and segregated it in the dark so that no functional stimulus can influence the regeneration event, the reappearance of the eye is considered the result of some "internal properties of the part"[xv] 40 41 .

Differently, the origin of acquired traits is strongly dependent on functional stimuli[xvi] . Those traits can be experimentally recognized because they vary their morphology in agreement with the amount or extent of external stimuli. One of the first examples introduced by Roux deals with the capacity of muscles to increase their size after prolonged use and more importantly with the fact that change is only achieved through a growth in their thickness and not in their length. Indeed thickness is what is required to perform a better function while an increase in length would make them more fragile.

He summaries this evidence through the "morphological law of dimensional hypertrophy" which states that organs "only develop in those dimensions which are required by the application of function" (Roux 2013, p. 41)[xvii] .

At this point of the story, a difference is worth noting. Roux identifies two different kinds of functional adaptation: the former is the property of active organs, which are able to increase -or eventually decrease- their size according to the variation of their activity. This is an active form of functional adaptation, which strictly depends from the existence of specific external stimuli inciting organs to react actively. Another form of functional adaptation is the one performed by the so-called passive organs, such as the vascular system and arguably the peripheral nervous one. According to Roux, "most of the structure and form of the blood vessels arises in direct adaptation to function […] the vessels of adult men and animals are not fixed structures, which once formed, retain their form and structural build unchanged throughout life. On the contrary they require even for their continued existence the stimulus of functional activity" (Oppel;Roux 1910, p.125[42] ).

When speaking of a functional stimulus in the case of blood vessels, Roux speaks of an unspecific internal stimulus coming from an organ, which is itself actively engaged in a process of -active- functional adaptation. Blood vessels irrigate those organs that call for an increase in blood supply because of an increase in their activity. From this point of view, functionality is both externally driven during the development of organs thanks to differentiating environmental stimuli and internally driven during the development of the vascular system thanks to an increase in the activity other organs.

"*La formation des parties ayant un role passif depend du fonctionnement embryonnaire des parties ayant un role actif*" (Roux 2013, p. 66). This also means, according to Roux, that dysfunctioning (hypo-functioning) active organs (e.g. one kidney) will not be vascularized in the same way as normal functioning ones or that hyper-growing tissues, with a strong metabolic activity, will be properly vascularized, thus also supporting tumor proliferation.

A further point about passive organs concerns their possible dysfunction. Here Roux's focus is on vascular dysfunctions also known as angiomes. He speaks about plane and cavernous angiomes which are both attributed to a shift from dependent (functional) development to an independent (dysfunctional) one.

Thus, blood vessel branching is dependent on the functionality of other organs.

However, while there are detailed explanations of the mechanisms responsible for accomplishing the first type of functional adaptation - at the crossroads between organs and external stimuli - the same precision is lacking with respect to mechanisms of the passive type.

Here we will try to build a coherent framework without forcing the fragmented structure of Roux's argumentation. Blood vessel branching is about finding the causes of the vascular branching, which from Roux's point of view, deals with the proximate cause of specific vessel bifurcating angles, lumen, wall thickness and direction.

Similar to bifurcating angles, we could approximately say that lumen, wall thickness and vessel direction also obey to an optimality principle: "la distribution du sang dans l'organisme se produit avec un frottement minimum dans les innombrables embranchements, c'est à dire que la circulation est rendue possible avec un minimum de force vitale et de material parietal". Indeed Roux says that all those morphological traits (lumen, wall etc..) are extremely fine tuned to the metabolic needs of the organism. However, which "optimal" vascular morphologies are due to inherited developmental rules of construction i.e. hydrodynamical forces, and which are due to the developmental interplay between the organism and the environmental stimuli i.e. passive functional adaptation is an open question.

In other words, "optimality" may be the result of natural selection and may also be the result of internal selection.

Arguably, the only trait which seems to be shaped by functional adaptation is the direction of blood vessels: passive functional adaptation, explaining angiogenesis, can only be framed within the selectionist approach by substituting external stimuli with internal ones.

However, angles, diameters and vessel wall, though being optimal traits according to the hemodynamical constraints, are not directly explained by a mechanism of internal selection. It seems that Roux comes back to his 1878 hypothesis of a "direct moulding" of those structure by hemodynamical forces (Kurz et al. 1997).

Let us consider for example the vessel lumen at the bifurcating points: "Au dèbut de chaque branche, la lumière des vaisseaux sanguins ne se presente pas sous une forme cylindrique, comme c'est le cas au milieu des branches, mais sous une forme conique caractéristique. […] la lumière adopte librement […] cette forme, c'est à dire sous l'effect à l'oeuvre à l'interieur d'elle". Here the hemodynamical role is not that of a posteriori functional constraints, which explains why, in terms of evolutionary adaptation, vessel branching has been internally selected to show this particular growth pattern. They are intended as physical forces in the same way as the hydraulic forces of a river shape its riverbed (e.g. "de la meme manière que pour un jet qui s'écoulerait librement" (Roux 2013, p.52).

However, if blood's flow shapes vessel lumen, vessels have to be there already. Their formation is partly subjected to hemodynamical laws, partly to passive functional adaptation. Primary directions are given by the composition of physical forces (flow speed and lateral pressure) while their final direction, towards points of irrigation, is obtained through functional adaptation.

As the reader will probably notice, there is a conundrum in Roux's argument: either he explicitly resorts to the principle of functional adaptation and explains the optimality of its outcome, or he calls for hemodynamical laws to be directly shaping the structure of the system without any need for an external stimulus. The main difficulty is that, even when speaking of hemodynamical laws, Roux maintains that the phenotypes produced are optimal thus confusing optimal developmental adaptations, the ones mechanistically produced by internal selection, with optimal evolutionary adaptation, due to the natural selection of highly efficient and inheritable vascular branching rules.

## A resourceful mechanistic explanation

At this point of the analysis, it will be clear enough that the need for a "mechanistic explanation" is among Roux's major concerns: embryological explanations are said to be mechanistic type-a in op-position to Haeckel's phylogenetic ones; at the same time hemodynamical forces moulding vessel angles are said to be mechanistic type-b with reference to their reducibility to physical-chemical laws. Finally functional adaptation, through its process of internal selection, is a mechanistic type-c explanation of infra-organismic change in opposition to a teleological one.

"Mechanistic" is thus a "Πολυμηχανος" concept[xviii] synonymous with at least three different kinds of causal explanations: analytic (vs phylogenetic), physical-chemical (vs not yet reducible) and historical (vs teleological).

Coming back to Roux's 1878 and 1881 theories of vascular morphogenesis in the light of this epistemological clarification, we realize that both of them, hemodynamical forces and functional adaptation, are "mechanistic" but in two clearly different senses.

As far as hemodynamical forces are concerned, they are mechanistic type-a and type-b because they seek developmental factors producing vascular architecture and recognize those developmental factors to be physical laws of construction.

Roux seems to suggest that certain traits of the vascular architecture are the result of a self-organizing process based on purely physical-chemical forces acting on the embryological matter.

As far as functional adaptation is concerned, it can be said to be mechanistic type-a because it aims at explaining the developmental production of phenotypic traits but at the same time it is mechanistic type-c because it explains their adaptation to the external environment through a selectionist, thus non-finalistic process.

In this second case Roux seems to suggest that environmentally attuned traits are the result of an adaptive mechanism that, in order not to be teleological (cfr. Lamarck), is presumed to be a selective one. In today's developmental biology, we would probably place hemodynamical forces and functional adaptation under different explanatory labels. Roux's explanation, making use of hemodynamical laws, is very close to what we would call today a "structuralist approach". In developmental biology, structuralism has a long tradition from D'Arcy Thompson (1917) to Brian Goodwin (1990[43] ) and more recently Stuart Newman (2003[44] ); it is concerned with the explanation of developmental regularities through the aid of physical-chemical laws[xix] .

Conversely, Roux's concept of functional adaptation points to the existence of adaptive mechanisms, which allow the organism to tune its development with the functional stimuli coming from the external and internal (embryological) environment.

In today's developmental biology, this reactive capacity of the organism would better go under the heading of "developmental plasticity": among the manifold adaptive mechanisms, internal selection has been proved to play an important role in immunological responses and in neural development (Corbellini 2001[45] ) but regulatory, genetically based or epigenetic mechanisms also play a major role[xx] [46] [47] .

Of course, Roux did not make himself explicit this epistemological differentiation between the different senses of "mechanistic" nor he could draw a clear distinction between a "structuralist" approach and one focused on the organism's adaptive capacity. The feeling we have while reading his work is that the notion of causality implied by hemodynamical forces gradually blends into the different notion of causality suggested by the use of the concept of functional adaptation. Moreover, this epistemological confusion is fueled by the fact that Roux sees both "structural" and "adaptive" traits through the lens of optimality[xxi] , which in the former case is the result of developmental rules of construction while in the latter is the result of a process of infra-organism selection.

However, we must remember that his main objective was to show the scientific value of mechanistic explanations with respect to historical (Haeckel's phylogenetic necessity) and vitalistic (based on immaterial final causes) ones. Hemodynamical laws and functional adaptation, though being different kinds of mechanisms, fulfilled this task: the former, with a focus on physical-chemical mechanisms aimed at explaining vascular morphogenesis through material (vs immaterial) proximate (vs phylogenetic) causes. The latter, differently, aimed at unmasking the myth of finality as the result of a goal oriented immaterial force by introducing mechanisms of internal selection able to account for final dispositions as un-oriented adaptations. Thus though the main difficulty that we encounter in trying to encompass Roux's scientific thought about developmental causes is the conceptual mixture expressed by the word "mechanistic", we are bound to recognize that the ambiguity surrounding this word makes it an eminently resourceful concept.

## Conclusions

In this essay, we have explored the work of the XIX century embryologist Wilhelm Roux (1850-1924) with particular focus on the role played by his research on the vascular system in the formation of his embryological theories.

In the "Introduction", we have outlined our epistemological analysis with respect to two of Roux's early works: his doctoral dissertation on blood vessel branching (1878) and his theoretical volume on functional adaptation (1881).

In section I "Wilhelm Roux (1850-1924) and the prelude to *Entwicklungsmechanik*", we have sketched out the epistemological background to Roux's academic formation: Darwinian revolution and biophysical research in physiology respectively shape the debates opposing historical to proximate causality and vitalistic causality to physical-chemical one.

In section II "Order in blood vessel branching: Roux's anatomical observations", we have introduced Roux's vascular observations: the identification of a regularity in vessel bifurcating angles and the verification that the whole vascular structure can be described through an optimality principle of minimal physiological work.

In section III "Functional adaptation and blood vessel branching", we have introduced Roux's embryological concept of functional adaptation, which is meant to be a transposition of the Darwinian logic of variation and selection inside the organism, and we show how Roux attempts to use it to explain the developmental constraints on blood vessel direction.

In section IV "Πολυμηχανος" mechanistic explanation, we have underlined the epistemological ambiguity of the key concept of "mechanistic" causality and notice how this prevents giving a perfectly coherent picture of Roux's thought in the two texts examined.

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## Endnotes

[i] The explanation of blood vessel branching through the concept of functional adaptation is not mentioned in Roux's 1878 doctoral thesis where the focus is on the explanatory role of hemodynamical laws. Indeed the concept of Func-tional adaptation was only introduced in 1880 in *Ueber die Leistungsfaehigkeit der Principien der Descendenzlehre zur Erklaerung der Zweckmaessigkeiten des thierischen Organismus* (Roux, 1895), later examined in *Der Kampf der Theile* and retrospectively applied to some aspects of blood vessel branching (vessel directions). I thank Silvia Caianiello for bringing this point to my attention.

[ii] On the coincidence of mechanistic and mechanical explanation: "the causal doctrine of the movements of part has been extended to coincide with the philosophical concept of mechanism" (Roux, 1895, p. 150).

[iii] In a passage from "Order and Life" (1936) concerning the contribution of Roux's Entwicklungsmechanik to the rise of a "true, non-dogmatic organicism", Joseph Needham clearly catches the difference between these two notions (stricto sensu and lato sensu) of causal explanation in biology. "The ideal axiom at the basis of all causality can only be stated in terms of the mathematical concept of function. Physical equations necessarily involve functions. But an important distinction must be drawn between mathematical and mechanical" (Needham, 1936, p. 25). Causal explanation, according to Needham, is a broad epistemological category in relation to which mechanistic (=mechanical) generalizations are a particular case. Coming back to Roux's developmental mechanics, Needham stresses Roux's distinction between explanations making reference to "complex component" relationships and explanations arising from "simple component'" relationships. The adjectives "simple" and "complex" respectively stand for the possibility or provisional impossibility of a physical-chemical reduction of those regularities. However, even if "the aim of Entwicklungsmechanik is thus the reduction of the phenomena to the smallest number of causal processes" (Needham, 1936, p.21) - that is relationship

between simple components- Roux was totally aware that such a level of fine grained analysis could not yet be accomplished (either technically, or theorically) during the nascent days of Developmental Mechanics and he himself performed many of his experiments at the coarse grained level of embryological "complex components".

[iv] G. A. Schwalbe's publications "Beitraege zur Kenntnis des elastischen Gewebes" (1876) (tr. eng. "Contributions to the knowledge of elastic tissues"), "Ueber das postembryonale Knochenwachstum (1877) (tr. eng. "On post embryonic bone growth") and "Ueber Wachstumsverschiebungen und ihren Einfluss auf die Gestaltung des Arteriensystems (1878) (tr. eng. "On shifts in growth and their influence on the formation of the arterial system") prove his interest for the mechanical relation between form (anatomy and growth) and function (physiology). Schwalbe was Roux's doctoral supervisor in 1878.

[v] The technique of wax injection is thought to have been established in the early XVII century by Jan Swammerdam (1637-1680), Frederik Ruysch (1638-1731) and Regnerus de Graaf (1641-1673) and furtherly refined through the centuries. For details on the history of this technique see Zampieri and Zanatta (2012). Further details on the technique used by Roux are available in section I "Methodik und Fehlerquellen" (tr. eng. Methods and sources of errors) of his dissertation.

[vi] It is worth noting that the diameter exponent parameter has been progressively extended to the analysis of other animals' branched vascular systems (es. mammifers) once more creating an interest - though differently from Haeckel's XIX century "biogenetic law"- for comparative and evolutionary analysis in morphological explanations (LaBarbera 1990).

[vii] A similar case of physical constraint on functionality is the role played by the gravitational field in explaining the "allometric scaling of bones in different sized animals" firstly pointed out by Galileo Galilei (1638 cited in Carter et al. 1991, p. 3). In this case "to have a comparable structural strength for their body mass" -the biomechanical rather than physiological optimal condition- "large animals would need bones which were thicker relative to their length than smaller animals. […] However" this "sheds no light on the means by which such scaling is achieved" (ibidem, p.3).

[viii] On the proximity between Lamarck's and Roux's concepts see Roux (2013, p. 32): "Au sujets des effects de l'usage et du non usage, auxquels nous ferons désormais référence par le concept d'adaptation fonctionnelle […]".

[ix] I thank Silvia Caianiello for highlighting the need to discuss this distinction. Indeed once that distinction is made, the opposition between Roux's and Lamarck's explanations of the organism's reactivity blends considerably and it could be fruitful to enquiry about their similarities (Silvia Caianiello, personal communication).

[x] Though an anachronistic term at the time, it is better to use the term "biological" in the sense of being restricted to living beings.

[xi] In the second half of the XX century many biologists and philosophers of biology started questioning the power of evolutionary theory as originally conceived by Darwin and further strengthened by his supporters from the 1930s to 1960s, to explain both the process of diversification within species and between species. Two different terms have been coined: microevolution to address evolutionary change within population (whose dynamics are formalized in the field of population genetics) and macro-evolution to address change between species and higher taxa. For a complete and highly readable text on the topic, see Gould (2002).

[xii] As previously outlined, Roux's own position concerning the inheritance of traits acquired by functional adaptation was fluctuating. Arguably, just a few years later, after having committed to Weismann's restriction of inheritance to cells making up the germinal line (Weismann, 1892, 1909), he would neglect the possibility of such a functional, inherently somatic inheritance.

[xiii] For an updated study on the fortune of the mechanism of selection in other contexts than population genetics, see (Heams et al. 2013, Caianiello 2013).

[xiv] Roux's transposition of the concept of natural selection at the developmental level is an attempt to rescue Darwinism from the resurrection of finalistic causes. It has to be pointed out, however, that the adoption of selection as a mechanism for complex adaptations during development displays great explanatory power at the levels of molecule and cell proliferation but it is less sharp with respect to tissue development where a mechanism for correlation is preferable with respect to a mechanism for competition.

[xv] Shortly afterwards regeneration would become a leit motif of embryological research at Anton Dohrn Marine Zoo-logical Station, in Naples (Morgan 1901, Sunderland 2010).

[xvi] The fact that the effects of functional adaptation could eventually be inheritable does not imply that we cannot distinguish between inherited traits and their first ontogenetic occurrence through functional adaptation.

[xvii] Together with this law, he introduces also "a physiological law of dimensional hypertrophy" and "a morphological law for dimensional atrophy".

[xviii] Tr. eng. "resourceful". Ancient Greek word quoted in the incipit of Homer's Odyssey to describe Odysseus's strategic nature.

[xix] It is worth noting that the same emphasis on physical-chemical explanation has a different meaning for Roux (against vitalistic causality), for D'Arcy Thompson (against the abstractness of heredity), for Goodwin (against the reduction of all phenotypic characters to evolutionary adaptations) and for Newman (against genetic reductionism). Structuralism is thus a label for a set of homogenous positions -the explanatory power of physical-chemical laws- that, nonetheless, support very different objectives.

[xx] Our post-cybernetic notion of regulatory mechanism (Rosenblueth et al. 1943) based on the concept of feedback was unknown to Roux. For him the concept of "regulation" had no mechanistic basis and has to be rejected as every vitalistic cause (see Oppenheimer 1967 for the later debate with H. Driesch on the concept of independent or "mosaic" and dependent or "regulative" differentiation).

[xxi] "The temptation to reduce the two kinds of optimality - the one based on the reactive plasticity of living entities, the other to strictly physical hemodynamical constraints- could also reflect the very early phase of Roux's research. He will only later admit that total reduction to physical-chemical laws is not yet viable, and biology must resign to work with complex components" (Silvia Caianiello, personal communication).

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