Determining Sex/Gender: Genes and DNA Precisely Do Not Predict the Development of a Genital Tract…[1]

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Summary

Biological research of the past decades that attempted to attribute the determination of sex to only a few genes has failed. Neither the gene SRY (sex determining region on the Y chromosome) nor additively added genes led to a reasonably consistent and convincing understanding of sex determination. With complexity already being discussed for quite some time in the natural sciences and biology under the terms 'system organization theories' and 'system biology', this way of thinking is now gradually being embraced in biological sex and gender theories: it concerns the investigation of developments and processes whose outcome is not already presumed by researchers.

Introduction

Beginning with some historical observations this contribution offers an introduction into developmental thinking and, drawing on current theories of sex determination, identifies the potential of such observations for more complex and more convincing theories of sex/gender determination than those hitherto used. The emphasis on development, on developmental processes constitutes a departure from the notion of predetermining elements. Instead it is necessary to take the entire organism and its interdependencies with its environment into account. This means that from the perspective of current biological science the focus has to be on the communication between the various parts of the cell as

1 | Original version in German.

well as on the communication between different cells, their integration in the organism and the influencing factors from their environment. Genes and DNA precisely do not predict the developments of an organism or, in this case, of a genital tract. Instead they merely represent one among many factors in the complex interplay of cells.

Preformation or development – opposing concepts

The debate whether physical features are already preformed in the earliest stages of the embryo or only develop over time, so that one can observe an increasing complexity of the developing organism, has in the past shaped notions in natural philosophy, biology and medicine about embryonic development and continues to do so.

Already in Greek antiquity we find two different models regarding this issue. Drawing particularly on the atomist Leucippus of Miletus (around 460 BCE) and Democritus of Abdera (460-371 BCE), one school of thought assumed that the semen of the parents[2] contained extracts (atoms) of all parts of the body. According to this theory, arms, legs and other body parts were present in miniscule units and constituted the basic elements of an embryo. In the genitals these features would supposedly agglomerate, with the features of the corresponding atoms of the female and the male semen competing and the semen present in greater quantity and strength asserting itself. The embryo would in this way be preformed. This school of thought is also referred to as the theory of pangenesis. It also forms an important basis of the writings of Hippocrates[3], only that according to him the semen does not constitute itself from the atoms of the parts of the body, but rather from the body fluids and body tissues.

A contrary view associated particularly with the name of Diogenes of Apollonia (499/98-428/27 BCE) and Aristotle (384-322 BCE) was the haematogenous theory of reproduction. This theory posits that the semen is formed from blood. The semen would then not be the extract of the parents' body parts – as posited by the pangenesis theory – but there would occur a real transformation process from blood to semen. Aristotle attributed this process to heat by which blood is boiled down to semen. And here he saw a major difference between the sexes: thus only the man – and here also only one who is not too old, or too young, or too fat – would have commanded sufficient heat for boiling the blood to semen. The woman, by contrast, due to the greater frigidity Aristotle attributed to her, would only have been able to form an incomplete pre-stage of the semen, so-

2 | According to Leukippos and Democritos both women and men had semen.
3 | The Corpus Hippocraticum comprises writings from between the 4th and the 1st century BCE.

called catamenias. That the woman had, as he believed, no complete semen was one of the reasons for Aristotle to reject the pangenesis theory, because it did not explain the presence of the uterus.

The 18th century debate over the preformation theories of the ovists and animalculists on the one hand and the epigenesis on the other represented another crystallization point, where the theories of preformation and development (transformation or developmental processes) were discussed so prominently side by side. In the late 17th century the preformation theories emerged. These theories presumed that in either the female conception contribution – described by the ovists – or in the male contribution to conception – advanced by the animalculists – the individual was already preformed in miniature or that at least the extracts of all parts of the body were already present. The corresponding theories of the ovists are particularly associated with the names of Regnier de Graaf and Marcello Malphigi. Animalculism is fundamentally linked to the use of the microscope invented in that time. While examining a drop of male semen under the microscope Antoni van Leeuwenhoek and Nicolas Hartsoeker among others discovered a host of moving animalculi – little creatures, a meaning that is reflected in the term 'spermatozoa' still used today (see Illustration 1). The essential point of the preformation theories is that from the very beginning on the complete individual or all its parts are preformed in the egg or the semen, so that there is no real development but a mere increase in size.

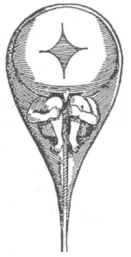

Illustration 1:
Preformation in the male semen, according to Nicolas Hartsoeker. (source: URL: http://www.hps.cam.ac.uk/visibleembroys/s1_4.html [04.07.2011]).

These preformation theories of the ovists and the animalculists fitted nicely into the prevailing social order and into society's established notions. It was presumed that a higher power – a god – had created the world at a particular point in time. Everything that existed, exists, or will ever exist can be attributed to this creator god. Correspondingly some scholars connected their theories on the preformation of the individual in the semen or egg with the Christian religious

notions of creation: Adam or Eve would already have contained all subsequently living human beings within themselves.

The preformation theories quickly became a target of criticism, since they did not serve to explain occurrences such as regeneration and the healing of wounds. This was illustrated by a popular experiment: if one cut a polyp (simple multicellular organism, Cnidaria) in half it was shown that overnight each of the two halves had formed a complete small polyp. These observations were hardly reconcilable with the assumption of a creator god. A further important point of criticism was that features of a child common to both parents could not be easily explained with the preformation theories or only in roundabout ways. Both points of criticism were repeatedly advanced by scholars of the time and ultimately had the effect that in the late 18th century developmental thinking, also regarding the views on embryonic development – epigenesis – gradually asserted itself.

Epigenesis no longer assumed that the individual was already completely preformed in miniscule units, with only a growth in size occurring, instead it was believed that first there was unformed matter from which only through developmental and differentiation processes increasingly complex, shaped matter developed. It was only as a result of these processes that body parts and organs of the embryo were formed. And neither would development have stopped with birth, instead transformations would have taken place all the time, and in this way regeneration and the healing of wounds would be possible. The detailed theory of epigenesis goes back to Caspar Friedrich Wolff – he described development and differentiation as necessary for embryonic development. While Wolff's ideas were first met with a guarded response, also because he analogized the force that was to fuel the development to other mechanical-physical forces, the epigenetic view gained currency with the observations advanced by Johann Friedrich Blumenbach. He had suggested a formation drive as the force fueling the development, in the sense of an activity that could only be performed by living things.

In the same way the preformation theories have to be considered against the background of social conditions, this applies to epigenesist as well. It is remarkable that as of the middle of the 18th century developmental thinking gained currency in all sectors of society. This was evident in scientific geographical and physical observations (genesis of the earth through cooling, electricity etc.), in philosophical descriptions (one now followed the theories of Spinoza, Spinozism) and even in theology (changes in the understanding of god, also drawing

on Spinozism). Last but not least the French Revolution made clear that social order too is not preordained by a god and thus unchangeable for human beings, but that society is shaped by human beings guided by reason. The importance of the transition to evolutionary ways of thinking has been variously emphasized in research, see for instance Lepenies 1978; Rheinberger 1981 and Engelhardt 1986. Alfred Schmidt (1984: 10) observed with a view to natural sciences: "The most important qualitatively new aspect of the situation forming around 1800 in the field of natural sciences is the ultimate triumph of evolutionary ways of thinking."

With evolutionary thinking to communalities of the sexes

The significance of evolutionary thinking should also not be underestimated for the biological-medical sex/gender theories. In the preformation theories the female and the male sex were presumed to make very different contributions to conception. The embryo was purported to be preformed in the conceptive matter of one sex, while the conceptive matter of the other sex fulfilled other functions. Both the ovists and the animalculists minimized the female contribution to conception. Thus even the ovists who believed the preformation to occur in the female egg held that the motive principle regarded as significant for development resided in the male semen. The animalculists reduced the female contribution to conception even further – it consisted, they said, solely in carrying and nourishing the embryo. On the basis of the descriptions of the conceptive matters further differences were identified. Also the places where eggs (ovaries) and semen (male testicles) agglomorated would have been different – up to the 17th century they had not even been differentiated terminologically, rather the term testicles was used both for the female and the male sex, even though individual differences were named. In addition there were supposed to be differences in the blood vessels supplying the ovaries and the testicles and in the vessels transporting the conceptive matter.

Further sex-related differences were identified for the genital tract, but particularly for breasts and pelvis. Developmental thinking reflects a significant change: epigenesis presupposed (mostly) equal contributions to conception by woman and man. Correspondingly one dispensed with differentiating terminologically between semen and egg or testicle and ovary and the conceptive matter of the woman and the man were both denoted as semen. But even though the terminological differentiation was retained by a few authors, it was still assumed that the contributions to conception were involved in equal measure in the

embryo and its development. Based on the mixed, combined contributions to conception it was thought that embryonic development would proceed via development and differentiation processes (see Voß 2011a: 85 ff., Voß 2011b).

If the preformation theories made it possible to link differential descriptions of additional features to the differences of contributions to conception, these became irrelevant with the assumption of (in most part) identical contributions. Now it was also possible to describe commonalities of the sexes regarding the places of formation, the incoming and outgoing vessels and other features of the genital tract. This is evident from a closer look at the works published around 1800. An example: The physician and professor of anatomy Jacob Fidelis Ackermann (Ackermann [1805] wrote in 1805: "Each individual can potentially contain the conceptive parts [genitalia] of both sexes"; later he added:

> "From the presented description of the conceptive parts [genitalia] it is evident that in every individual both kinds of genital organs are present (in their rudiments), but that only one sex emerges outright and that the penis is analogue to the clitoris, the prostate to the uterus, the urethra to the vagina, the testicle to the ovary, the ductus deferens [carrying-away duct] to the tubes [Fallopian tubes: oviducts, footnote, HV], the scrotum to the external labia."

Even though Ackermann differentiates here between the female and male genital tracts – this is already clear from the differentiating terms –,something else seems to have been important to him, namely the similarities of the organs of the female and male sex. He builds on the assumption that every embryo initially, i.e. in the first stages of development, contains both genitals and only with further development and differentiation a more or less unambiguous sex emerges. This observation is by no means trivial but marks a significant change of perspective: every embryo would at first have the potential to develop either into a female or a male direction. Sex-related differences could therefore not be fundamental but merely relative. They would not be describable as being radically different, as an either-or, like recent sex/gender research has identified for the biological-medical sex/gender theories since the 18th century, but would move within the framework of a temporal relative or a more-or-less. This was far from being a minority view. It is found both in the works of the Romantic natural science and the speculative natural philosophy but also in empirically oriented authors such as Ackermann. In the course of the 19th century this theory became the dominant perspective of those who concerned themselves in biology and medicine with the development of sex in embryonic development. The contro-

versy was carried out on an entirely different level. The debate was over whether in these sex-related rudiments, which had the potential to develop both as female and male, the points of departure for both sexes would be present one next to the other (which would make them hermaphrodite) or whether both sexes had a common point of departure which then differentiated in different directions (and more or less unambiguously). A quote by the physician Heinrich Wilhelm Gottfried Waldeyer (later Waldeyer-Hartz; Waldeyer 1870: 152 f.) illustrates the self-evident way in which the embryo's initially both female and male potential is propounded as well as the point of controversy described above:

"But a different point, also not insignificant for teratology [study of abnormalities of physical development, footnote HV], follows with certainty from the observed, namely that the primordial disposition of the individual even in the highest vertebrates is a hermaphroditic one. Until now one has attempted to interpret the strange comportment of the genitals in their initial development in such a way that a neutral common, indifferent condition as it were would exist, from which development proceeded either to one side or the other, so that sometimes a male and sometimes a female individual is created. But here one has relied far too much on the comportment of minor things, for instance that of the external genitals. Here indeed there exists an indifferent, neutral primordial condition as it were, which then evolves either towards the male or the female side. This can however be nosurpriseto us since we have in the external genitalia of both the man and the woman anatomically the same structures that only develop in the different individuals in different directions. […] But if one looks at the development of those structures which constitute the nature of the two sexes, the two gonads, then an indifferent, neutral, as it were, primordial dispositionis difficult to envisage.[4][…]; in other words, every individual is on a certain level of their development a true hermaphrodite."

Today, too, the view that the genital furrow or the genital ridge (the first cells from which the genital tract evolves during embryonic development) has the potential to develop both in a female and a male direction is still the dominant position in developmental biology.

Every human being is both female and male at the same time

Others went even further. They held the view that this condition in which female and male appeared together is not limited to the embryo or the early stages of the embryo, but that human beings combine female and male features within themselves all their lives. This view too was not altogether new –a tradition for

4 | Other authors were not of this opinion, which probably led Waldeyer to explicitly address this subject. The works of the medically trained publicist Johanna Elberskirchen, who also contradicted Waldeyer's view, are of interest in this context (see Leidinger 2008, Voß 2011a: 97f., Voß 2011b).

this perspective in terms of intellectual history emerges for instance with respect to the spherical people in Aristophanes' speech in Plato's Symposium and with the Chinese notions of Yin and Yang (see Römer 1903; Neuer Berliner Kunstverein 1986). Descriptions that every embryo has the potential both for female as well as male development and that the first stages of development are sex-related indifferent enabled science to tie into these traditions. One of the representatives for such a perspective around 1800 is Wilhelm von Humboldt, particularly known for his theoretical writings on linguistics, but who was also interested in natural philosophy and attended lectures on his subject (also see: Rosenstrauch 2009: 100, 107 ff). Humboldt wrote:

> "But the supreme and consummate beauty not only requires unification but the most precise balance of form and material, of artifice and freedom, of mental and sensual unity, and this one only achieves if one welds together the characteristic of both sexes/genders in one's thoughts and forms humanity from the most intimate union of pure masculinity and pure femininity. But to even find such pure masculinity and femininity is inordinately difficult, and from experience well-nigh impossible." (Humboldt 1959b [1795]: 81)

A little later he adds (Humboldt 1959b [1795]: 102): "Of these two characteristic features of the human form, whose specific difference disappears in the unity of the ideal, there rules in every sex preferably one, while the other is in no way lacking."

Manfred Herzer has suggested in initial overview research that such a view had established itself by around 1800 and at the end of the 19th century represented a common notion in the Bildungsbürgertum[5] (see Herzer 1998). With this Herzer contradicted the representation that observations describing human beings as mixtures of female and male parts had only emerged and gained a certain currency around 1900.This understanding was induced by the vehement controversies over the publication of "Sex and Character" ("Geschlecht und Charakter") by the young and also medically trained Viennese philosopher Otto Weininger. In this otherwise deeply anti-Semitic (Weininger was himself a Jew who converted to Protestantism in 1902) and antifeminist essay Weininger had also propounded that every human being represented a mixture of female and male features. There were (also) vehement objections against this view – for instance by the antifeminist Leipzig-based neurologist Julius Möbius, already controversial in his lifetime, and by the women's rights activist Grete Mei-

5 | Briefly, a 'Bildungsbürger' was a member of the pre-war bourgeois German elite whose status was marked less by birth than by a solid classical education.

sel-Heß, trained in philosophy, sociology and biology (see Voß 2010: 186, 355 f.). More interesting, however, is that controversies unfolded over who had been the first to advance this theory. Wilhelm Fließ, Otto Weininger, Hermann Swoboda and Sigmund Freud were involved in the controversies over priority. Magnus Hirschfeld also joined the fray, but without claiming priority. But Weininger had already acknowledged the tradition right at the beginning of his observations, thus preempting the senselessness of such a debate over priority:

"The idea of this kind of bisexuality of all living things (as a result of the never perfectly complete sex-related differentiation) is very ancient. Maybe it has not been alien to Chinese myths; in any case it was very much alive in Greece. The personification of the hermaphrodite as a mythological figure testifies to this; as does the account of Aristophanes in Plato's Symposium; indeed, even in later times the gnostic sect of the Ophites considered the primeval human being to be male/female."[6]

Chromosomes, hormones, sex/gender

If the historical observations from developmental biology have shown that these in no way strictly differentiated between female and male sex-related development, but that rather commonality and sameness was central to the debate, then what is irritating today is the self-assuredness with which a strict two-gender difference is presumed, partly with reference to (supposedly) biological findings. Even though in the early 20th century differences in the chromosome sets between female and male individuals were also observed, influential biologists of the time concluded that on the level of the actually developed appearance (in the so-called phenotypical features) an uninterrupted series of transitions between male and female of all sex-related features would show. Chromosomes were first examined in various species of insects, showing that in certain species a chromosome could be lacking in one of the sexes that was present in the other, and that in other species one of the sexes displayed a chromosome that had a different size and structure than in the other sex, and in 1923 corresponding descriptions were carried out for human beings by Theophilus Shickel Painter. He concluded that in human beings all male individuals had each one X and one Y chromosome, and all female individuals had two X chromosomes.[7] These de-

6 | Weininger himself had thoroughly revised the 1st edition published in 1903, so that the 2nd edition constituted a changed version. While contemporary critique reacted almost exclusively to the revised version, the reprint from 1980 used the 1st edition making it available to modern research. The textual differences are often not observed. For the textual differences see Hirsch 1994.

7 | They were termed Xand Y at the beginning of the 20th century (1905 and 1910) by Edmund Beecher Wilson and Nettie Maria Stevens.

scriptions however in no way contradicted the assumption of an uninterrupted series of transitions. Richard Goldschmidt described such transitions, based on the assumption that chromosomally there existed two sex variants. He argued that the sex development of an individual depended on the quantitative and temporal distribution of the female and the male factor. These factors were said to be formative substances for the sex, with the gene's effect always ensuing via formative substances which in this case would be hormones.[8] While often one of these sex-related factors predominated permanently in an individual, these could also change. This development would then for instance be marked by the predominant male factor and would then continue in a female direction, because the female factor would then predominate. Goldschmidt described the point of reversal as the turning point. The point when the reversal occurred determined the degree of development of femininity or masculinity in the corresponding individual (see e.g. Goldschmidt 1927: 10-37; Goldschmidt 1931: 1-16). An unambiguous chromosomal attribution was thus compatible with a very variably perceived appearance of phenotypical features in the individuals of one species – and also in human beings.

Already at the beginning of the 20th century also regarding hormones research findings were by no means clear-cut. Rather, experiments showed that it was impossible to separate hormones considered as sex-related according to female or male organisms of origin unambiguously. Bernhard Zondek was one of the important representatives of hormone research. He was able to detect in the urine of the male horse (stallion) a surprising amount of estrogen, a hormone then defined as female. These findings and also others published in the journal "Nature"cast doubt among researchers and fundamentally questioned the unisex effect of hormones(see Oudshoorn 1994: 24 ff.; Sengoopta 2006: 117 ff.; Satzinger 2009: 295, 376 f.).

However, political developments prevented such findings pointing more to complexity and multi-causality from being followed up on both in genetic and in hormone research. Their protagonists Goldschmidt and Zondek were Jewish scientists in the German Reich. Both were forced to emigrate in the 1930s from Nazi Germany and no longer found such favourable conditions for continuing their research (see Satzinger 2009). At the same time other concepts were pursued– simpler concepts of the effect of genes in the US with which Goldschmidt's models competed. The curtailing of research opportunities had a disadvantageous effect on this competition and impeded the reception of Gold-

8 | The term 'hormone' was coined in 1905 by Ernest Henry Starling for substances that are transported via the blood from the place of their formation to the place of their effect.

schmidt's ideas also beyond Germany. On the other hand, the Nazis took over the lead in research, also regarding biological sex theories. Thus Adolf Butenandt became director of the Kaiser Wilhelm Institute for Biochemistry in 1936. He was an advocate of a clear distribution of roles between woman and man propagated by the Nazis and also in hormone research represented the theory of the clear sex separation of female and male hormones (see Satzinger 2009). Although his hormone research yielded contradictory results, he did not discuss these and simply excluded them in his publications (Satzinger 2009: 388 f.). Helga Satzinger wrote about his work: "His concept of sex closed itself to scientific counter-arguments which at that time were formulated primarily by Jewisch scientists." (Satzinger 2009: 295 f.) Satzinger also emphasized his anti-Semitism; "which was used, whenever convenient, to discredit a scientific opponent" (Satzinger 2009: 296). A letter to his mother from 1930 already reveals Butenandt's anti-Semitic stance with regard to Bernhard Zondek: "The only discordant note was injected by Zondek – a very despicable Jew! – who, with a certain arrogance and in an ironic tone, attempted to denigrate my work and its validity. I gave a retort that made the audience laugh heartily and rendered Mister Zondek subsequently speechless!" (quoted from Satzinger 2009: 293).

Later Butenandt made a career for himself in the Federal Republic of Germany and continued to dominate research, including as president of the Max Planck Society. Helga Satzinger (2009: 399) summarizes the significance of the political events and their effect on scientific knowledge with focus on biological gender theories: "In the preceding years the concept of genes and hormones causing fluctuation between and mixing of the sexes had been widely discussed, and the dominance of the bipolar model did not establish itself until the 1930s owing to the absence of the representatives of the former model, who were forced to emigrate."

Current theories of sex/gender determination – including multicausality

So now the biological sex/gender model that came to establish itself – at first almost unchallenged – was a strictly bipolar one. Here one drew on Painter's descriptions of a homologous chromosome combination of two X chromosomes for the female sex and a heterologous combination of an X and a Y chromosome for the male sex in the human being. The fact that the heterologous chromosome combination showed itself in the male sex, thus that the Y chromosome appeared here as a special factor, led to the assumption that the Y chromosome

represented the deciding factor in the determination of sex. While a female genital tract would form as a general development without the Y chromosome, it was believed that for a male genital tract to form an active developmental step was necessary. This orientation towards chromosomes was connected with the view that testicles were particularly significant for the development of the male sex – and the differentiation of the sexes in general. Since the late 18th century testicles had been in the focus of research as the masculinizing organs par excellence. They were thought to induce the male formation of physical and physiological features, some authors also emphasized their significance for the development of psychological features and (im-)mortal capabilities. Only a little later, since the beginning of the 19th century, did various authors with a similar range also describe ovaries (or female testicles) as important for the forming of the female sex. That the female sex was considered to be temporally delayed was a commonly held view in observations on sex/gender in biological-medical science. One attempted to explain the pre-existing order of the sexes/genders in society – and there the men dominated; it was necessary to find a scientific justification for their dominant position. While there were intense debates about this in the 19th and early 20th centuries, the assumption of a far-reaching and, in contrast to ovaries, exclusive significance of the testicles dominated research since the middle of the 20th century. This was in particular a result of experiments undertaken by Alfred Jost at the end of the 1940s and their reception. He had removed the gonads of rabbit embryos in early stages of embryonic development and subsequently observed a consistently female development, regardless of which chromosome combinations there were. Thus the view established itself that for male development gonads (testicles) were necessary as an active developmental step, whereas female development would merely take its course – passively (for a detailed discussion see Voß 2010: 245 ff.).

Focusing on the X and Y chromosomes in connection with the emphasis on the testicles shaped the research of the following decades in two ways: on the one hand the Y chromosome was now the unique object of focus and identified as the factor that activated the development of the testicles, on the other hand, in the following decades only male development was investigated. This androcentric focus was only tempered in the 1980s by an essay by the geneticists Eva M. Eicher and Linda L. Washburn. They explained simply and convincingly that ovaries too are very complex organs, so that there was no reason to assume that these could simply come about, without an active developmental step (Eicher et al. 1986). Now also female development came to the attention of research.

In 1966 the search on the Y chromosome was narrowed down to the short arm of the Y chromosome. There one searched for the gene that would cause the formation of the testicles, the so-called testis determining factor). Various authors successively proposed different genes. However, their significance as a testis determining factor had to be ruled out repeatedly, because the postulated gene turned out to be either missing in cases where testes had formed nevertheless, or that no testes had formed despite the gene being present, or that it was detected in so many copies in the human being's overall set of chromosomes (or the gene's homologue in the set of chromosomes of mice) that a significance limited only to the formation of testes was unlikely. Finally, in 1990 the gene Sry was suggested as the testis determining factor. It is currently still frequently described as the most significant factor of sex determination, even though here too contradictory results soon appeared: in some cases testes developed in its absence and in other cases they did not develop despite Sry being present. Also for the female development various genes have been suggested since the late 1980s which were believed to activate the formation of ovaries in the sense of an ovaries determining factor. One of the genes currently being discussed in this respect is Dax1 that can be located regularly on the X chromosome (dosage-sensitive sex reversal, adrenal hypoplasia congenital, critical region on the X chromosome). But here, too, contradictory findings quickly appeared (for a detailed discussion see: Voß 2010: 245 ff.).

In recent decades the contradictions that showed up in the findings have resulted in simple models of gene effects being increasingly discarded also in biological research on sex/gender determination. While for a long time the understanding predominated that one single gene was responsible for the formation of a complex organ structure – like the ovaries and testes – today one tends to favour the view that a network of various genes and other factors are necessary for the formation of testes or ovaries. Meanwhile around 1.000 genes are described as expressed in the corresponding phases of embryonic development. For around 80 of these there is at least some degree of, by no means consistent, evidence.

At this point already one basic element of multicausality becomes clear: many genes and their products interact in networks. They are expressed in differing degrees in terms of time and space. And the expression in no way differs according to sex – the popularly held belief that in one sex a gene is expressed and in the other not is wrong. Rather, all genes both in the individuals regarded as female and those regarded as male are, as a rule, expressed. Differences can only be detected in the quantity and the temporality of expression – and these

differences are in no way to be understood as sex-related. The differences are as a rule significantly greater within one group – for instance between the single individuals in the male group – than the differences that can be measured between the groups of female and male individuals. This is an indication that individuality has been a significant, long neglected factor. Thus, in every individual manifold genes, their products and additional factors interact in specific ways in quantitative and temporal terms. Even when a gene which is present in other individuals is absent, structures similar to the other individuals can come about by the gene's effect being substituted by other genes. But this can also explain the individual differences of appearance between human beings – they could be adduced to individual differences of expression. A final observation should suffice on the genetic level: just as we meanwhile know that the XX chromosome combination and the XY chromosome combination are by no means the only existing possibilities of combining the sex-related chromosomes X and Y, but that also the combinations X0, XXY, XXXY etc. occur, and that a set of chromosomes regarded as typically female can combine with an appearance (so-called XX men) regarded as typically male, and a set of chromosomes regarded as typically male can combine with an appearance (so-called XY women) regarded as typically female, so we should fundamentally question the labeling of X and Y as sex-related chromosomes and their differentiation from the other chromosomes. For most of the 1.000 genes that are described as being possibly involved in the formation of the genital tract, do regularly precisely not appear on the chromosomes X or Y, but on the others, the autosomes. In fact only very few of these genes are regularly localized on the X or Y chromosomes, so that already labeling these chromosomes as sex-related chromosomes is misleading (for a detailed discussion see Voß 2010: 283 ff.).

It has become clear so far that with the new findings we arrive also in terms of chromosomes and genes at complex and individual possibilities for the formation of sex. But with that we still remain on this chromosomal and genetic level, a two-dimensional level, according to which, as repeatedly explained, the genes would already contain all information necessary for the formation of an organism. But an approach that accords chromosomes and genes the crucial role, that decouples them from the cells, the organism and surrounding factors, or only describes these factors merely as subordinate auxiliaries – as slaves of the genes –constitutes a too simple and meanwhile already disproven view. It would be comparable to the preformationist theories of the ovists and animalculists and the pangenesis theory – development would be pure

development of already existing information, processuality would be ignored, influences of surrounding factors would remain excluded. As described above there were, on the one hand, political and societal reasons for the focus on genes, to the detriment of cellular and organismic factors, on the other hand, the decryption of the structure of the genetic material DNA (deoxyribonucleic acid) by James D. Watson and Francis Crick in the 1950s, based in particular on the findings of the X-ray analyses performed by Rosalind Franklin, led to the assumption that with DNA one had now found the key to life. Funding programs conducted subsequently favoured gene research, while research focusing on further cellular and organismic factors became marginal and had to make do with relatively little funding.[9]

Meanwhile there is a rethinking process underway. It is assumed now that genes and their products operate in networks. At the same time, the results of the human genome project aimed at determining the base sequence of the entire human chromosome set were somewhat sobering: The number of genes in humans is probably not significantly higher than that of the unremarkable barely 1mm long nematode Caenorhabditis elegans. Thus other factors have moved more into the foreground – factors of the cell which make it possible in the first place that a concrete product is created from a DNA sequence (from a gene) which can then take effect in the cell. Observations on this subject are also by no means new – every student of biology and biochemistry gets to learn something about processes such as transcription, transcriptional modification, transport mechanisms, translation, and translational modifications. However these subjects are rarely followed up on their implications: If this processuality and its multi-phased cellular regulation is taken seriously then the significance of DNA, of the genes becomes a relative one. Apparently complex cellular regulation is required for the approx. 2% coding regions – i.e. which represent something like genes to be selected from the DNA sequence. On the way from the gene (of the DNA sequence) to the product actually effective in the cell, sequence changes occur directly, with various chemical molecules being taken up and the spatial structure of the forming molecule produced and actively regulated. It is only in this way that the product is formed which then takes specific effect in the cell (for a detailed discussion see: Voß 2010: 283 ff.).

DNA does thus not merely constitute a piece of information that only needs to be read. Rather, it is only in embryonic development that a specific unit of information is produced through cellular processes, embedded in the entire organism and dependent on parental influences and those of the wider environ-

9 | See for instance the epigenetic research by Conrad Hall Waddington which was successful, but did not receive the same attention as the findings of genetics (Slack 2002, Speybroeck 2002: 61 ff.).

ment, using a DNA sequence. Which DNA sequence is expressed and which product is formed from it depends on cellular processes – in which numerous factors are involved that are regulated in a complex way – and is sensitive to surrounding influences for instance from the parental organism and the wider environment.

This contribution has made clear that sex development – the focus was on sex determination– proceeds in a variable way. Numerous factors are involved, it ensues processually and the result is at no point predetermined. The popular belief that as a result of sex development only the two forms of the genital tract result in male or female is, after an analysis of current biological and medical research, no longer tenable.

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