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Donation and Acceptance in Biological Inheritance: The Long Path from Darwin's Gemmules, DNA and Membranes to Uniqueness and Kinship

Günter A. Müller[1,2]

[1]Institute of Diabetes and Obesity, Helmholtz Center Munich, Research Center for Environmental Health, Oberschleissheim, Germany
[2]Media, Culture and Society, Department of Media Studies, Faculty of Arts and Humanities, Paderborn University, Paderborn, Germany
Email: guenter.al.mueller@t-online.de

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Abstract

The inheritance of features within plants, animals and men as species as well as individuals represents one of the oldest concepts of thinking about biological phenomena of mankind. From the beginning, it has been linked to the transfer, i.e. donation + acceptance, of some materials from the mother organism or parents to the daughter organism or children, respectively. Despite some speculations about the mechanistic basis of inheritance, which cumulated in the formulation of the "Pangenesis" theory with "Gemmules" operating as matter of inheritance by Charles Darwin, the nature of the matter of biological inheritance remained obscure until the seminal finding of bacterial transformation by Frederick Griffith in 1928 and the subsequent identification of the transforming principle as DNA by Avery, McCarthy and MacLeod in 1944. This turned out as the starting point for a series of key findings of molecular biology, such as the deciphering of the genetic code, which finally gave rise to its central dogma with fundamental consequences for life science and society, such as the exclusion of the possibility of the inheritance of acquired traits. From then on at the latest, inheritance has been intimately linked to DNA as the mediator or carrier material for genetic processes which is both necessary and sufficient for the synthesis of proteins and as consequence of the DNA-centric view of inheritance for the self-assembly of cellular structures as well as the development of the complete organism. Here, some of the most influential settings and presumptions of this view will be delineated in concert with the resulting exclusion of other biological matter, such as membranes and organelles, and concomitantly of the process of self-organization and autopoiesis from biological inheritance.

Keywords

DNA-Centric View of Inheritance, Darwin's Gemmules, Membrane Landscapes, Non-Genetic Matter, Science and Technology Studies

1. Introduction—The Emergence of the Phenomenon of "Like-from-Like"

This study is aimed at the description of some of the (f)actors which contributed to the neglection of non-genetic matter, in particular biological membranes, in favor of DNA and genes for a sufficient explanation of the phenomenon of biological inheritance. At first, the conception of "Donation + Acceptance" as the foundation of all "like-from-like" phenomena is explained (chapter 1). Then, a brief summary of the long and complex story about the origin of the term biological "inheritance" will be presented (chapter 2), followed by current "state-of-the-art" definitions, which can be found in text and reference books (chapter 3). One of the first suggestions for the type of matter engaged in the transfer process along "Donation + Acceptance" was made by Charles Darwin with his conception of "Gemmules" which is briefly introduced (chapter 4). Then, a long and complex path followed from the postulation of "Gemmules" to the discovery of DNA as the carrier of the information for the synthesis of proteins, encompassing a number of detours and roadblocks, which is covered in short (chapter 5). This path was accompanied by the apparent exclusion of non-genetic matter as the carrier of the information playing a critical role in the self-organization (autopoiesis) of biological membranes (chapter 6). The motivation for attributing explanatory adequacy or sufficiency to DNA *vs.* explanatory background to membranes for a balanced understanding of the phenomenon of biological inheritance is discussed next (chapter 7). In a backward loop to Darwin's "Gemmules" and DNA, it is asked whether blood (containing "Gemmules" according to Darwin) or DNA provides more adequate or sufficient explanations for the uniqueness *vs.* individuality of the body (chapter 8) as well as for kinship *vs.* heredity (chapter 9). Finally, the putative contribution of STS to clarify the relationship between adequate and background explanations for the phenomenon of inheritance and its apparent contingency is acknowledged.

The phenomenon of "like-from-like" has long been well known to people, especially breeders of plants and animals. It simply refers to the fact that biological organisms—through either asexual or sexual reproduction—produce organisms with characteristics that are (almost) identical to or (at least) like their own, such as, organisms with eight legs typically and reliably producing organisms with eight legs again, or short-lived organisms emerging again from short-lived organisms. The phenomenon of "like-from-like" does not apply equally to all traits and all organisms. But it applies to many essential characteristics of all organisms and for this reason must be considered one of the most important pheno-

mena of the living world. Within each biological lineage, there are traits that typically recur with high reliability from generation to generation. Accordingly, there are reliable similarities within each biological lineage. The conception of the inheritance of traits refers to processes that take place between generations along the "like-from-like" phenomenon, i.e. it adequately explains the reliable occurrence of traits within biological lineages. The conceptions of inherited and heritable traits refer to characteristics of organisms to which the phenomenon of "like-from-like" applies, i.e., to those traits that reliably recur within biological lineages.

The "like-from-like" phenomenon, i.e., the conception of the inheritance of traits, ultimately corresponds to ideas of common sense. Humans have known for a long time—probably with the first appearance of *Homo sapiens* on earth, at the latest with the transition of the hunter-gatherer way of life to the sedentary lifestyle of farmers and cattle breeders and the concomitant inventions of private property, patriarchy and maternal monogamy during the Neolithic revolution—the occurrence of many typical similarities or even identities between parents and offspring with a high degree of reliability. It is possible that the Neolithic revolution even provided the social and cultural conditions for the perception of the "like-from-like" phenomenon. Presumably, in the typical life world of hunter-gatherer during the paleolithic and mesolithic eras (Eibl-Eibesfeldt, 1976; Pfeiffer, 1978; Leakey & Lewin, 1979; Reader, 1981), there was neither the need nor the possibility to recognize the inheritance of biological features within plants, animals, and humans.

At this point, it may be relevant to note that it has been hypothesized on the basis of ethnographic, archeologic, ethologic and psychoanalytic findings that for the inheritance of goods and wealth from people to their descendants, a crucial condition must be met: Long before the case of inheritance, already at the time point of conception, some materials, such as blood or sexual factors, must have been transferred from the former to the latter or acquired by the latter through the former. Only in this way can the donors be sure that the heirs are in their biological lineage and this seems to represent the most widely accepted prerequisite or justification for the inheritance of private goods and wealth, from their initial introduction into the market up to the corresponding laws for their inheritance as realized in most countries at present. Thus, the process of societal inheritance seems to presuppose the conception of biological "Donation + Acceptance". Marxism-oriented, materialistic or realistic historians, anthropologists and ethnologists, such as Ernest Bornemann (1973 & 1976), Wilhelm Reich (1936), Geza Roheim (1950), V. Gordon Childe (1951), Bronislaw Malinowski (1975), and Johann Jakob Bachofen (1975), have repeatedly emphasized that the invention of (private) property and personal goods along the transition from hunter-gatherers to farmers and cattle breeders during the Neolithic revolution inevitably brought about the introduction of patriarchy and monogamy, in order to ensure security in the transfer of any kind of materials, i.e. individual biological factors in concert with private property, from the parents, but above all from

the father/husband, to the offspring (Reich, 1936; Childe, 1951; Bornemann, 1976). Due to the establishment of the process of societal inheritance at a very early stage in human history, it can be speculated whether this causally induced the conception of "Donation + Acceptance" as an explanation of the process of the inheritance of traits.

Nowadays, the existence of the phenomenon of heredity seems to be self-evident to us, but apparently both the social and the biological one is based on presuppositions, namely on the existence of private property. Since private property has most likely been introduced with the Neolithic revolution, i.e., the transition from hunter/gatherer to agriculture/cattle breeding, which at the same time led to the co-development of patriarchy and monogamy (obligatory for women, at least) by men (because those would like to know for sure that they are bequeathing their property to the "right" children with absolute security).

Analogously, one may ask the question of the basic assumption(s) for biological inheritance. What is the critical requirement for the recognition of the "like-from-like" phenomenon? This is the precise knowledge who mated with whom and what offspring came out of it. In the case of plants and animals, it must have been (sedentary) plant and animal breeders who first became aware of the phenomenon of heredity, i.e., after the invention of agriculture and animal husbandry during the neolithic revolution. And as far as humans are concerned, recognizing the phenomenon of similarity or even identity between parents and offspring presupposes monogamy (at least of the mother). Because if "every man with every female" and *vice versa*, similar characteristics of the offspring can hardly be traced back to certain parent pairings. One could therefore speculate that without the invention of private property and the legislation of patriarchy/monogamy, neither the need for societal inheritance would have arisen nor the recognition of biological inheritance might become feasible, respectively! The knowledge of biological heredity thus presupposes a social and discursive construct, the neolithic revolution, but for this very reason it is not a mere social construct or even arbitrary. Of course, there is a material basis for biological inheritance. But only the interaction between this materiality and societal-discursive practices, in particular patriarchy and private property, as well as the discourse about that constitutes the phenomenon of biological inheritance in mankind.

Regardless of the historical accuracy of this admittedly not undisputed connection, people of the period of the neolithic revolution at the latest must have had conceptions at their disposal that refer—either in a forward or backward way (see below for definitions)—to the repeatedly reliable recurrence of features within biological lineages and the underlying mechanisms. In contrast, the conceptions of the inheritance of differences or variabilities have developed only recently. Charles Darwin was probably among the first to introduce it, based on his thinking in terms of evolutionary changes in populations rather than in the development of individual organisms (Darwin, 1868).

The phenomenon of the "like-from-like" phenomenon is already dealt with in

some of the oldest scientific treatises on biological phenomena, such as those of Hippocrates (460-370BC) (Hippocrates, 2012, 2023) and Aristotle (388-322BC) (Aristotle, 1963, 1991). Hippocrates and Aristotle not only acknowledged the existence of the phenomenon of the "like-from-like", but they also tried to explain it. Their explanations, however, differed significantly from each other in essential aspects. Hippocrates believed in contributions from both parents, while Aristotle attributed the formative power on the offspring exclusively to the male seed. Hippocrates developed a conception about the underlying mechanism that was not shared by Aristotle but was taken up much later by Charles Darwin (1868, 1869, 1871a, 1871b) in his "Pangenesis" theory. But there are also some similarities between the two concepts. For example, according to both theories, the phenomenon of the "like-from-like" can only be explained by the process of "donation" and "acceptance". During "acceptance", the sexual substances of woman and man (today usually called gametes) come together and merge, resulting in a new organism (today usually called zygote). The gametes (at least those of one of the two parents) contain a certain material (factor) that becomes part of the zygote and is responsible for the fact that it has some of the characteristics that are specific to the parents—already during or after conception—in addition to those that the parents share with other individuals of their species. Thus, during conception, the parents "donate" to the offspring by means of their gametes through the newly created zygote any material that is important for their development. This material is "accepted" by the zygote and causes its development in a manner similar to the parents. Most theories on the phenomenon of "like-from-like" have the structure of "Donation + Acceptance".

Despite the fact that from today's point of view the concept of "Donation + Acceptance" as a mechanistic basis for the phenomenon of "like-from-like" is self-evident or even trivial, it should be stated that "Donation + Acceptance"—realized by cell division, cell fusion or intercellular material transfer (see below)—does not have to causally lead to similar daughter cells or offspring in both unicellular and multicellular organisms. It would be conceivable that the donated and accepted materials do not induce any specific phenotype at all in the daughter and offspring organisms, except that life as the "overall-feature" is realized in them, or that a phenotype corresponding to their species (e.g. human and not turtle) is triggered in them, which, however, does not vary between individuals and thus is not responsible for the establishment of any similarity to the mother or parent organisms. In the first case, the classification to the corresponding species, in the second case, the similarity to the mother or parent organisms has then to be produced after "Donation + Acceptance". Identical or similar environmental conditions, such as incubation conditions in cultured cells, blood circulation in body cells, water in marine animals, brood care in mammals, education in humans, would be conceivable as factors outside "Donation + Acceptance", leading to individuation. In this case, the conception of "Donation + Acceptance" would not explain the inheritance of biological traits, nor the inherit-

ance of differences, variances, or variabilities between biological traits. However, the intuitive persuasiveness and immediate plausibility of the conception of "Donation + Acceptance" seems to have been so overpowering from the outset that it has hardly been seriously and sustainably questioned subsequently. Furthermore, it cannot be ruled out that the introduction of private property and the consequent need to pass it on to the descendants was the driving force behind this desire of the parents, i.e. above all of the patriarch, that the materials donated and accepted do guarantee specificity and individuality. The individual descendants have already received materials at the beginning of their lives which is unique and characteristic for their parents or patriarchs and have also accepted those. And this biological phenomenon should be recapitulated with the societal inheritance at the end of the lives of their parents or patriarchs.

2. Historical Understanding of the Term "Biological Inheritance"

In fact, the term "heredity" was first used for the socio-cultural process. For example, Hippocrates and Aristotle never used the metaphor of "heredity" and terms such as "inherited", "hereditary", "hereditable", or their ancient Greek counterparts, to explain the biological phenomenon of "like-from-like", but they did use it to describe the socio-cultural transfer of property, goods, and wealth. This raises the question of when these terms have first been used in a biological context and when the metaphor of biological inheritance has first been formulated. Surprisingly, these interesting historical questions have hardly been adequately addressed by historians interested in the history of biology. Among the few exceptions is Sapp (2003a), who believed that he had identified Charles Darwin as the originator of the metaphor of biological heredity, i.e. as a noun, for the first time in 1859, that is, in the heyday of the industrial and Manchester capitalism in the United Kingdom, in his "*The Origin of Species*" (Darwin, 1859). As a result, this apparent coincidence gives further support for the speculation about the capitalistic driving force for the emergence of the scientific fact of the transfer of biological traits between individuals, starting from the phenomenon of "like-from-like" and ultimately leading to its metaphorization with the term "heredity".

However, the *Oxford English Dictionary* (OED, online version) locates the first occurrence of the verb "to inherit" to describe the phenomenon of "like-from-like" as early as in 1597, namely in Shakespeare's drama *Henry IV*. (Part II, Act 4, Scene 3), and four years later in 1601 in the comedy *All Well That Ends Well* (Act 1, Scene 2). Shakespeare also used the metaphor of heredity in the context of the phenomenon of "like-from-like" as an adjective. In the tragedy *Antony and Cleopatra*, he used "hereditary" (Act 1, Scene 4). A little earlier, in 1597, the composer Thomas Morley used "hereditary" in a biological context, namely in his treatise *A Pleine and Easie Introduction to Practicall Musicke*. And even earlier, in 1570 and 1571, according to the OED, the metaphorical use

of the adjective "hereditary" to describe traits that are apparently naturally transmitted from parents to offspring can be traced in the works of the Scottish humanist George Buchanan (1570) and the French theologian, pastor and church reformer John Calvin (2022).

Notwithstanding the apparently first documented written use of "to inherit" and "hereditary" with reference to the phenomenon of "like-from-like" by Shakespeare and Morley in 1597, the noun "inheritance" appeared in the same context according to the OED and J. Sapp's note (Sapp, 2003b) for the first time in Darwin's *Origin* (1st edition) (Darwin, 1859). Many more examples can be found in this book. In earlier writings, including the first written record of his theory of natural selection (Darwin & Wallace, 1858), Darwin does not seem to have used the term "heredity" in a biological context. However, the adjectives "inherited" and the verb "to inherit" appear in this work co-authored by Darwin and Wallace (1858: p. 49), but interestingly only in the passages written by Darwin. Even earlier, Darwin (1845) used the adjectives "inherited" and "hereditary" to characterize biological traits, such as instinct, habits, and structures.

And by analogy with the fact that the adjective "hereditary" had been used in connection with the phenomenon of "like-from-like" by Morley as early as in 1597, the OED locates the earliest occurrence of the noun "heritability" in a biological context in printed form in the textbook *Principles of Biology* by Herbert Spencer (1910), and a little later in the treatise *Hereditary Genius* by Francis Galton (1869).

Even more important than the question of the historical development of the metaphor of biological inheritance is the question of why this metaphor has developed in our thinking about the biological phenomenon of "like-from-like". It is probably not by chance that the linkage of the adjectives "inherited", "hereditary", etc. or of the nouns "heredity", "inheritance", etc. with the conception of "Donation + Acceptance" had emerged only in modern times, in the heyday of the Renaissance of the late 16th century and industrial capitalism in the second half of the 19th century. At those times, the feudal or entrepreneurial parts of the population managed to accumulate huge amounts of private property, individual wealth and personal goods. This necessitated the invention of a—(preferably) rationally justifiable—mode of transfer after (or shortly before) the death of the owners and proprietors. Those declared the process of transfer to the respective biological offspring as intuitively correct, intellectually plausible and as a reflection of "common sense" (i.e., apparently of the will of the majority of the population) and, in addition, as fulfillment of either natural law (analogy to brood care) or positive law (rich *vs.* dispossessed people). Consequently, transfer of property, goods and wealth to biological offspring has been regarded as the only possible way of practical realization of the conception of "Donation + Acceptance". The prevalent socioeconomical structures and political power relations fostered the implementation of the sociocultural process of inheritance as being without alternative and inviolable in virtually all countries of the Western and

industrialized world to this day.

And from this conclusion with all its manifold economic, cultural and political effects, it is only a small step to the assumption that the transfer of some biological materials must have taken place between the donor and the acceptor as an indelible inseparable "bond" of togetherness, and thus represents the crucial prerequisite for societal inheritance—"what else?". Thus, both the societal and the biological conception of "Donation + Acceptance" is based on the transfer of materials from parents to their offspring. Considering the time span between the invention of private property (see above) and the use of the terms "heredity" or "inheritance" for biological transfer, it can be speculated whether their use in biological thinking and research since modern times has been driven forward or even causally triggered by the practice of societal inheritance. In any case, the term "heredity" in a biological context must be considered as a metaphor derived from societal heredity.

Finally, regarding these reflections on the historical development of the term "heredity", it is worth pointing out an important commonality between its societal and biological use. Both uses have no implications regarding the type or nature of the materials to be transferred in future or already transferred in past. On the one hand, private material goods, such as houses, or their derivatives or substitutes, such as money, or intellectual property, such as licenses and patents, on the other hand, individual biological characteristics, such as eye color, or the underlying molecular structures and mechanisms, such as DNA or cell membranes, including the copying process of DNA or biogenesis of membranes, or the "agency" for the synthesis of cellular proteins, such as genes, can be inherited. But that's not all. Both societal and biological inheritance requires the continued and reliable existence of specific and sophisticated external worlds, i.e., the maintenance of certain environmental conditions. For the former, the functioning of state systems and the obeying of rules for enforcing inheritance claims after the death of the parents, such as probate courts and written last wills, for the latter the existence of factors and the operation of conditions in the immediate vicinity of the developing offspring during and after conception, such as nutrition and gravity (e.g., for appropriate development of the legs of mammals) are of uttermost importance. None of these transferable materials and factors, whether being matter or information, should be prioritized, since all of them will contribute in a cooperative process to successful inheritance.

Nevertheless, along the historical practice of societal inheritance, as well as along the history of research on biological inheritance, the importance of certain matter and certain factors has been emphasized, and other entities have been downranked or even excluded. The incomplete description of the—human and non-human—actors which form a complex network rather than a linear causal chain of biological inheritance is manifested best in the (degree of the) impossibility to deduce the inherited trait, i.e., the phenotype, from the nature of the transferred materials, in general, and the DNA sequence of the transferred genes,

i.e., the genotype, in particular. The elucidation of the potential reasons for these incomplete as well as difference-generating molecular analyses with regard to the complete cycle of study of biological inheritance, which includes but is not limited to the design, interpretation and publication of the corresponding experiments, as well as the unraveling of the putative consequences for future biomedical research should be the subject of future Science and Technology Studies (STS) of life sciences, in general, and genetics and molecular biology, in particular.

3. Current Understanding of the Term "Biological Inheritance"

According to Martin Battran (2023: p. 1197), "biological inheritance" is generally understood to mean mechanisms that ensure that individual organisms that communicate with each other—in the broadest sense through an unidirectional or bidirectional flow of (natural) materials—and thereby become phenotypically more similar to each other. Although related and unrelated individuals of a local population become more similar to each other—even over generations—if, for example, they practice jointly learned behavioral traditions, biological inheritance is nowadays equated with genetic inheritance, i.e., the transmission of genes or genetic processes, according to both scientific and popular views. For example, Toepfer (2011: p. 620) defines: *Heredity is the transmission of characteristics of an organism to its offspring, especially insofar as these result from the specific structure of their hereditary units* (*genes*). Similarly, a modern encyclopedia of biology *LexBiol* (1999-2004) states: *In the biological field, the term* [*heredity*] *is generally limited to the transmission of genes from one generation to the next*. Accordingly, the modern synthetic theory of evolution also attributes similarities between parents and offspring, i.e., the phenomenon of "like-from-like" (see above), exclusively to the possession of the same genes (Fisher, 1918, 1930; Haldane, 1937; Dobzhansky, 1937; Huxley, 1942; Mayr, 1942; Rensch, 1947; Kutschera, 2015). Thus, as Martin Battran (2023: p. 1198) has pointed out, current textbook genetics and evolutionary biology are essentially based on transmission genetics (Morgan, 1923; Brookes, 2002; Rheinberger & Müller-Wille, 2009), relying on the assumption that everything species- and population-specific that parents transfer to their offspring is at least indirectly completely encoded in the genome.

The problematic aspect of this view, which has been repeatedly recognized during the past decades (Jablonka & Szathmary, 1995; Sarkar, 1996; Sterelny, 2000; Griffiths, 2001; Dall, 2005; Stegman, 2005), becomes clear when one realizes the many ways in which organisms 1) acquire "agency" that is important for their development, survival and chances of reproduction—i.e. their "fitness"—2) exchange "agency" with conspecifics of the same generation and 3) send "agency" directly to their own, directly or indirectly to other descendants of the population or even to individuals of other species (horizontal inheritance),

for whom this "agency" is also useful. The question to be addressed in this study is therefore whether it is justified to understand heredity as an expression of donation and acceptance, transmission and acquisition of genes alone as the only carriers of developmental "agency", or whether—possibly necessarily—other levels of biological organization, i.e., material pathways of transfer, beyond the genetic level must be taken into account.

The directed transfer of material with causal significance for the development of the organism from donor to acceptor organisms (e.g. from mother to daughter cells during cell division in asexual reproduction, from parents to offspring during conception in sexual reproduction) is defined as inheritance of biological features or traits. This classical theory of inheritance can therefore be described as the conception of the "donation + acceptance" of traits. At variance, the inheritance of biological differences refers to the inheritance of traits specifying a biological feature or characteristics that can be marked with a well-defined value (e.g., the one and only one specific height, e.g. of 175 cm or the property of having exactly six legs). In this sense, it is possible to speak in a synonymous way of the inherited or heritable trait or the inheritance of the trait. A distinction must be made between this and the inheritance of variance or differences at the level of similarity or non-similarity, which refers to a whole set of possible values, such as height (e.g., from 120 to 210 cm). In this sense, the inheritance of a difference or the inherited or heritable difference means the inheritance of the variation or the inherited or heritable variation of a certain trait in a given population at a given time. These definitions lead to the two different conceptions of heredity, on the one hand the conception of the inheritance of traits or features, or of the inherited or heritable traits, and on the other hand the conception of the inheritance of differences, variances, or variabilities, or of inherited or heritable differences, variances, or variabilities. In this study, various conceptions of the inheritance of biological traits are discussed, including specific reference to the inheritance of differences and variability. At this point, it is only important to emphasize that the relationship between the inheritance of traits and the inheritance of differences is complex, but of great importance. A misunderstanding of this relationship has led to many deep-seated and long-lasting misconceptions throughout the history of heredity.

The conceptions of inherited and heritable traits refer to characteristics of organisms to which the phenomenon of "like-from-like" applies, i.e. to those features that reliably recur within biological lineages. The difference between both conceptions is that the conception of the inherited trait is backward-looking, while the conception of the hereditable or hereditary trait takes into account the future development. A trait of an organism is inherited if its occurrence in that organism can be explained by the course of an inheritance process that links that organism to its predecessor, such as the mother cell with its daughter cells or the parents with their offspring. In contrast, a trait of an organism is considered heritable or hereditary if it is probable that the offspring organisms of that organ-

ism will be endowed with that trait as a result of an inheritance process linking the former to the latter, such as daughter cells to their mother cell or offspring to their parents. A trait of an organism is therefore heritable or hereditary if it can be transferred to offspring organisms.

The multitude of hereditary processes may be subdivided and further characterized by the following differentiations and discriminations: Vertical inheritance as transfer between organisms belonging to the same biological lineage, such as from mother to daughter cells or from parents to offspring; horizontal inheritance as transfer between organisms belonging to different biological lineages, such as between cells or cell lines derived from different tissues or organisms of different species, e.g., adipocytes and erytholeukemia cells, or between different animal species, e.g. mice and men); downward inheritance as transfer from older donor to younger acceptor organisms, such as from mother to daughter cells or from parents to offspring; upward inheritance as transfer from younger donor to older acceptor organisms, such as from cultured cells obtained after a high number of passages to those of a low number; heredity at the individual level as transfer between multicellular organisms, such as between plants or animals; heredity at the sub-individual level as transfer between cells, such as between bacteria, unicellular fungi, cultured cells or somatic and germline cells of multicellular organisms; inheritance at the super-individual level as transfer between biological communities that happens beyond the level of the individual (uni- or multicellular) organism, such as between populations of organisms of the same or different species or between ecosystems.

Inheritance at "each of these levels" is basically conceivable as "vertical" or "horizontal", "downward" or "upward" as well as (sub-/super-)individual. Based on these distinctions, $2 \times 2 \times 3 = 12$ different modes of inheritance are conceivable, among them for instance between cultured cells "horizontal", "upward", "sub-individual" or between patient collectives "vertical", "downward", "super-individual". Typically, classical, or canonical inheritance, as typically dealt with in "school biology", is understood as a "vertical", "downward" and "individual" phenomenon. And even if scientists concede in principle the possibility of the operation of the other non-canonical modes of inheritance (at least under special circumstances), they do not attribute any significant biological relevance to them. However, the considerations in this article clearly demonstrate that the non-canonical "horizontal" transfer of non-genetic matter, i.e. biological membranes, in general, and of subcellular organelles and plasma membrane landscapes, in particular, at the "sub-individual level" is of particular importance for the inheritance of traits.

As outlined above, the concept of "Donation + Acceptance" represents the only explanation for the phenomenon of "like-from-like" and is thus considered as theory of the inheritance of biological traits par excellence. Ultimately, this also makes comprehensible the link of the term "heredity" with this conception and the phenomenon that can obviously be explained by it. Terms such as "he-

redity", "inheritance", "hereditary", "inherited" or "hereditable" come from a socio-cultural environment and refer primarily to the transfer of property, goods, wealth from parents to their offspring. The use of these terms in the field of biology and life sciences has therefore to be evaluated at a first glance as the introduction of a new metaphor for describing a biological phenomenon. Human descendants inherit goods and wealth from their human parents, just as offspring organisms and daughter cells inherit certain traits and features from their parent organisms or mother cells. In the socio-cultural environment, "heredity" means the process of transferring or acquiring property from people to or by people who have a close biological relationship, i.e., are related at the individual level. In the biological context, "heredity" is the process of transferring or acquiring traits from organisms to or by organisms that are in a biological lineage. Thus, the concept of biological inheritance is a typical example for a metaphor. But the use of this metaphor is now, i.e. for at least the past 150 years, so self-evident and "automated", i.e. without any reflection, that hardly any notice is taken of its origin. But it is of significance that "inheritance" and related terms have not always been used to explain the biological phenomenon of "like-from-like".

4. Darwin's "Gemmules"

The apparent universality of the conception of "Donation + Acceptance" is also manifested in its compatibility with the theories of preformation and epigenesis of the 17th century. These differ only in the nature of the material that is passed on from the parents via their gametes to the zygote as the starting point of the offspring, but not with regard to the fact that in order to explain the phenomenon of "like-from-like", materials must be transferred from the parents to the offspring (Farley, 1982). According to the preformation theory, the materials transferred via the gametes is a miniature version of the mature organism with all the corresponding characteristics, while the theory of epigenesis rejects this possibility and assumes the de novo formation of the offspring with their characteristic configuration from uniform matter and substance (building blocks), that do not resemble the adult organism and constitute its shape (structure). Both theories agree that the explanation for the phenomenon of the "like-from-like" must rely on the "Donation + Acceptance" of materials between parents and offspring, between gametes and zygotes (Haller, 1788; Pinto Correia, 1997; Benson, 2002). Operation of "Donation + Acceptance" also applies to the theories of Jean Baptiste de Lamarck, Charles Darwin and August Weismann. However, those theories differ in the acceptance (Lamarck [Lamarck, 1809; Battran, 2023] and Darwin [1869, 1871a and 1871b]) or rejection (Weismann, 1889 and 1892) of the possibility of acquiring new characteristics by the organism during its lifetime and their incorporation into the phenomenon of "like-from-like". Darwin even attempted a mechanistic explanation for linking this phenomenon to the acquisition of traits, i.e., to Lamarck's thesis of the inheritance of acquired traits (Darwin, 1871b). In his famous theory of "Pangenesis", he argued that the

traits acquired by the parents produce so-called "gemmules", which are then transferred to the offspring during conception and subsequently induce in them the development of traits similar to those that triggered the production of the "gemmules" in the parents (Figure 1 and Figure 2).

Importantly, "gemmules" and the Pangenesis theory are compatible with both the "unfolding" or preformation (Figure 1) and the "*de novo*" or epigenetic theory (Figure 2) of development of organisms. After the emergence of the modern embryology in the 17th and 18th centuries, the theory of preformation initially dominated scientific discussions. It was propagated by the most well-known naturalists and philosophers, among them Gottfried Wilhelm Leibnitz as its most famous supporter. Based on careful observations, they were led

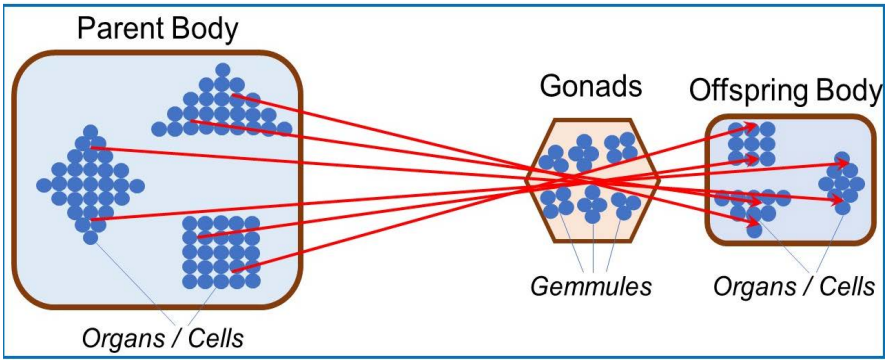

Figure 1. Hypothetical model for the role of "gemmules" in the inheritance of biological features according to Darwin's Pangenesis theory. The various organs and cells of the parent body release "gemmules" (blue circles) which correspond in shape to the (sub)structures (triangle, quadrate, rhombus) of the releasing organs and cells and then accumulate as miniature version in the gonads. After conception, the "gemmules" as "shaping matter" associate in the offspring body, thereby giving raise to the (re)configuration of larger shapes of those organs and cells, from which they had been initially derived from ("unfolding" or preformation version of Pangenesis).

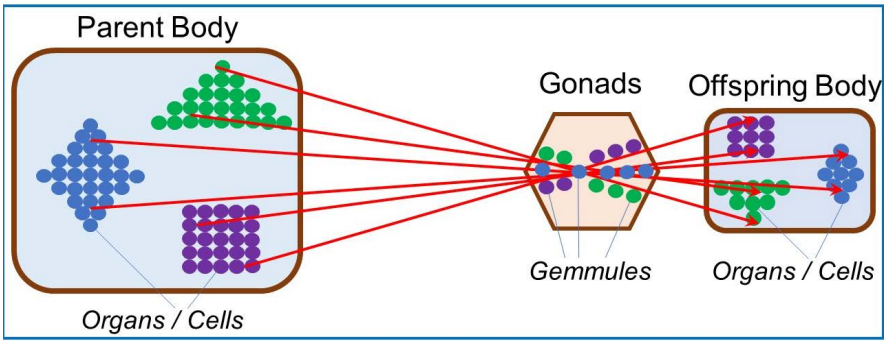

Figure 2. The various organs and cells of the parental body release "gemmules" (colored circles) which are characteristic for their substances rather than their shapes and consequently do not represent simple representations of their (sub)structures accumulate in the gonads. After conception, the "gemmules" as a matter of substance or material associate in the offspring body, thereby giving raise to the initial formation of the shapes of those organs and cells, from which they had been initially derived from ("de novo" or epigenetic version of Pangenesis).

by logical conclusions to assume that the future organism is already contained in the egg or sperm thread as an already completed and viable miniature version equipped with all specific features, which has only to grow to adult size after birth. A breakthrough in the supposed confirmation of this theory came when the Dutch naturalist Antoni van Leeuwenhoek (1677) produced magnifiers with up to 270-fold magnification and used them to examine the sperm of humans and animals. He believed that he could recognize internal structures in the sperm, i.e., the miniature versions of the organs of the future organisms. As with the unfolding of a flower from the bud or the development of an insect from its pupa, the development would encompass only the processes of growth and expansion. In this context, one also spoke of "evolutio" (Latin) in the meaning of "unfolding". The preformationist Albrecht von Haller (1788) wrote in his "Grundriß der Physiologie für Vorlesungen": "*dasjenige*, *was sich im vollkommnern Kinde zeigt*, *schon im zärtern Embryo vorhanden*…, *obgleich die Lage*, *Gestalt und Zusammensetzung in den ersten Zeiten sehr von derjenigen entfernt schien*, *die sich nachher zeigt*".

Although all parts of the later organism are said to be already present in the embryo, they are often difficult to observe, as they typically differ from the adult organism in size, consistency and color, a dilemma that was to be solved a few years later again by Antoni van Leeuwenhoek. Charles Darwin was thereafter convinced that only a mechanism of transfer of specific substances and materials, which do represent miniature versions of substructures, e.g., parts of organs or vessels, of the future organism (rather than of the total structure or organ) during conception could explain the transfer of acquired traits from parents to offspring in a scientifically plausible way. August Weismann, on the other hand, believed neither in "Pangenesis" nor in the existence of materials such as Darwin's "gemmules". He concluded that traits acquired by the parents cannot be passed on to the offspring via the transfer of any materials and substances during conception. And from this, in turn, it followed for him that there could be no inheritance of acquired traits at all. Nevertheless, Lamarck, Darwin, and Weismann, in their respective theories of heredity, took the conception of "Donation + Acceptance" for granted, and without this their lines of argumentation would have remained meaningless.

Those conceptions of the inheritance of traits, which have just been presented, have recently proven their fruitfulness: 1) The conception of "Donation + Acceptance" in the—vertical and horizontal—inheritance of traits at the sub-individual level, namely between cells *in vivo* as well as *in vitro* (for definitions, see above). Incubation in cell culture of donor cells, that have a certain trait, in the vicinity of acceptor cells, that do not express this trait, reflects typical "Donation + Acceptance". During this process, the donor cells release certain biological materials—small membrane vesicles or micelle-like structures loaded with proteins, phospholipids and/or nucleic acids (see below)—which after transfer to the acceptor cells are then taken up by them and finally induce in them the corresponding features that are similar to those of the donor cells. These materials

can be understood as "gemmules" and the associated mechanism of inheritance of traits at the sub-individual level as "Pangenesis" in the Darwinian sense. 2) The conception of preformation in the vertical inheritance of traits at the sub-individual and sub-cellular level, namely between cells and between membrane systems, respectively. Biological membranes, such as the plasma membranes, the membranes of the endoplasmic reticulum (ER) and the Golgi apparatus, as well as mitochondria, chloroplasts and peroxisomes, are inherited from the mother cell to the daughter cells by growth/replication in the mother cell, division of the mother cell, distribution/transfer to the daughter cells and subsequent growth/replication in those. During growth/replication, prefabricated components, such as proteins and phospholipids, are incorporated into the "precursor versions" of the "daughter" membranes provided by the mother cell, whereby the growing/replicating "daughter" membranes or cells acquire characteristics that are like those of the "mother" membranes or cells. Thus, the inheritance of cells, i.e. at the subindividual level, or between their membrane systems, i.e. at the sub-cellular level, seems to be compatible with the preformation theory, in that their biogenesis does not take place *de novo*, but through the growth/replication of already preformed structures. Thereby the existence of lineages of membranes between cells and organisms becomes manifested, which operate parallel to the lineages of soma and germ cells. 3) The theories of "Pangenesis" and "preformation" are compatible with the inheritance of acquired traits at the sub-individual or sub-cellular level, i.e., between cells or their membrane systems. Characteristics and structures of the membrane systems of donor or mother cells can be specifically altered during their lifetime by environmental factors (in *vivo*) or by incubation conditions (*in vitro*). The newly acquired features and structures of the membrane systems are then transferred to the acceptor or mother cells, where they can expose their altered characteristics immediately (epigenetic version of "Pangenesis") or after growth (preformation version of "Pangenesis").

5. The Path to the "DNA-Centric" View of Inheritance

Scientific progress is often the result of an effort to combine and reconcile old theories or old assumptions with new scientific data produced by newly developed methods or technologies. Thus, the gain of scientific knowledge can by no means be traced back to the mere (experimental) testing and verification or falsification of hypotheses, as envisaged by certain theories of the philosophy of science, such as the logical positivism according to Rudolf Carnap (1961) or critical rationalism according to Karl Popper (1972). This certainly holds also true for the concepts of "Donation + Acceptance" with regard to the explanation of the phenomenon of "like-from-like" in the 17th to 20th centuries.

In the second half of the 17th century, gametes or germ(line) cells were described for the first time, i.e., cells that do not contribute to the function and physiology of an organism, but rather to its replication and reproduction, and discriminated from soma or somatic cells. This justified the separation of the so-called germ from the somatic cell lineages. Reegnier de Graaf (1672) discov-

ered follicular cells of the ovary and believed that he had identified a mammalian egg for the first time. Around the same time, Antonie van Leeuwenhoek (1673) invented the light microscope and by using it observed cuboid entities for the first time, which he from then on referred to as "cells". Among the first cells van Leeuwenhoek (1677) described were spermatozoa during the microscopy of male seminal fluid. At about the same time, Marcello Malpighi (1686/1975) thought that they have biological rudiments or precursor features of structures of the adult organism from very early embryonic developmental stages in front of the microscope. From this, the classical theory of preformation developed very quickly (see also above). According to it, the emergence of an organism from the corresponding predecessor organisms proceeds "only" through growth, enlargement and unfolding of all those structures already existing in them. This "cell-centric" view of inheritance became the preferred mindset of many materialistic thinkers in the 18th century (Haller, 1788; Pinto Correia, 1997; Benson, 2002).

In the context of "heredity" it may be important that with the discovery of gametes or germ cells, the thesis was immediately formulated according to which those cells operate as "vehicles" with the help of which organisms manage to "donate" some of their characteristics to their offspring. Here, of course, the conception of "Donation + Acceptance" was "operating" in the background as a presupposition or fixed setting. And, of course, this background had critical impact on the design and execution of experiments with the new light microscopic method, as well as on the interpretation of the data produced with it. Those experiments were therefore less performed to test a previously formulated hypothesis in order to subsequently confirm or reject it—just as the canonical philosophies of science of logical empiricism or critical rationalism interpret the development of scientific progress (Hempel, 1966; Stegmüller, 1969). Rather, the experimental settings were planned in such a way and the data were interpreted in such a way that the newly acquired knowledge at the microscopic level could be incorporated as new details into the conception of "Donation + Acceptance", and that hopefully "precisely" and without any problems. In this way, no scientific revolution or paradigm shift was triggered according to the thinking of the philosopher and historian of science Thomas S. Kuhn (1962), but rather merely a new version of the conception of "Donation + Acception" has been created, which could be called a "gametocentric" view of the inheritance of biological traits.

About a century passed until Ernst Haeckel (1866) formulated the hypothesis that the materials "donated" by organisms to their offspring during conception, which is so important for their development and ultimately responsible for the phenomenon of "like-from-like", have to be located in the nucleus of the germ(line) cells. Shortly thereafter, Oscar Hertwig (1878) concluded from a study of the reproduction of the sea urchin that during its fertilization the fusion of the two cell nuclei takes place, which came from both the male and the female parents

(Hertwig, 1884). A few years later, Herman Fol (1877) reported the observation of the penetration of spermatozoa of the starfish into the egg and the subsequent transfer of the complete intact nucleus into the egg. Thus, in the 1880s, many scientists found a sound explanation for the phenomenon of "like-from-like", namely the transfer of nuclei from the parental organisms to their offspring organisms. And this explanation was vehemently defended against any criticism by the leading embryologists and developmental biologists at those times, among them Eduard Strasburger (1978), August Weismann (1889 & 1892) and Wilhelm Johannsen (1911) and remained the canonical view and textbook knowledge for more than a century.

For Weismann, the findings, and interpretations about the role of the cell nucleus in fertilization were decisive arguments against the theory of "Pangenesis", with which Darwin had mechanistically explained the Lamarckian inheritance of acquired traits. Although some biologists did not agree with Weismann's argumentation and continued to adhere to the thesis of cytoplasmic inheritance, many of them were convinced of the crucial function of the nucleus during the phenomenon of "like-from-like" (Sapp, 1987, 1994 & 2003a). And it is again important to point out that the new data and interpretations obtained at the light microscopic level served to (merely) incorporate details into the conception of "Donation + Acceptance" and never to seriously question this conception. Through this apparent trajectory of theoretical and practical thought and action in biology, a new version of the conception of "Donation + Acceptance" has been created once again, namely the "nucleocentric" view of the inheritance of biological traits.

Something similar happened during the next phase of the "path to DNA" (Olby, 1994). When Mendel's laws of heredity (Mendel, 1865) were rediscovered in 1900, biologists began to think about how these rules would "translate" or "manifest" themselves at the molecular level. In the first decades of the 20th century, Thomas Hunt Morgan and his collaborators developed the so-called "chromosome-centric" view of inheritance of biological traits and thus another new version of the concept of "Donation + Acception" (Morgan, 1909, 1910, & 1919; Morgan et al., 1915). According to this, not the entire cell nucleus is involved in the phenomenon of "like-from-like" or is essential for its explanation. Rather, certain specific substances and characteristic structures of the nucleus are responsible, or more precisely, necessary, and sufficient for the reliable recurrence of similarities between organisms and their offspring, namely the chromosomes. Decades earlier, Friedrich Miescher (1871) had already made this substance visible by light microscopy by specifically staining the nucleus, but without being able to link it to a specific cellular function. Thus, it was left to Morgan to incorporate further details into the conception of "Donation + Acception", based on his data from studies on the fruit fly.

The next step of extreme impact was a further reduction of the material substances and structures that were held responsible for the phenomenon of "like-

from-like", from the complete chromosome to one of its constituents, namely DNA. This reduction is attributed by many geneticists as well as philosophers and historians of science to Oswald Avery, Colin MacLeod, & Maclyn McCarty (1944), but the credit for the decisive impetus for the design of the corresponding experiments and their interpretation belongs to Frederick Griffith (1928) and his seminal finding of the transforming principle in bacteria. As a consequence, the transfer of DNA from organisms to their progeny organisms has been accepted by entire generations of life scientists, molecular biologists and geneticists as the only process that is necessary and sufficient for the phenomenon of "like-from-like". The "chromosome-centric" view of inheritance became a "DNA-centric" view of the inheritance of biological traits, which in turn represents "only" another version of the conception of "Donation + Acceptance". But from this version, with its radical reduction to only a single type of molecule (for depiction of the DNA-centric view of inheritance, see **Figure 3**), the problem arose as to how the transfer of DNA—from a chemical point of view a relatively "boring" linear, "one-dimensional", polymeric macromolecule, since it is only made up of four different building blocks in varying sequence—can causally explain the phenomenon of "like-from-like".

According to the proponents of the "DNA-centric" view—and alternative

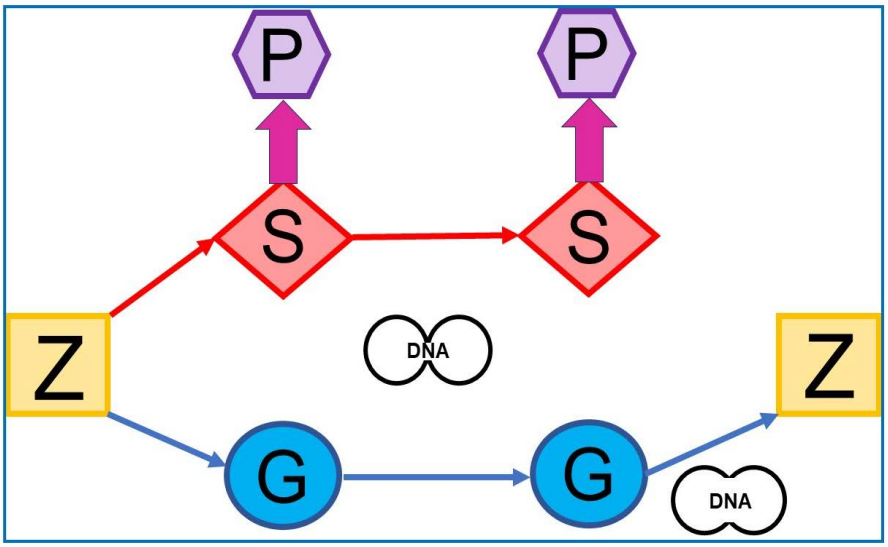

Figure 3. "DNA-centric" view of the conception of "Donation + Acceptance" for the explanation of the "like-from-like" phenomenon. During early development of the zygote (Z), produced by the parents, the somatic (S) and germ cell (G) lineages become totally separated. The entirety of S, which is copied by cell division and then become differentiated, creates the phenotype (P) of the organism. G which is also copied by cell division during adult life may ultimately lead to a Z of the next generation upon cell fusion without any direct effect exerted by S (which is in full agreement with Weismann's theory of the "germ plasma"). In course of both cell division and fusion, DNA is thought to be the only matter to be transferred from the mother to daughter S and G as well as from the parental G to the offspring Z, respectively.

concepts hardly appeared afterwards—the solution to this was provided in the following three decades and culminated in the elucidation of the spatial structure of DNA as a double helix by James B. Watson & Francis Crick (1953a). For it is precisely this structure that intuitively makes DNA appear perfectly suited for its task as a material to be replicated and transferred and equipped with the capability of inducing specific features in daughter organisms or offspring. Thereby, the phenomenon of "like-from-like" becomes reduced to a single principle or factor. The combinatorial and repetitive nature of DNA and its length entail a complexity that should be sufficient for the unambiguous and reliable recurrence of organisms with all their specific features. And the apparent "logic" of the semi-conservative mechanism of replication of DNA at a first glance in the wake of its structural clarification by Watson and Crick (1953b) was experimentally proven by M. Meselson & F. W. Stahl (1958). This apparent "logic" and straightforwardness of the process of copying DNA become mirrored by the striking consistency of the machineries of transcription and translation for the DNA-guided synthesis of proteins, the molecular analysis of which culminated in 1961 in the complete elucidation of the "genetic code" by M. W. Nirenberg & J. H. Matthaei (1961). The precision and reliability of these processes directly and intuitively implied that they are responsible for the reliable recurrence of the features between mother and daughter cells as well as between parental organisms and their offspring and thus that the phenomenon of "like-from-like" could be explained mechanistically by those processes. According to this canonic view, that is all that is needed, and certainly not "Pangenesis", "Gemmules" and "preformation" (Maynard Smith, 1993).

With the discoveries of the processes of transcription and translation and the formulation of the "Central Dogma of Molecular Biology" derived from them, i.e. the unidirectional information flow from DNA to RNA (via transcription) to protein (via translation), which Francis Crick (1958 and 1970) was probably the first to express, it was established that "reverse translation", i.e. from protein to DNA, from phenotype to genotype, from somatic cells to germ(line) cells, simply cannot happen. The impossibility of "reverse translation" was in complete agreement with the statements of August Weismann about the non-operation of "Pangenesis" and the non-existence of "gemmules", which Charles Darwin had proposed as mechanisms for the inheritance of acquired traits (see above).

The discovery of Watson and Crick and the implications for the inheritance of biological traits that are or appear to be associated with it received eminent attention in the following decades—both by researchers from a wide range of life sciences and by scientifically interested laymen around the world. For both groups, the "DNA-centric" view of inheritance of traits, i.e., the DNA-based version of the conception of "Donation + Acceptance", represent the generally accepted and hardly ever questioned "facts" about biological inheritance. The "DNA-centric" view represents a milestone in scientific biology, and not only for genetics and molecular biology. Taken together, the "old" conception of "Donation + Acceptance" for the inheritance of traits has evolved over the centuries

from the "pre-microscopic" versions of Hippocrates, Aristotle and others to the "cell-centric" version of the 17th century to the "gametocentric" version of the 18th century to the "nucleocentric" version of the 19th century to the "chromosome-centric" version of the first half of the 20th century and finally to the "DNA-centric" version of the second half of the 20th century. There is no doubt that the depth of the molecular details about the structures and mechanisms involved has increased tremendously along this path up to present times. But the basic assumptions have remained unaltered. Certainly, those have critically driven and shaped the process of experimental research about the phenomenon of "like-from-like", including the interpretation and publication of the produced data and thereby paved the path for many discoveries of huge biomedical significance. Nevertheless, those basic assumptions have to be disclosed as "set in advance" at least, albeit not arbitrarily, if not discussed, questioned and—if required—modified, precisely because of this.

6. The Exclusion of Non-Genetic Matter by the "DNA-Centric" View

As just explained, according to the "DNA-centric" view of the inheritance of biological traits, only the replication of DNA and its transfer from the predecessor to the successor organism or from the parental to the daughter cell in combination with DNA-instructed protein synthesis in the successor organism or daughter cell are required to explain the phenomenon of "like-from-like". Accordingly, those three processes are assumed to be sufficient for the reliable and continuous recurrence of biological traits within biological lineages. It is important to note that the "DNA-centric" view claims validity for all genotypic and phenotypic traits that occur reliably and continuously within a lineage, with one exception. This refers to reliably and continuously occurring "cultural" phenotypes. For the "DNA-centric" view, "cultural" phenotypes are reliably passed on not only because DNA is replicated and transferred, but also because cultural conditions are copied and transferred. On the basis of this idea, various theories of a "two-fold", i.e., genetic and cultural inheritance, as well as the inheritance of "memes" as carriers of "cultural/immaterial" "agency" have been developed (Cavalli Sforza & Feldmann, 1981 & 2002; Boyd & Richerson, 1985, 1996 & 2000; Maynard Smith, 1998; Dawkins, 1999; Cavalli Sforza, 2001; Laland & Brown, 2002; Durham, 2002), in analogy to the inheritance of genes as carriers of natural/material "information" (Dawkins, 1983 & 1989; Dennett, 1995, 2001a & 2001b; Wimsatt, 1999; Aunger, 2000 & 2003; Laland, 2002). It is possible that "dangerously anthropomorphic" parallels between the inheritance of genetic (and non-genetic matter; see below) on the one hand and the inheritance of customs, rites, traditions, and cultural goods on the other hand could be discerned at the levels of the development of individuals and the evolution of populations.

But how can the reliable and continuous recurrence of "non-cultural" genotypic or phenotypic traits within a biological lineage be adequately explained by

the replication and transfer of DNA? This is probably only possible if the characteristics of the organism in question (parental cell or predecessor organism) consists of nothing other than the possession of certain DNA molecules with certain sequences, i.e., of certain genes. Only in this case will the replication of DNA produce new entities/specimens of these particular DNA molecules, i.e., genes, which will then be transferred to the daughter cell or successor organism during cell division and conception, respectively, where they will guide protein synthesis. Thus, the mechanisms of replication and transfer of DNA provide a sufficient explanation for the reliable and continuous recurrence of genotypic rather than phenotypic traits.

However, this is not the case for the reliable and continuous reoccurrence of ("non-cultural") phenotypic traits within a biological lineage, which only emerge during individual development, and which cannot simply be produced by DNA replication, DNA transfer from ancestral to progenitor organisms and DNA-guided protein synthesis. Otherwise, the development of phenotypic traits would have to be adequately explained solely by the presence of a particular set of genes (and possibly their interactions). Rather, the development of phenotypic traits in progeny organisms critically depends on the transfer of non-genetic matter, encompassing biological membranes, in general, and subcellular organelles and plasma membrane landscapes, in particular, from the parental cell or predecessor organism as well as the action of environmental factors. Both of them must also reoccur in reliable and continuous fashion during development. In fact, the "DNA-centric" view claims to provide a sufficient explanation for the inheritance of all reliably and continuously recurring ("non-cultural") traits and phenotypes. According to it, the inheritance of phenotypic traits is explained by the inheritance of genetic materials and nothing else. The "DNA-centric" view of inheritance is ultimately a logical continuation of the "nucleocentric" view originally formulated by August Weismann and visualized as the so-called Weismann diagram (shown in a modified version in **Figure 3**).

The "DNA-centric" view of inheritance represents only one version of the conception of "Donation + Acceptance", according to which the transgenerational or intercellular transfer of DNA from predecessor to successor organisms during "acceptance", i.e., fusion of gametes or division of mother cells, adequately explains the phenomenon of "like-from-like". However, albeit the conception of "Donation + Acceptance" in its general form is based on the existence of materials and factors to be transferred, it is neutral towards their nature. In the "DNA-centric" view of inheritance, the transfer of genetic materials—mentioning of the transfer of non-genetic matter is not necessary for a sufficient explanation (see below)—only takes place in the short period during "acceptance", and thus with the beginning of the development of the new organism. Thus, immediately after "donation", which corresponds to the stage of fusion of gametes (transgenerational transfer) or division of mother cells (intercellular transfer) (**Figure 4**), the resulting acceptor organisms, the zygotes and daughter cells, respectively, possess

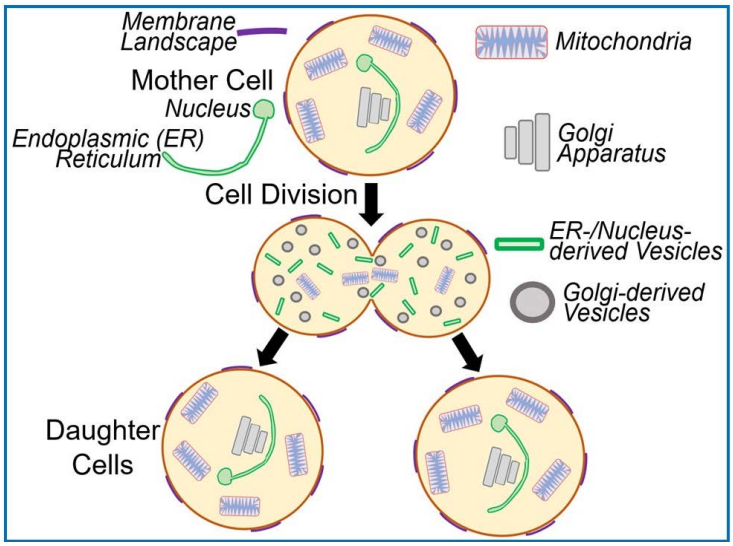

Figure 4. Data-based model for the transfer of organelles and "plasma membrane landscapes" between mother and daughter cells during cell division. In course of cell division of (mammalian) mother cells the membranes of their nuclei, endoplasmic reticulum (ER) and Golgi-apparatus are fragmented into small vesicles which become distributed by chance between the daughter cells along with their plasma membranes including the corresponding "membrane landscapes" and their mitochondria (see Du et al., 2004) After completion of cell fission, the vesicular structures re-assembly to functional nuclei, ER and Golgi-apparatus by fusion and then grow along the secretory pathway, in concert with the plasma membranes and their "landscapes". Prior to the next cell division, the mitochondria increase in number by the incorporation of pre-synthesized proteinaceous components and phospholipids at appropriate sites and subsequent fission.

many genotypic (the parental alleles of the genes) as well as phenotypic traits, including cellular membrane systems, organelles, proteins, RNA (which are sometimes localized in very specific positions or sections of the zygote or daughter cell, respectively).

According to the "poly-matter network" view of inheritance, the organism develops or unfolds, as it were, from a complex "tangle" of different genetic and non-genetic matter, which is completely present at start of its development when the fusion of the gametes or division of the mother cell is completed. Thus, at the the subindividual cellular level development seems to follow the original preformation rather than the epigenesis theory. Furthermore, the "DNA-centric" view of inheritance apparently interprets the development of the organism from the zygote or daughter cell as occurring in a closed system without any additional transfer of materials, until the next cycle of "Donation + Acceptance" becomes initiated. In contrast, in a conception of a "poly-matter network" of "Donation + Acceptance" (for greater details, see below), which recognizes the transfer of genetic materials alone as being insufficient, a continuous inflow and outflow of non-genetic matter, among them extracellular membranes and vesicles (**Figure 5**), micelle-like

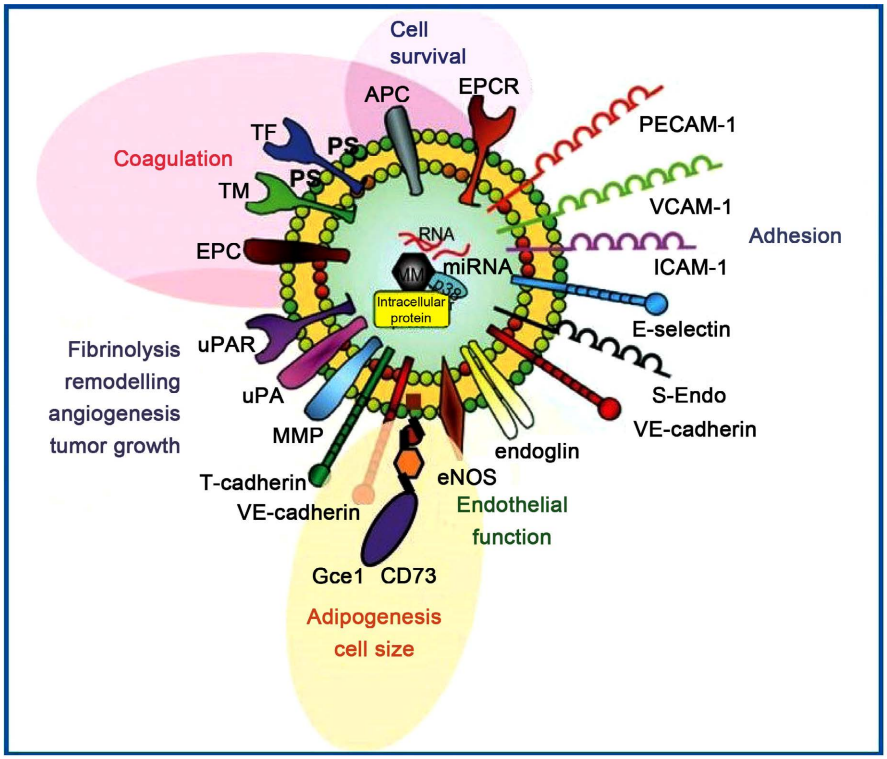

Figure 5. Data-based model for the structure of typical extracellular vesicles (EVs), as adapted from Müller (2012) with permission from Taylor & Francis Inc., as candidate "Gemmules". EVs are surrounded by a typical phospholipid (PS, phosphatidylserine) bi-layer with inserted transmembrane proteins (TM), such as tissue factor (TF), urokinase plasminogen activator receptor (uPAR), matrix metalloproteinase (MMP), cadherins, endothelial nitric oxidase (eNOS) and various cell adhesion proteins (PECAM, VCAM, ICAM) as well as glycosylphosphatidylinositol-anchored proteins (GPI-APs), such as glycolipid-anchored cAMP-binding and phosphodiesterase ectoprotein (Gce1) (Müller et al., 2008) and 5'-nucleotidase (CD73). Importantly, it is thought that groups of those membrane proteins regulate specific (patho)physiological processes and integrated pathways in concert upon their transfer from donor to the acceptor cells, such as coagulation, angiogenesis, tumor formation, endothelial barrier, cell adhesion as well as adipogenesis and cell size, respectively. Moreover, the aqueous lumen of EVs may harbor RNAs coding for enzymes, such as glycerol-3-phosphate acyltransferase GPAT3 (Müller et al., 2012), and microRNA (miRNA) as well as cytoplasmic proteins, captured by carrier proteins, such as heat shock proteins, which in course of their intercellular transfer induce phenotypic switching, such as stimulation of lipid synthesis (Müller et al., 2009, 2011a & 2011b). Not indicated in this model is the possibility that EVs are equipped with specific "membrane landscapes", constituted by transmembrane and cytoskeletal proteins in concert with GPI-APs (see below), which become transferred from donor to acceptor cells.

structures (**Figure 6**), "plasma membrane landscapes" (**Figure 7(a)** and **Figure 7(b)**), proteins (e.g. prions) and non-nuclear nucleic acids (e.g. microRNAs) may happen during the complete cycle of the individual life, from its very beginning—fusion of gametes or division of the mother cell—through development into an adult organism in course of the complex interplay between growth and differentiation to its death and is regarded as necessary for a sufficient explanation, i.e. is explanatorily sufficient. Thus, the conception of a "poly-matter

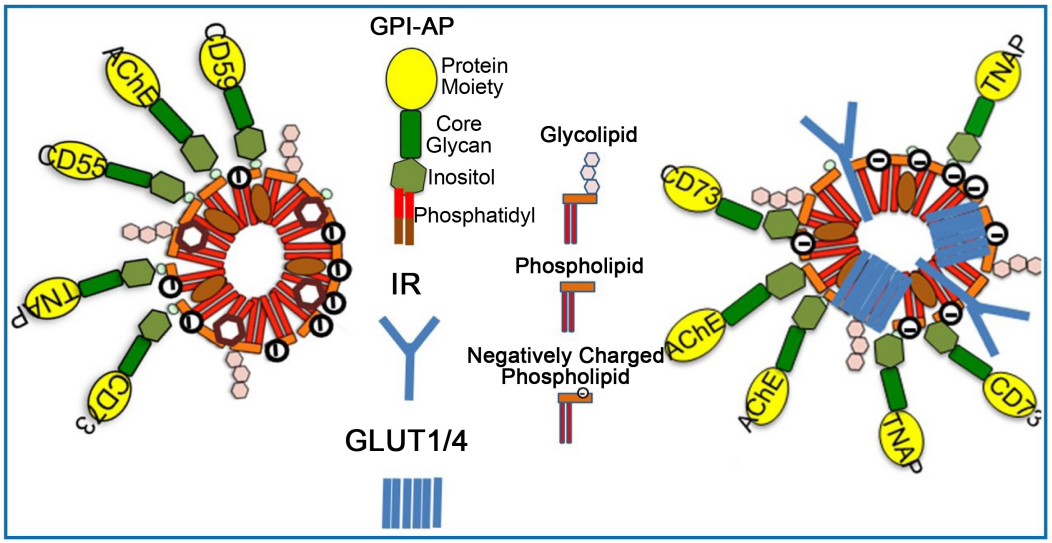

Figure 6. Data-based model for the structure of typical micelle-like GPI-AP complexes, as adapted from Müller et al. (2020) and Müller & Müller (2022) with permission from mdpi Inc., as candidate "Gemmules". GPI-APs are known to become released from donor cells into micelle-like complexes which consist of (lyso)phospholipids and (lyso)glycolipids at appropriate ratios, often resulting in a negative total surface charge, with inserted membrane proteins, which are equipped with single or multiple transmembrane-spanning regions, such as the insulin receptor (IR) and the glucose transporter proteins 1/4 (GLUT1/4), respectively. The structure of GPI-APs with the hydrophilic protein and core glycan moieties at one end and the amphiphilic phosphatidylinositol at the other end leading to pronounced overall amphiphilicity perfectly fits to their role in being transferred between the outer phospholipid leaflets of the plasma membranes of donor and acceptor cells.

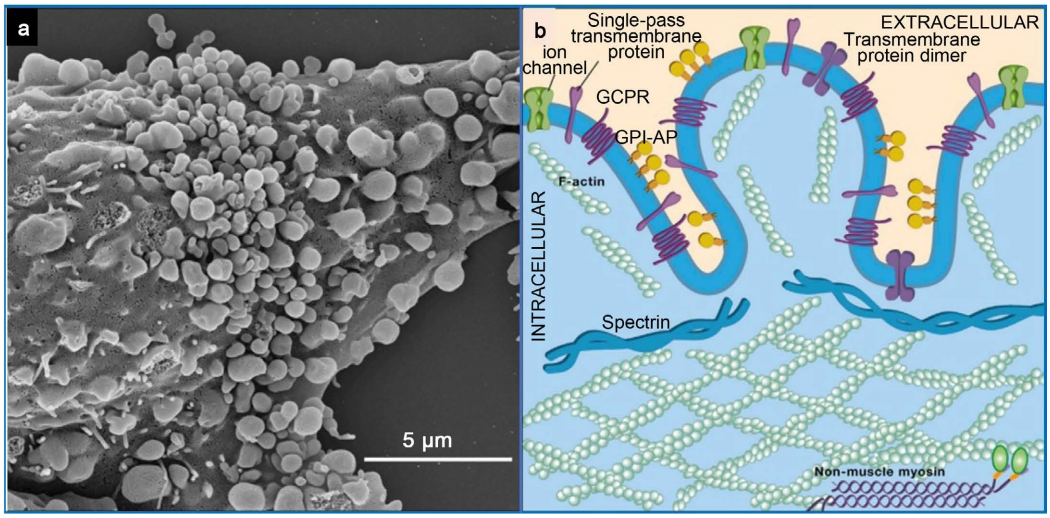

Figure 7. Experimental representation of a typical plasma "membrane landscape" and its presumed molecular structure, as adapted from Jacobson et al. (2019) with permission from Cell Press. (a) Bleb-like protrusions on the surface of Chinese hamster ovary cells in the process of spreading on an appropriate substrate as imaged by scanning-electron microscopy. (b) Model for a "membrane landscape" or compartmentalization of plasma membranes by blebs and/or bleb-like protrusions as well as intermittent valleys and incisions as it becomes organized by the underlying network of cytoskeletal elements, among them F-actin, spectrin and non-muscle myosin, with resulting restriction of the lateral mobility of their proteinaceous constituents, such as G protein-coupled receptors (GCPRs), GPI-APs, ion channels, single and multiple spanning transmembrane proteins.

network" of "Donation + Acceptance" deals with the developing organism or replicating/differentiating cell as an open system. This conception also considers the necessity of the transfer (donation) of a complete set of soluble small- and high-molecular-weight factors (e.g. nucleotides, amino acids, proteins, enzymes) from donor to acceptor cells to establish a functional expression system for the genome of the organism, which has been addressed as "First Question", "Production Force" or "Transcriptase System" by Muying Zhou (2018a, 2018b & 2020).

7. The "DNA-Centric" View of Inheritance as a Sufficient Explanation

The statement that the occurrence of event X is explanatorily sufficient for the occurrence of event Y is not to be equated with the statement that X is causally sufficient for Y. Explanatory adequacy does not mean causal conditionality. In other words, the fact that a factor is causally necessary does not mean that it is also necessary for an adequate explanation. Whereby here by "X is necessary for Y" it is to be understood that there is no sufficient explanation for Y that does not mention X. For each phenomenon, many causal factors and conditions can be identified that must be present for this phenomenon to occur. But in order to explain the occurrence of the phenomenon, there is no need to name all these factors and conditions. Otherwise, an explanation would be made practically impossible for many biological phenomena. Only an appropriate set, i.e., an adequate selection, of factors and conditions, which make the occurrence of the phenomenon plausible to understand, must be named in the corresponding explanation. The other factors and conditions, classified as "self-explaining", trivial or operating by nature, should be kept in mind as "explanatory background" that does not need to be emphasized separately.

But who or what now decides which factors and conditions involved in the occurrence of a biological phenomenon are to be counted as the explanatory background, only, and which are to be counted as the explanatory foreground, which must be mentioned in any case. The origin of those processes of distinction, differentiation or exclusion is a typical question of *Science and Technology Studies* (STS) (Bellinger & Krieger, 2006; Beck et al., 2012; Lengersdorf & Wieser, 2014; Bauer et al., 2017) and will be the subject of a future study with regard to replacement of the "DNA-centric" view of the conception of "Donation + Acceptance" and the resulting exclusion of a "poly-matter network" view of the inheritance of both innate and acquired features.

In this regard, it could be interesting to clarify the reasons for and the consequences of the specific design of the bacterial transformation experiment ingeniously performed by Frederik Griffith (1928): "Who" decided that the matter of inheritance has to be heat-stable, to be taken up by (bacterial) cells as "naked" molecules—after their "unphysiological" release from bacteria, albeit with extremely low efficacy (but selectable using bacterial mutants) and to induce a rather "simple" pathological phenotype, i.e. production of a capsule, virulence and

lethality for mice. This experimental setting unavoidably led to exclusion of heat-labile matter that can only be taken up by acceptor cells upon packaging into specific macromolecular complexes, such as vesicles and micelle-like structures, with the help of vesicular and insertion mechanisms, respectively, albeit at high efficacy, and manages to trigger complex physiological phenotypes, such as stimulation of glycogen and lipid synthesis (Müller & Müller, 2022; Müller et al., 2021; Müller & Müller, 2022, 2023b; Müller et al., 2009, 2012, 2011a, 2011b & 2021). In short, the specific experimental design of bacterial transformation as used by Griffith unambiguously favored the identification of nucleic acids rather than other biological macromolecules, such as (nucleo)proteins (originally thought to act as matter of inheritance on basis of their complex structure (Koltsov, 1928; Mirsky, 1943) and membranes which actually have been excluded from the very beginning as the matter that upon "donation" and "acceptance" induces a specific phenotype in the acceptor cells and thereby may be regarded as explanatorily sufficient for the "like-from-like" phenomenon.

According to the "DNA-centric" view of inheritance of biological traits, DNA is explanatory sufficient for the development of reliably and continuously recurring phenotypes that contribute to the phenomenon of "like-from-like". However, this does not mean that the "DNA-centric" view claims that DNA is causally sufficient for this. If it were to insinuate this, it could be refuted very easily, since not a single phenotype can be causally explained by DNA. Naked DNA molecules pipetted into an empty Eppendorf vessel do nothing and certainly do not produce a living organism. Non-genetic factors (matter), i.e., extremely complex, highly organized, multi-molecular machineries, consisting of enzymes and RNAs, in the cytoplasm of the cell, and environmental conditions, such as nutrition for the availability of vitamins and amino acids, are causally necessary for the replication of DNA as well as for the direction of protein synthesis—via RNA—by DNA. The machineries must be transferred from the cytoplasm of parental to daughter cells or of gametes to zygotes during cell division and fusion, respectively, in order to contribute to the development of the phenotypic characteristic "P" of a successor organism. Furthermore, the appropriate environmental conditions must be maintained. In short, without any doubt DNA (and RNA) represents a necessary but not a sufficient condition for "life". In the absence of the biochemical-cellular apparatus for "reading" the "information" encoded by DNA (and RNA), these macromolecules are "dead" (Chetverin, 2010), which also holds true for virus particles, i.e., virions, outside a host cell.

But despite of the fact that DNA is causally not sufficient for the development of a phenotype "P", it might seem reasonable to attribute all non-genetic factors causally required for the development of "P" in their entirety to the explanatory background, and therefore not to explicitly mention them in a sufficient (adequate) explanation for the development of "P". Thus, DNA would be explanatorily sufficient for the development of "P" (Van der Weele, 1999). Thus, the "DNA-centric" view assumes the explanatory adequacy of DNA for the devel-

opment of reliably and continuously recurring (i.e. heritable) phenotypic traits. At the same time, it implies that none of the non-genetic factors and (environmental) conditions that are also causally necessary for the development of these "P" need to be included in a sufficient (adequate) explanation for "P", and this is exactly what most developmental and molecular biologists believe today. Accordingly, developmental processes are characterized by those as a sequence of activations and inhibitions of gene expression, in the sense that upstream genes produce chemical substances that activate or inhibit downstream genes, and this then continues to hold true for the next set of genes at the next lower level of hierarchy.

From here, it was only a small step to the last and still accepted version of the "unfolding" or preformation theory of biological development, according to which it has to be understood as a cascade of gene-induced gene expressions functioning with the precision of a clockwork (Raff & Kaufmann, 1991; Wolpert, 1991; Olson, 2002). In order for these cascades of hierarchically arranged gene expressions to take place, a multitude of non-genetic factors (matter, environmental conditions) must of course be operative. But it does not seem necessary to name them in explanatorily sufficient descriptions of the molecular sequence of developmental processes. How is this strategy of "devaluation" or exclusion of non-genetic factors as a mere background for the (sufficient) explanation of the development of heritable phenotypes justified? A common argument is that DNA is the "blueprint" driving the synthesis of multiple proteins that is critical for the "assembly" of a phenotype from heritable traits. By contrast, non-genetic factors are thought to "only" contribute the matrix and structures, as well as the appropriate conditions that are required for the "assembly" of a phenotype in its entirety. This "blueprint" or "construction plan" has been given another metaphor, the metaphor of *information*. A fairly widespread interpretation of this metaphor is that of information as a "recipe" (as in cooking) or as "agency". Accordingly, phenotypes with their heritable traits are to be understood as "the roast", for the production of which the DNA/genomes/genotypes provide the "recipes" and the non-genetic factors (matter, environmental conditions) make available the appropriate ingredients (Jacob & Monod, 1961; Dawkins, 1986 and 1996; Williams, 1992). Another popular interpretation of the metaphor of information understands it as a "program" with which the genome decides which heritable traits of the phenotype are executed or "unfolded" during and for development (Bonner, 1965; Wolpert & Lewis, 1975; Fox Keller, 2000 & 2002).

Information theory, formulated at the end of the 1940s (Shannon, 1948), works with purely quantitative parameters and is detached from content and meaning. Information is not an entity here, but rather a purely stochastic phenomenon that affects the statistical rarity of signals (Kay, 1995) and ultimately leads to pattern formation. The mathematical definition of information is thus also indifferent to biological aspects such as function or value and does not allow, for example, to distinguish between functional and non-functional DNA sequences

(Chatzidinmitriou-Dreismann, 1996; Mahner & Bunge, 2000; von Sternberg & Shapiro, 2005; Mattick & Dinger, 2013). Therefore, a mathematical, purely quantitative definition cannot be the basis for a concept of information in biology, in which qualitative aspects (value, function, purpose) play a paramount role.

The idea of information in biology was initiated by Erwin Schrödinger (1944) when he dealt with the question of order in living beings and their long-term preservation as well as the highly ordered structure of genes as information carriers with their highly regular and lawful effectiveness or "agency". The idea of (development) determining genetic information was concretized in the early 1950s during the "Cold War" phase, after DNA (and not the proteins favored until then) had been identified as genetic material (Griffith, 1928; Avery et al., 1944), its constitution and configuration had been elucidated (Watson & Crick, 1953a, 1953b) and the molecular nature of point mutations (Ingram, 1957; Nirenberg & Matthaei, 1961) had been recognized (Olby, 1994). According to this, the genetic information of any one of its cells alone should define a multicellular organism and even allow the production of artificial, fully functional pro- and eukaryotic cells (Gibson, 2010). In biology, this idea driven by information theory is still dominating to the present day: Heredity is exclusively genetic, i.e. defined by the concept of information, according to which evolution has to be understood as (complex interplay of) frequency shifts of genes/information, i.e. qualitative and quantitative changes of genetic information in the reproductive allele pool of a population or ultimately of its "agency".

8. Blood and DNA—Matter of Body and Uniqueness

Despite the rather vague "scientific" understanding of what genes and genetic information "are", most people and laymen apparently have no doubt about it when it came to the question of the meaning and agency of genes and genetic information give answers like the following: *I think our basic personality is in the genes*, *our attitude to life*, *our basic mentality*, *for example*. *Of course*, *we will be influenced and shaped by our experiences throughout our lives*, *but* "*the material*" *is there from the beginning*. *And this material must be in our genes*, *or what else could it be*? At a first glance, this sounds overwhelmingly deterministic, but it is important to note that genes are commonly interpreted as a kind of foundation, or possibly just as the stuff that life "works" on. Consequently, life experiences are evaluated as not so unimportant to shape people as a person. This assumption is surprisingly very much in line with modern genetics and molecular biology, which describe the relationship between genes and the environment as intimate, but extremely complex. However, the belief that genes define the "framework" within which the individual has been developed or still can develop is remarkable. Often this claim is based on the experience of people about (individual) differences and similarities between their (twin) sister or brother and themselves. They consider that they are different "on the surface"

and that these differences are due to the fact that they live different lives, but that they are more or less similar in what people often name their basic constitution. From this experience of similarity, it is concluded that the "basic constitution" of personality is influenced by genes. This common view thus reflects a certain dogma of molecular biology that in the cells of the body the basic control of their components and processes is hidden in their genes in the "depths" of the cell nucleus, while the "skin" on the surface, i.e. the plasma membrane, of the cells, is exposed to a wide variety of environmental factors and becomes changes in its structure, i.e. shape and composition, in the course of life by gene-controlled reactions which ultimately determine their life and destiny. In course of this idea of genes as a determining factor for personal identity, which is manifested in many public and published narratives of the most diverse genres, another bodily component, which in past centuries was attributed a comparably important effect, namely blood, is considered as more or less irrelevant.

Being a unique personality is a crucial element in the conception of uniqueness in the Western world, starting with the age of enlightenment, at the latest. According to the understanding of most people, blood cannot be identity-forming. The major argument for this relies on the knowledge of a very limited number of different blood groups, such as A, B, AB, 0, and others, which would enable the differentiation of only four to a few dozen types of people in the world, while the almost endless variation of possible gene combinations corresponds to the expectation that all people are unique individuals and is compatible with the common view that those are causally responsible for the interindividual differences. However, there may be no (direct) causality between uniqueness in personality and uniqueness in genes. But in the strong cultural anticipation of uniqueness, the relationship between genetic uniqueness and uniqueness in personality actually seems to be understood in a common sense as (direct) causality rather than a correlation. Apparently, it is frequently assumed that the unique set of genes of each human individual vouches for his or her unique personality.

On the other hand, the reference to a causal relationship between genetic uniqueness and uniqueness in personality is often being recognized as flawed and potentially threatening. The reason for this discomfort presumably is that if the set of genes of an individual determines the personality of the individual, then monozygotic twins would be considered two versions of the same person, which those would strongly emphasize that they were not. Monozygotic twins typically claim that they were both quite unique and very different, even if they happened to have identical genes. Numerous monozygotic twin pairs have reported to follow their own little "research project" to mutually observe their development from childhood to adulthood, and they concluded that physical things, such as visible appearance and physiognomy, are of genetic origin, while psychological traits and personality are less influenced by genes. Monozygotic twins often state that they are very similar, but that in fact they are completely different people. Their understanding of how genes work is that there is a germ to the personality

at conception (in the genes), but from then on it develops in close interaction with the circumstances through life both in the womb and after birth. And they are often very sure that personality is shaped primarily by social experiences in life. They expect as the main goal of education by their parents to ensure that they develop different and unique personalities.

It is undisputed that individuality, uniqueness, and kinship have been considered as the core elements of personality in the modern Western world. Identity and value are gained by being autonomous and distinguishable from other people, but identity is also acquired by being connected to certain other people in a certain way. The question that needs to be answered is: How are these three prominent aspects of personality connected to the Western perception of the human body and its crucial components, such as DNA, genes, proteins, and their assemblies into subcellular structures, and how are they reflected in them? Or, by abandoning the anthropocentric view, is it feasible to combine the "personality" of organisms, be it that of humans, animals, or cells, with disdainful matter, be it blood, genes, proteins or their subcellular assemblies.

The Western concept of personality and uniqueness is culturally co-constructed with the concept of the body and inextricably linked to it. With the autonomous indivisible individual as the primary entity that carries meaning, the individual body is also a primary place for meaning. The body, parallel to the person, the animal, and the organism, is considered individualized (Giddens, 1991). The conception that the boundaries of organisms, in general, and of animals and persons, in particular, coincide with the boundaries of their physical body or with their material shape is an idea that is supported by the biological and medical understanding of the animal and human organism and its constituent cells. Traditionally, the body and its cells are understood as indivisible and distinct entities, with clear boundaries between the inside and the outside, between the self and foreign, between the "depth" and the "surface", separated by the skin and the plasma membranes, respectively. A person, an animal, or an organism seems to reside within a body. The individual body symbolizes the person, the animal, the organism, i.e. "is" the person, the animal, the organism and thus is the "property" of the person, the animal, the organism (Elias, 1978; Larsen, 1998).

The body is perceived as both being given and made—understood as an inseparable mixture of natural and environmental/social processes. This perception is integrated into the laymen's knowledge that human bodies, but also animal bodies, are socially shaped in course of human activities to a certain extent and are made meaningful to the "carrier" of the body through culture, for example by the way he or she decorates their own body, but also animal bodies, what they eat, drink, how they move, etc. However, the components of the human as well as animal body—its flesh, its fluids, its organs, and its cells—are mainly understood as "pure nature". According to the prevailing Western epistemologies, the "natural" processes are best studied by the natural sciences. Genetics, (molecular

and cellular) biology, biochemistry, physiology, and medicine are understood as the suppliers of hegemonic knowledge about the components of the organismal body, in general, and the animal and human body, in particular, including our own bodies and matter, as well as about the material components of the entire living organismal world. In this way, "natural" and biomedical classifications and categories have the potential to have a huge impact on the self-image of humans. But these classifications and categories do not transform in an unchanged version from the natural sciences into people's everyday lives and life worlds. Laymen interpret, negotiate and fight for biological knowledge and biomedical classifications and categories in a variety of ways which thus represent meaningful vehicles for self-understanding in their everyday lives and in their living environment.

As already stressed, the categories of genes (DNA) and cells were dealt with in the foreground of explanations of the "like-from-like" phenomenon. In addition to the reasons mentioned above, genes (DNA) and cells have become an obvious choice in this context, as they are increasingly understood as the substances and components of the body that are most fundamental to personality, identity, and kinship according to the Western view (Conklin & Morgan, 1996; Nelkin & Lindee, 1995). Genes and cells (somatic as well as germline cells) are to be considered as the substances and matter of the body. However, this should be interpreted more as an analytical strategy and less as a descriptive categorization. The conception of substance and matter has been an important analytical tool for anthropologists with an interest in kinship, identity, and personality. The usefulness of the concept may be largely due to its breadth of possible meanings, as Janet Carsten (2004) has argued.

Although genes (DNA) have been seen as a natural bodily substance to discuss when it comes to personality, identity, and kinship, it may be instructive to compare the focus on genes with a focus on blood. The reason for the juxtaposition of these two substances relies on a "movement" from blood to genes as a substance or matter of kinship in modern Western thinking. David M. Schneider (1968), a pioneer of anthropological studies of Western kinship, argued that Americans defined relatives by blood and that: "*The blood relationship is… a relationship of substance*, *of shared* [*concrete*] *biogenetic material*". According to Schneider, this understanding of kinship is in a state of dependence on science, in which science is given the power to define what kinship "is". In Schneider's text, and in much of the subsequent literature on contemporary Western kinship, terms such as "blood," "biogenetic substance" and "biological bonds" are used interchangeably and without further discussion. Janet Carsten has pointed out that both "blood" and "biogenetic substance" remain unexplored as symbols in Schneider's text, and that it would be useful to focus on the concepts separately as well as how they relate to each other (Carsten, 2004). Thus, in future studies, it should be explored 1) how the conceptions of genes and other body substances, such as blood, cells, surfaces, membranes and

"membrane landscapes" differ from each other and 2) whether and how genes, blood, cells, surfaces and membranes belong to different chains of meaning. Consequently, in a future report (Müller & Müller, manuscript submitted) genes, blood, cells, surfaces, membranes and "membrane landscapes" have been examined as matter of the body that influences the constitution of human (and animal) organisms, in general, and the configuration of the human (and animal) body from its basic physiological functions to personal identity and uniqueness, in particular.

To gain further insight into how genes are understood as part of uniqueness given by nature, it may be useful to take a step back and have a look at the idea of the beginning of individual life, as it is prevalent in modern Western countries. Concepts of identity, personality, and kinship are co-produced with the social meanings given to bodies and the substances of the body. This is particularly evident in the common views of emerging bodies, as those arise through the process of reproduction, and embryonic and fetal development (Schneider, 1968). How do bodily substances correlate with core elements of the current conceptions of "the person", the "individual" and the kinship in Western reproductive theories and state-of-the-art embryology?

Informed by biology and biomedicine, the prevailing popular view of conception in the Western world is that there are almost exclusively only two physical substances or materials engaged, the (human or animal) egg cell from the female organism (oocyte) and the (human or animal) sperm cell from the male organism (spermatocytes). These cells, the gametes, each contribute half of the genetic substance or matter to the embryo, according to the Western bilateral kinship system. In this context, oocytes and spermatocytes gain their primary importance by being carriers of genes which became transferred during the phenomenon of "Donation + Acceptance".

The oocyte and spermatocyte fuse together and the DNA, i.e., the genome, of the new being is formed. The fertilized egg is perceived as being of a different order than the cells from which it originated, which is the basis for one of the dominant (albeit very controversially debated) Western ideas of when a person begins. Thus, a new human being, or animal organism in general, gains moral value at conception. This view is based mainly on the argument that the DNA (genome) of the fertilized egg is of unique composition and that the fertilized egg is therefore different from the maternal body in which it is located. Of course, this has been controversially discussed since centuries. People of the Western world do not agree on when to attach human or animal value to the development of new life. This controversy is well documented, for example, in the public debates on abortion and stem cell research. Suggestions as to when a "person", an "animal", an "organism" begins range from conception to when it can be said that the fetus develops feeling and/or thinking to when the fetus would be viable outside the maternal organism prior to its natural birth. The arguments vary, but one can see a culture-specific commonality in the tendency to look for solid,

structural, and mostly biological markers and materials, when the fertilized egg, the fertilized embryo, the fetus should be called an individual organism (Carsten, 2004). This gives biology and life sciences the defining power for an apparently socially constructed category and moreover leads to the impression of the individual organism being a category given by nature.

In the context of "nascent life," both genes and blood represent the realm of nature, but in slightly different ways. While DNA, genes, genomes become biology or nature in a deterministic meaning and vouch for the "given" with regard to both the uniqueness of the organism and its basic kinship relationships, bodily fluids, such as blood, become nature as part of specific education or care, as a substance that the maternal organism itself can influence to a certain extent through lifestyle and life world choices and through which it can realize its relationship with the offspring. The quality of "nature" that it offers becomes an achievement, an action, which more or less completely blurs the separation of nature and education or care.

9. Blood and DNA—Matter of Kinship and Heredity

In the Western world, blood has long been considered as the symbol of kinship. This is expressed best in phrases such as "blood relatives" and "our own flesh and blood", which delineate groups of belonging such as "blood lines" following certain social rules. In former times, the idea of blood as a substance or matter of kinship was based on the belief that conception itself was the mixture of male and female fluids, with the fluids understood most commonly as purified blood (Jones, 1996; Fox Keller, 2008 & 2009). Charles Darwin, for example, believed that certain traits are inherited through certain body fluids, in first line the blood, albeit he did not focus on it in his Pangenesis theory explicitly, and did not state that the specific material entities, called "gemmules" (see above), and transmitted from the human or animal parents to their offspring are definitely constituents of blood. By contrast, Gregor Mendel (1865 & 1870) was the first to propose that heredity does not rely on the blood but is stored in discrete units of "agency", that are passed on through spermatocytes and oocytes, the nature of which however remained vague and mysterious.

Blood as a symbol of kinship is still, depending on the area, country and society, more or less of societal relevance, and the above phrases are still actively used in several life worlds and languages. In the 20th century, it may be argued that blood has been replaced by DNA and genes as a general material of kinship and as a specific matter of heredity. Or, following Strathern's reasoning (Strathern, 1995), "flesh and blood" may only be of symbolic value, but this phrase nonetheless represents a symbol of what Western people believe to be true in the literal sense. Those who are connected by matter are related, and it is the act of reproduction that creates the connection through matter. Genetic connections can be traced and technologically tested (e.g., DNA testing for paternity), and as such they become a concrete tracking device and proof of a specific kinship

bond. Genes as a connecting body matter are not only understood as fundamentally inclusive, since a genetic bond cannot simply be broken, reversed, or denied. Rather, genes are also to be understood as fundamentally exclusive, since a genetic bond cannot be socially constructed (In this sense, the offspring emerging from a forced marriage must not be regarded as socially constructed but in fact are connected through genes to their parents who produced them, albeit for reasons other than love). However, it is not clear what consequences actually arise from those genetic connections, since genetic bonds do not "automatically or mechanistically" lead to social relationships. In a way, counting relatives or biological ties through blood or through genes has more or less the same meaning. Thus, a specific kinship relationship is thus thought to correspond to a certain "set" of common matter, which during the century of molecular biology has been shifted from blood to genes.

In this context, genes are understood as small material units that move through generations, and thereby produce certain "sets" of non-specific as well as specific genetic relatedness regarding the same species (e.g., mankind) and being member of the same kinship line. The percentage of shared genes (between parents and offspring) is coupled with the question of which specific genes are shared. In this way, genes act more specifically than blood as a kinship matter. Genes operate as more concrete tracking device for connections than blood and have the potential to produce specific connections between specific individuals, regardless of the actual "amount" of genetic kinship. Specific one-to-one kinship ties can be singled out and have the power to gain social relevance, as Strathern stated (Strathern, 1992): "*While blood could be seen as a symbol of a communicative event, genes are the bits of information themselves*." While blood becomes inevitably diluted from generation to generation, genes move (seemingly) unchanged through generations, crossing the stream of time and life that the idea of the blood lines indicates.

In conclusion, both blood and genes are categories of the body, but the chains of meaning and contexts in which they are embedded are very different. Genes are associated with the language of science and technology and with ideas of the future and hope, and often with certain mystery and fear, while blood belongs in the context of everyday life, concrete reality, disease and injury, and the old time and past. Genes provide undeniable, static, and lasting contributions to identity, while blood is perceived as more in motion, as a dynamic, processual entity. Blood *works*, *works* within bodies and *works* between people, animals, organisms. In fact, this differentiation has been narrowed to the view that while genes belong only to nature and are undeniably important for the formation of identity, blood—which moves between nature and education or (brood) care, between biology and social life—is important for the living and survival in community with other people, animals and organisms by determining the quality of the social bonds between them.

However, Western concepts of personality delineate the individual as a social

and moral actor and emphasize individual qualities such as uniqueness and authenticity as core values. The concept of personality and the cultural values it reflects precede the era of the gene. Nevertheless, the concept of the gene, as it has been and is still often presented in popular science and as it is often interpreted by laymen, is shaped in such a way that it fits perfectly as a means to this self-concept. Accordingly, genes can not only prove that each individual organism is unique, but also anchor the social value of uniqueness in nature. Genetic relatedness is inherently given. It is definitely exclusive and definitely inclusive. Genes individualize humans, animals, organisms. Genes connect people, animals, and organisms with each other, making them unique. Genes give each individual organism a "core" that can be further shaped and modified by the society of organisms and their life worlds. In a two-fold act of meaning production, people's bodily substances and matter, such as blood and genes, are charged with meaning and then that meaning is interpreted by people through these substances and matter. This co-production of matter and identity, or self, to a certain extent, sediments cultural values as physical conditions and thus as naturally given or as a natural setting. And accordingly, the way in which genes are understood as guarantors of the core elements of personality, kinship and identity seems to be determined solely by their natural quality.

10. Conclusions—Inheritance, Contingency and STS

Biological inheritance which has been a matter of intense scientific and public interest for centuries, meanwhile seems to be settled regarding the materials transferred and the laws and molecular mechanisms controlling that transfer. However, along the path to the present "DNA-centric" view of inheritance, the preformed opinions, critical settings, basic assumptions and terminology underlying the recognition of the "like-from-like" phenomenon, the "donation-acceptance" conception, kinship and heredity, have been masked by a variety of human and non-human actors of varying agency. The unraveling of (some of) the most prominent actors, which represents the aim of the present review/hypothesis paper, clearly indicates that the phenomenon of inheritance can adequately be understood only as a complex network of many human and non-human actors, encompassing among others private property, laboratory procedures, practices of individuality, materiality of cellular structures and developmental processes, rather than as a mere representation of a scientific fact or social construct driven by intention.

In adaptation of the Actor-Network-Theory (ANT), which has been introduced as a methodological variant of STS by Latour (1984/1988, 1996), Latour & Woolgar (1979), Callon (1986/2006) and Law (2004) in the 1980s, many human and non-human, living and non-living actors (organisms and things) have been involved in the production of the substance or matter of inheritance, among which are mini-organisms, homunculi, relatives, mono/dizygotic twins, cells, gametes, organelles, membranes, nuclei, chromosomes, genes, DNA, "gemmules",

blood, blood groups, proteins, vesicles, complexes, as well as farmers, cattle breeders, Western people, patriarchs, scientists, laymen, lawyers as well as private property, goods, wealth, habits, instinct, education, school system, health care system, social and welfare system introduced during the past centuries in the Western world. These actors have been or still are components of complex, flexible, dynamic networks that have produced or are still producing adequate explanations for the like-from-like phenomenon, each of them based on the setting or presumption of "Donation + Acceptance", starting with the cell-centric and gametocentric, followed by the nucleocentric and chromosome-centric and finally culminating in the DNA-centric view or network. Apparently, each transition from a former to the following network results in a reduction in size, mass, and/or complexity of the newly defined matter of inheritance, i.e., from cells via nuclei and chromosomes to DNA. This reductionism, the criterion and aim of natural sciences per se, is necessarily accompanied by the stepwise exclusion of matter with each network transition which is regarded as superfluous to be mentioned in adequate or sufficient explanations for the "like-from-like" phenomenon. Certainly, reductionism provides a powerful tool for the generation of differences and distinctions which are aimed at the creation of classifications and order of the "things" of the human and non-human world to cope with contingency with the aid of natural sciences, in general, and biology, in particular.

According to Luhmann (1993), contingency is explained as follows: *contingent is something that is neither necessary nor impossible*; *that is*, *what it is* (*was*, *will be*) *can be*, *but is also possible in other ways*. *The term thus refers to the given* (*to be experienced*, *expected*, *thought*, *fantasized*) *with regard to possible otherness*. Luhman was referring to Aristotle, who saw contingency as neither necessary nor impossible. Contingency is therefore based on differentiations, distinctions, inclusions, exclusions, and constructions that could always be made in this way, but also differently. In this respect, the term means negation of necessity and impossibility. Human beings want or need to manage contingency, i.e. limit the risk of disorder, uncertainty, the unexpected, threats. This risk arises from uncertainties for which there is no explanation available. In the cultural history of man, many strategies and mechanisms of coping with contingency or suppression have been developed in order to make the natural world more predictable, calculatable, safer, including political ideologies (Holzinger, 2006), conspiracy theories, law, religions (Blumenberg, 1959; Lübbe, 1998), social systems (Luhmann, 1993; Rorty, 1992), but also the natural experimental sciences (Heidelberger, 2006; Wuchterl, 2011). In this regard, the processes and terms of societal inheritance as well as biological inheritance derived thereof (see above) with the different networks or views of "Donation + Acceptance" (ranging from "cell- to DNA-centric") for the explanation of the phenomenon of "like-from-like" have to be regarded as admittedly very successful strategy or mechanism of mastering or suppression of contingency.

Thus, the acts of reductionism to a DNA network and elimination of other matter networks, such as "membrane landscapes", including of all human and non-human actors involved, respectively, may be interpreted as strategies or mechanisms of mastering or suppression of contingency which is caused by the apparent complexity and disorder of cells, as apparently manifested in their proteins, cytoplasmic content, organelles and membrane landscapes to scientists as well as laymen before the observation of bacterial transformation. The identification of a linear, regularly shaped macromolecule and unique polymer of high order, consisting of sequences of just four different building blocks and forming a simple double helix, i.e., the DNA, rather than of macromolecular complexes exhibiting a huge variety and number of three-dimensional conformations, sophisticated configurations and elaborated structures (as holds true for proteins, cytoplasm, organelles, membrane landscapes) as the only matter of biological inheritance led to a sudden and unexpected, but to the highly desired decrease in contingency and increase in order. Regarding biological inheritance, the stepwise transitions from the cell-specific via the other networks, to the DNA-specific network have seemingly paved the path to the generation and recognition of more phenomena in nature that proceed either necessarily or not at all and couldn't be otherwise.

Nevertheless, or even the more so, the identification of the nature of the matter excluded and the delineation of putative consequences for each of the relevant actors arising from the exclusion must be elucidated for each network transition, possibly or preferably with support of STS, in general, and ANT, in particular. This will provide initial evidence as to whether the processes of differentiation, of inclusion and exclusion, themselves are subject to contingency or could be explained adequately. However, in agreement with the principles of ANT it is not feasible and even not useful to try to unravel these networks regarding strict and unambiguous causal relationships, i.e. as the primary and secondary actors of effect and consequence (Latour, 1987). STS must focus solely on the description of the actors involved and of the network they form rather than to provide any evaluation and assessment of the contribution and impact of specific actors.

Each actor gains its agency solely through formation of a network with other actors (Latour, 1996). This process has been called translation. Four phases of translation can be discriminated which help to elucidate the integration of heterogeneous actors into a network: *Problematization*, *interessement*, *enrolment*, *mobilization* (Callon, 1986/2006): *Problematization* is the process in which a problem occurs and is also perceived as a problem (e.g., transfer of private property from parents to offspring). This also creates the certainty that there could be a solution to the problem that has arisen (e.g., of paternity by testing the matter of inheritance). This solution becomes a "portal" through which all stakeholders have to enter the process. *Interessement* is then the connection of different interests to this possible solution (e.g., BioTech companies engaged in PCR-based

paternity tests). *Enrolment* encompasses all the negotiation processes of convincing all actors of their participation in the solution (e.g., financial support for parents and BioTech companies), and *mobilization* is the communication of this collectivized conviction to the public (e.g., DNA as a more reliable substitute for blood to delineate kinship). All those actors mutually will become involved and integrated into the network if they are able to translate their requirements for each other. The foundations of the translation are, however, not defined or set a priori, but arise in the meaning of "emerge" during the translation. It's not about the creation of identities with regard to, for instance, "gemmules" (**Figure 1** and **Figure 2**), extracellular DNA and vesicles (**Figure 5**), micelle-like GPI-AP complexes (**Figure 6**) or "plasma membrane landscapes" (**Figure 7**), but about the recognition and acceptance of differences, small shifts that can (but don't have to) harmonize when translated. Along these philosophical axioms, Latour makes it clear (Latour, 1987) that he is guided by a Not-Kantian philosophy that even refers to the presocratic thinkers *via* Deleuze, Whitehead, Nietzsche, Leibnitz and Spinoza, and does not retreat behind the assumption of *a priori*-categories.

Accordingly, the phenomenon "biological inheritance" is generated by multiple networks and chains of transformation which must be documented and contextualized in a manner that enables "inheritance" to speak for itself, omitting any efforts to explain it on the basis of a predefined or set context. Studies taking into consideration some of the central aspects of STS and ANT and dealing with the phenomena of diabetes mellitus (Müller, 2016), health (Müller, 2017) and GPI-APs (Müller, 2018; Müller & Müller, 2023a) have already been published. No doubt, the "DNA-centric" network of inheritance is a very powerful one that has managed to displace all the previous networks mentioned above. Moreover and much more important with regard to future societal, political and ethical consequences, it led to the exclusion of specific actors from the inheritance network, among them the so-called "membrane landscapes". The reconstructed network of inheritance that considers "membrane landscapes" in addition to DNA and the other actors, the so-called "poly-matter network" of biological inheritance, will be described in another study (see G. A. Müller; manuscript submitted).

In agreement with ANT, it is not possible to decide a priori what actors are acting, and what of them are critical or not. Power and domination, which are characteristic of a specific network, can only be made visible with the aid of trials in the sense of try, search, and examine for spurs, marks, and inscriptions. Since those are in motion or exert impact, they will thereby (and only thereby) become detectable for the other actors. Scientific knowledge about biological inheritance originates from practical exercise, among them experiments (e.g., bacterial transformation), that is performed by actors of the corresponding network (i.e., F. Griffith, respectively) with the aid or despite the resistance of other actors (e.g., heat stability of DNA, heat lability of proteins) and that produces this knowledge as a result or "fact". In this sense, reality becomes realized, which ap-

parently represents a constructivistic rather than a social constructivistic approach. Practical exercises and realizations must not be considered as being performed solely by social actors, such as force and power, since this would result in impermissible reductions. The stabilization of the "DNA-centric" network of inheritance in the 2nd half of the 20th century was founded on the enlargement and empowerment of the agency (e.g., genetic engineering) and mobility (e.g., distribution of model organisms) of actors, which can only arise from their association or connection. Detailed descriptions of the (apparent differences between the) translation, i.e., of the *problematization*, *interessement*, *enrolment*, and *mobilization* processes, of the interacting human and non-human actors for the "DNA-centric" and "poly-matter network" conceptions of biological inheritance remains a desideratum for future STS.

Author's Contributions

100%.

Conflicts of Interest

The author declares that he has no financial interests.

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