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Sex Determination and the Human Person

MYRON A. PENNER
Trinity Western University
myron.penner@twu.ca

APRIL M. CORDERO
Point Loma Nazarene University
acordero@pointloma.edu

AMANDA J. NICHOLS
Oklahoma University
amanda.nichols@oc.edu

Abstract: For many species that reproduce sexually, how sex is expressed at different points across lifespan is highly contingent and dependent on various environmental factors. For example, in many species of fish, environmental cues can trigger a natural process of sex transition where a female transitions to male. For many species of turtle, incubation temperature influences the likelihood that turtle eggs will hatch males or females. What is the case for *Homo sapiens*? Is human sex expression influenced by contingent environmental factors like we see in fish and turtles, with whom we share common ancestry and DNA? Our paper explores the current biological science of sex determination and how it applies to philosophical and theological accounts of the human person. We argue that while human sex determination is not susceptible to environmental cues to the same degree we see in other species, there is sufficient variability among the pathways of human sex development to complicate simplistic biological categories of male and female.

Keywords: Sex, Sex determination, Sex transition, Gender essentialism, Persons

Introduction

This paper applies current scientific understanding of the ways sex determination can occur in *Homo sapiens* to a philosophical and theological understanding of human persons.[1] We seek to present science-informed data for a narrow slice of philosophical and theological anthropology and demonstrate how the biological variance of sex expression in *Homo Sapiens* can contribute to understanding what it means to be human. More specifically, we will argue that sex determination science supports two conclusions significant for philosophical and theological anthropology. First, human biological sex is *contingent*: for any human person *S*, the biological features that constitute sex expression for *S* could have been otherwise. Second, humans possess a degree of genetic infrastructure to express sex differently throughout lifespan: for example, humans who follow a typical pathway of male sex determination possess some genetic infrastructure for female sex expression throughout lifespan. And similarly, humans who follow a typical pathway of female sex determination possess some genetic infrastructure for male sex expression throughout lifespan. We conclude that these two features of human biology undermine any biologically based gender-essentialism.

We proceed as follows. First, we outline a few preliminary concepts that will be important for presenting and interpreting the scientific information we introduce throughout, as well as for the applications we develop in the final section. Second, we survey and describe both typical and non-typical developmental pathways for sex development in humans. Third, we apply current science to answer the initial question that motivated our research: are there physically possible scenarios for human embryos where changing environmental factors in utero would have resulted in an expression of sex different from how sex was expressed without the environmental intervention? And fourth, we apply our current understanding of sex determination, including our best answers to the central question addressed in the previous section, to some philosophical and theological issues relevant for understanding human persons.

1. Preliminaries

On Science-Engaged Theology

We are a multidisciplinary team with two natural scientists (Cordero in biology, Nichols in chemistry) and a philosopher (Penner). While none of us is an academic theologian per se, Penner has experience in philosophical approaches to theology as well as in philosophy of science. Both Cordero and Nichols are natural scientists

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[1] "Sex determination" refers to the process by which gonads develop into either ovaries or testes (Schnebly 2021).

who have experience collaborating with theologians and philosophers in thinking about the scientific enterprise, as well as how science (conceived of as both a set of claims about the world and as a set of methods for investigating the world) connects to theological understanding, and vice versa. Moreover, each of us identify as Christian and are motivated to integrate our best information across disciplines into a unified theological narrative. As such, we have the following approach to science-engaged theology.

In terms of epistemological resources for theology, we adopt a domain-specific, non-hierarchical version of the Wesleyan Quadrilateral. That is, we acknowledge that in addition to scriptural texts, reason (including science), experience, and tradition are also domains of epistemic authority for theological reflection. By "domain-specific" we mean that each point on the quadrilateral has its specific area of expertise. In very general terms, the expertise of scripture is to present the experience of a people formed by their interaction with, and response to, the God of the Bible–including the experience of the people formed by their interaction with, and response to, Jesus of Nazareth. The expertise of reason, including science, is using our best tools of observation and inference to inform beliefs, explanations, models, and understanding of the world. The expertise of subjective experience is to provide a first-person perspective on the world. And the expertise of the Christian tradition is to provide historical wisdom and perspectives on the nature of faith. It makes sense to separate scripture, reason, experience and tradition when describing their particular domains of expertise, but that shouldn't lead one to think that each domain is isolated from the others. Rather, there is substantial overlap. Scriptural texts, for example, are neither produced nor interpreted without the influence of experience (of both authors/editors, and interpreters) and tradition.

By "non-hierarchical" we mean that no specific point in the quadrilateral is epistemologically superior to the other points simply by definition. For example, it would be an epistemological mistake to give scriptural texts epistemic authority over scientific methods and practice if, say, one was investigating the chemical composition of stars in a distant galaxy. Similarly, it would be an epistemological mistake to give tradition unquestioned authority about how to best interpret scripture or experience. Our understanding of theological method involves letting the appropriate domain "take the lead" in responding to theological questions, depending on the content and the context. Thus, for some but not all theological questions, scripture will have the most normative force. And, for some but not all theological questions, science will have the most normative force. So too with experience. Although our take on the Wesleyan quadrilateral is non-hierarchical, we do employ a division between the four domains. We see scripture, reason, and experience as first-order domains for theological authority and tradition as a second-order domain. This is because we see tradition as reflecting how people in times and places other than one's own have engaged the primary domains of scripture, reason, and experience. We agree with the twentieth century Rabbi Mordecai Kaplan who said, "The ancient authorities are entitled to a vote, not a veto" (Kaplan 1966, 263).

Based on the preceding perspective on epistemological authorities relevant for theological reflection, we see science-engaged theology as letting science (as an expression of reason) take the lead in providing data to address theological questions that concern the nature and functioning of biological organisms and physical systems. As a result, in order to understand and connect the ways in which biological sex expression is connected to our philosophical and theological understanding of human persons, the place to start for understanding how sex is expressed in humans is biology, not the Bible.

Biology, Sex, and Gender

One challenge for both specialists and non-specialists in reading biological science material, whether that material is from textbooks, journal articles, laboratory websites, and the like, is that terms are not always used consistently across times and formats. Sometimes what a term means changes over time because as new discoveries are made–sometimes quite rapidly–scientists in later eras will use a term common to biologists but give it a different or more precise meaning. Another challenge is that sometimes biologists will use a simple shorthand term of convenience to describe a more complex and nuanced concept or process, assuming that specialists will make the necessary caveats; the danger here is that non-specialists reading the simpler term might mistakenly take the biological content at face value, without the necessary caveats. And finally, another challenge both for specialists but particularly for non-specialists is that biologists themselves are not always uniform: they sometimes differ with respect to the terms that they use and the comfort levels they have in using shorthand terms of convenience. These difficulties can be compounded when specialists in disciplines other than biology refer to biological concepts.

Consider the terms "biological male," "biological female," and the broader category of "biological sex." In humanities contexts, these terms are sometimes used to distinguish anatomical and physiological aspects of human biology typically important for reproduction from more socially constructed concept terms like "man," "woman," and the broader concept of "gender."[2] Moreover, as Katrina Karkazis (2019) notes, in political contexts, "biological sex" (and related sub-categories of "biological male" and "biological female") can be used by policy makers to justify exclusionary practices based on allegedly clear and irrefutable science that distinguishes "biological male" from "biological female." However, such "clarity," is achieved by selecting only some of the biological factors relevant for sex determination, dismissing others, and ignoring cases where the selected factors do not apply. Says Karzakis (2019, 1899), "[t]his intentional gerrymandering of sex opportunistically uses the idea of "biological sex"—which lends a veneer of science and thus rationality to any definition—to remove certain individuals from a category based on intolerance." It is natural for people outside of biology who want to understand our sexed existence, and the relationship if any there may be between sex and gender, to look to biology for neat and tidy descriptions of "biological male and female." But the reality is that biologists tend to not operationalize categories of "male" and "female" in ways that will satisfy a quest for clear, distinct, and universally applicable definitions.

For biologists, the more general, conceptual starting point is not sex, but reproduction. Reproduction, of course, is the process by which members of a species replicate, bringing about new members of the species. Some species reproduce sexually, and some reproduce asexually. In species that reproduce sexually, genetic material from two types of reproductive cells ("gametes") combine to form a new member of the species that begins as a single-celled zygote. In most species that reproduce sexually, the two types of gametes necessary for reproduction are produced by members of two, biologically distinguishable subsets of the species. For example, a typical mammal species will have one subset of the species that produces smaller gametes ("sperm") and another subset that produces larger gametes ("eggs"). However, not all species that reproduce sexually do so by combining gametes from members of two distinct subsets of the species. For example, an individual earthworm produces both the large and small gametes necessary for reproduction. And as we will see below, for species of fish like the blue headed wrasse, some members of the species can produce eggs at one point in lifespan, and then transition at a later point in lifespan to produce sperm.

Notice that at no point in the preceding paragraph did we use the terms "male" or "female," when discussing reproduction in general and sexual reproduction in particular. In fact, it is possible that introducing those terms would have obscured

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[2] This is not to say that the biological terms themselves are contextless and free from social influence (Fausto-Sterling 2020).

the more general points being made about the variability of how gametes are produced among species that reproduce sexually. Nonetheless, it does make sense when talking about specific populations of sexually reproducing species to use "female" as shorthand for "members of the species who produce the larger gametes necessary for reproduction," and to use "male" as shorthand for "members of the species who produce the smaller gametes necessary for reproduction." That is, it makes sense to do so with the caveats that "male" and "female" do not refer to, and thus should not be thought of, as universal, fixed, distinct, and comprehensive sub-populations across species. And it does make sense in some contexts, when talking about *Homo Sapiens*, to use "female" as shorthand for "members of the species who produce the larger gametes necessary for reproduction," and to use "male" as shorthand for "members of the species who produce the smaller gametes necessary for reproduction" with the preceding caveat about these terms not being fixed and universal across species in view. Moreover, an additional biological caveat when using "female" and "male" in reference to *Homo sapiens* is the recognition that while there are typical developmental pathways involving a range of factors that enable gamete production within the species, there is also a range of non-typical developmental pathways such that in those instances, the convenient shorthand terms do not easily apply. All of this to say that when we use "male" and "female" in what follows, we are meaning them as terms of convenient shorthand with the previous caveats in mind.

While this paper focuses on sex determination, and specifically genetics, gonads, and genitalia (Joel 2012), it is worth noting that much research in human biology suggests a relatively low degree of sexual dimorphism (the degree to which sex-specific traits other than genitalia differ within a species). However, one can mine data for male-female group differences leading to false positives and reporting bias, including unjustified emphasis on marginal findings and post hoc rationalization for differences (Eliot, Ahmed, Khan & Patel 2021; Maney 2014; Rippon, Eliot, Genon & Joel 2021). Consider brain development for example. A popularly held assumption asserts that male and female brains are markedly different. Research refutes this claim showing that human brains are a *mosaic* of male and female characteristics (Eliot, et.al., 2021; Joel 2015; Joel 2021). The data show that "brains of men and women do not belong to two distinct categories nor are aligned along a female-male continuum" (Joel 2021, 166). While one's sex has an influence on brain development, binary sexed categories provide little if any information about the structure of an individual's brain. DuBois and Shattuck-Heidorn (2021) also challenge the notion of binary male-female categories with respect to gonadal hormones, secondary sex characteristics, and neuroanatomy. They argue, for example, that there is significant variation in gonadal hormone levels in relation to diet, activity level, body fat, and many other factors, and that "estrogens and testosterone play an important role in the biologies of people, regardless of sex assigned at birth or gender identity" (DuBois and Shattuck-Heidorn 2021, 6). Similarly, Shattuck-Heidorn, Danielsen, Gompers, Dov Bruch, Shao, Boulicault, Marsella & Richardson (2021) show that the research on sex differences in Covid 19 outcomes are unsupported by the data. All of these studies reveal that while gonads and genitalia are typically dimorphic, the sexed-binary framework is not a fruitful approach for explaining all human biological traits.

Notice also thus far that we have restricted our discussion mainly to biological aspects of sex, and have not addressed issues relevant to the social and cultural constructs of gender. That is because doing so is beyond much of the scope of our paper. The main focus of our paper is to reflect philosophically and theologically on data from the biological science of sex determination in humans. We trust that the philosophical and theological conclusions we draw based on the science of sex determination will be applicable to facets of philosophical and theological reflection on gender given the complicated and nuanced perceived relationship between gender and biology. While making extensive application from the biology of sex to discussions of gender is beyond much of what we set out to do here, in our concluding section we do make one such application where we critique biology based gender essentialism.

Essence, Contingence, Fish, and Turtles

There are many species for which sex determination is highly contingent on a range of environmental factors. That is, there are many species for which whether or not a member of that species expresses sex as male or female at a given time depends on a particular arrangement of environmental factors. Moreover, the sex expressed by individual members of these species could have been different than what is actually being expressed, and can transition naturally across lifespan from one sex to another. For these species, the expression of sex is a contingent, not essential property. We'll discuss some specific examples of this shortly, but first a little metaphysical housekeeping.

We use "contingent property" to refer to a property or feature that a thing can have in some scenarios, but fail to have in other scenarios possible for them. We use "essential property" to refer to a property or feature that a thing must have in every scenario possible for them–if *P* is an essential property of *X*, every time and place *X* is, *X* exemplifies *P*. We leave it to the reader to fill out the metaphysical backstory for understanding the concepts of "property exemplification" and "possible scenarios" according to their preferred metaphysical account of these phenomena. We will use the language of "possible worlds" as a convenient shorthand for complete possible scenarios. As such, we'll talk of an essential property of *X* as a property *X* has in every possible world in which *X* exists, and we'll talk of a contingent property of *X* as a property *X* has in some possible world but not in every possible world in which *X* exists. But there are other equivalent ways of referring to the relevant modal concepts, and we make no claim about whether possible worlds are concrete entities, abstract objects, combinations of metaphysical simples, or can be understood in some other way.[3]

Let's apply these modal concepts to actual world examples. Note that many species of reef fishes can change their sex between male and female during their lifetime, and blue headed wrasse is one such example. Differentiation between male and female depends on external factors such as reef size and ratio of males to females. There are two types of blue headed wrasse males: initial phase (IP) and terminal phase (TP), and all blue headed wrasse fish are born either as females or IP males. While females and IP male gonads differ (females have ovaries and IP males have testes), both sexes are morphologically similar and have yellow cigar-shaped bodies. On smaller reefs, most of the fish are female while on larger reefs, there's roughly a 50/50 split between females and IP males. In some cases, there can be harems of females with one TP male.[4] When this TP male is absent or not dominant enough, one IP male can join the population and transition to a TP male, or one of the females can begin the process of a sex change. In this latter case, behavioral changes are observed first as the female acts like a territorial TP male. Within 8-10 days, there is complete gonadal and morphological change where the formerly female fish now has testes, can fertilize eggs, and looks like other TP males with larger, blue bodies. Blue headed wrasse are one example of organisms for which, due to their "highly competitive, complex, social groups, it is critical for individuals to rapidly assert and maintain behavioral dominance in order to achieve gonadal/morphological changes that lead to higher reproductive success" (Lamm et al 2015, 2).

Sex determination being influenced by the environment is not just seen in fish. The red-eared slider turtle is another example of an organism where the

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[3] For an excellent survey of different views on possible worlds, see Menzel 2021.

[4] Reproduction among the wrasse can occur in two ways. In some populations, the multiple IP males and females spawn (release egg and sperm directly into the water). Alternatively, harems of females with one male also exist. The TP males are classified as either non-territorial (NT) or territorial (T).

environment influences sex determination. However, instead of the composition of the social group signaling sex changes as with the blue headed wrasse, the ambient temperature of the turtle eggs determines the gonadal sex for most of the turtles. For example, if the turtle eggs are incubated at 26°C, most of the turtles will develop as male. Conversely, if the eggs are incubated at 31°C, most of the embryos will develop into females. Exploring the mechanisms of temperature-dependent sex determination is an active area of research (Capel et al. 2020).

Clearly, for both the blue headed wrasse and the red eared slider turtle, biological sex is a contingent property of members of those species. Consider some particular blue headed wrasse who, in actuality, remains female across lifespan. Now "rewind the tape" on the life story of that wrasse and consider a different possible scenario unfolding where that exact same fish is signaled to transition into a male member of the species. Using the language of possible worlds specified above, there are some worlds in which that fish is female, and other worlds in which the same fish is male. Thus, while that fish happened to be female throughout its life, things could have gone differently for it. Had plausible and possible environmental factors shifted such that she was signaled for transition, she would have become a male.

Moreover, consider some particular male red-eared slider turtle egg whose egg was incubated at the optimal temperature for hatching approximately 50% males and 50% females in the population incubated at that temperature. Now "rewind the tape" on the life of that very same turtle and consider a different possible scenario where there's a change in the turtle's environment–perhaps some significant environmental disaster occurs–and as a result the incubation temperature rises a few degrees. Suppose also that this now leads to that very same egg hatching a female, as opposed to male turtle. Again, using the language of possible worlds, there are some worlds in which the turtle is male, and other worlds in which the same turtle is biologically female. For the red-eared slider turtle, sex is a contingent property.

So, we've seen that for species like the blue headed wrasse and red-eared slider turtle, sex is a contingent, and not essential property. Female blue headed wrasse are not essentially female. It's easy to imagine scenarios where for some particular wrasse that happens to be female, had things gone a bit different for them, they would have been male instead. So too with the red-eared slider turtle: male and female turtles in this species are not essentially so. But what is the case for humans? Is sex in humans contingent in the same way that it is for fish and turtles? Socrates, presumably, was a biologically male human. If we "rewound the tape" on Socrates' life and changed environmental factors early in development, are there possible worlds in which Socrates is biologically female?

2. Genetic Variation of Sex Expression in Humans

In order to consider the possible developmental pathways available to Socrates, we need to understand the ways that these pathways can be altered.

DNA, Genetic Mutation, and Epigenetic Modification.

Information encoded in the genome, an individual's DNA, typically determines a particular sex development pathway. During embryonic development one's chromosome constitution drives the primitive, undeveloped reproductive organs to differentiate into a testis or an ovary. Subsequently, the presence of specific hormones lead to the formation of internal and external genitalia. In humans, XX individuals (those whose genome contains two X chromosomes) typically develop female sex organs while XY individuals (those whose genome contains both an X and a Y chromosome) typically develop male sex organs. Two ways the typical trajectory of sex development can be altered is by either mutations to our genetic code or by epigenetic modifications. Decades of research have explored the effects of mutations to DNA sequences that affect sex determination, while research on the effects of epigenetic modifications in humans is new and limited.

Genetic Mutations. The first cell emerging from the combination of sperm and egg has the full complement of DNA to create the human body. This cell multiplies eventually leading to a fully developed fetus. Copying errors can occur during DNA replication causing a mutation. Consider an example where a copying error occurs and the string "ACCGTTAGGA" is incorrectly copied as "ACGGTTAGGA." Each letter represents one of the four nucleotide base molecules in DNA: A = adenine, C = cytosine, G = guanine, and T = thymine. Inside the nucleus, these nucleotide bases pair up creating the iconic double stranded DNA.[5] In the sequence above, notice that the third base changes from a "C" to a "G", cytosine to a guanine; a substitution. The various types of mutations occur at random during DNA replication, division, and recombination as the cells multiply.[6]

Through a multitude of complex molecular mechanisms, sequences of DNA bases are transcribed by RNA which are then translated into proteins (a process known as "transcription and translation") that form the human body. In short, if a gene is "turned on", transcription and translation occurs, and we say that the gene gets

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[5] The human genome is made of 3.2 billion bases of DNA, but the number of bases is not as important as their sequence.

[6] Some types of mutations are more common than others based on their location in the genome (Loewe 2008).

expressed. If it is “turned off,” expression is hindered.[7] Mutations can affect either the DNA protein coding sequences (i.e. genes) or the regulatory sequences of DNA, and both can lead to changes in the development of an individual.

Epigenetic Modification. Not only the nucleotide bases, but the whole DNA structure itself plays an important role in development. Our 3.2 billion nucleotide bases (A’s, C’s, G’s, and T’s) wrap around a “ball-like” cluster of proteins called histones that help package the DNA into a compact form called chromatin.[8] The three dimensional chromatin structure can change via epigenetic modification which involves additions or deletions of molecules. These changes make the gene sequences less accessible for transcription thereby regulating gene expression and influencing sex development.[9]

Sex Determination

The chromosomal constitution of the embryo is established at fertilization based on the initial egg and sperm that join, but it isn’t until week six to seven in utero that gonads begin to differentiate into testes or ovaries. Male and female genitalia also develop from a common early tissue that eventually differentiates into male or female sex organs. Once the testis or ovaries begin to develop, their hormones initiate a cascade of molecular changes resulting in numerous physiological differences between males and females (e.g. producing either eggs or sperm, size of mammary glands, shape of the front of the pelvis, size of bones, size of muscles, distribution of hair, etc.). Significant genetic mutations or epigenetic modifications early in the development cascade could lead to alternative, non-typical sexual development pathways.

Sex determination and the development of gonads leading to male or female anatomy depends upon whether or not genes get expressed at different times and

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[7] This gene regulation occurs through the on/off binding of a DNA binding protein in the cell that recognizes a specific DNA sequence (or “switch”) near the gene, thus controlling the molecular machinery that eventually leads to the production of proteins.

[8] See images of DNA, histones, and chromatin on the National Institute of Health (NIH)’s National Human Genome Research Institute website (Gahl 2022).

[9] Two processes, DNA methylation and histone modification, alter the 3D organization of chromatin within the nucleus without changing the underlying DNA sequences. Unlike methylation which only diminishes gene expression, some histone modifications increase gene expression while others drive it down. The variability of histone modification is another difference from methylation. While DNA methylation is a very stable epigenetic change that gets passed from mother to daughter cell, histone modifications can come and go in response to stimuli in the cellular environment (e.g. hormones).

places in the course of development. A Rube Goldberg contraption is a helpful analogy for understanding how gene expression and epigenetic modifications follow on from each other during development. Based on preceding events in development, each regulatory DNA switch turns its gene on or off (switches the molecular mechanism that leads to building proteins on or off) which in turn sets up the next set of patterns and events in development, referred to as a signaling pathway. Evidence suggests that these DNA switches are regulated epigenetically (Carey 2012).

Researchers talk about the pathway toward male or female anatomy as a process of fate commitment or "canalization". In other words, a set of genetic or environmental switches determine gonadal (testes or ovaries) differentiation activating one pathway (toward male or female anatomy) while repressing the other. "At the chromatin level, this transition is reflected in a reorganization of histone marks around sex determining genes. Genes associated with the female pathway lose their repressive mark when the ovarian pathway is activated, and genes associated with the male pathway lose their repressive mark when the testis pathway is activated" (Garcia-Moreno et al 2018, 20). Once a pathway is initiated, a cascade of signaling proteins lead to development of gonads followed by genitalia. While the genes for the alternate developmental pathway continue to exist, they are inhibited.[10]

Typical Pathways of Sex Development

The typical pathways of development for XY and XX individuals have been well documented over the past decade. Here we provide a brief overview of each typical pathway before discussing non-typical pathways.

During week 6 in the typical pathway for human development, the undifferentiated germ line cells (future egg and sperm cells) move to their final location in the body and proliferate making about five thousand new bipotential cells (can become either egg or sperm). Simultaneously, a set of somatic cells (not egg/sperm cells) begin to make a protein called WT1. WT1 is a regulatory protein that turns on other genes for both sexes.

XY Typical Pathway. If a Y chromosome exists in the genome, the WT1 protein binds to a segment of the Y chromosome and switches on the making of SRY protein (see Figure 1 Red Path). SRY protein then binds on to the DNA and switches on the

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[10] This forms the basis for what we call "the ongoing presence of a parallel pathway" in Section IV below.

transcription factor SOX9 protein (not on the Y chromosome). SOX9 creates a protein signaling pathway with FGF proteins (cell signaling proteins) that drive the production of each other. This self-sustaining SOX9-FGF triggering loop ensures the development of testis. This commitment by the SOX9-FGF loop is referred to as a "latch" that ensures that cells that started to follow the male route do not waver due to random noise in the system (e.g. random activation of a gene that promotes female development). Testis formation leads to differentiation of internal and external genitalia by action of hormones secreted by the fetal testes which include the action of various cells and the release of androgens including testosterone.

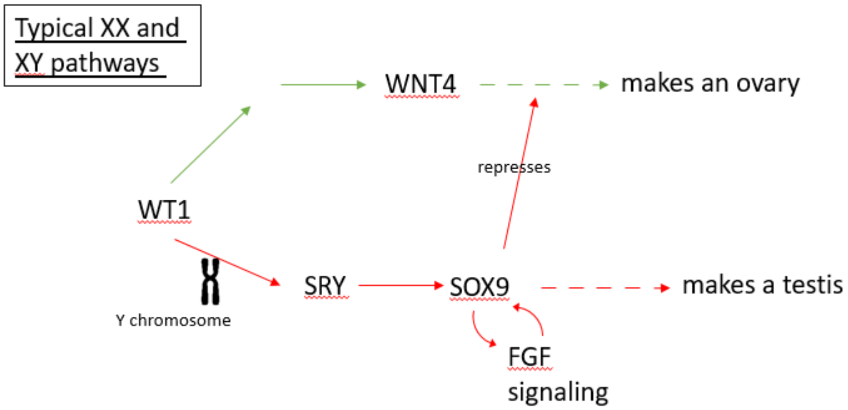

Figure 1: Typical Pathways for XX (green path) and XY (red path) individuals[11]

XX Typical Pathway. For individuals with XX chromosomes, the typical pathway differs from XY since there is no Y-chromosome or SRY gene (see Figure 1 Green Path). Nevertheless, WT1 still turns on other genes, as it does for both sexes, including turning on a family of signaling proteins named WNT4. WNT4 activates the female signaling pathway promoting female ovarian development. Cells of the rest of the body (somatic cells) rely on signals from the ovaries to switch on and off pathways for developing female anatomy.

In males, FGF-SOX9 is a powerful inhibitor of WNT4 activity, so while WT1 turns on WNT4 in both males and females, in males the activity of WNT4 gets inhibited. Likewise, the WNT4 pathway in females strongly inhibits the male specific pathway. The female-promoting pathway that centers on WNT4 uses a "latch" to ensure that any weak and random activation of male-promoting genes cannot interfere with typical development.

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[11] Adapted from Davies 2014, 150.

Contrary to common perceptions, developing male or female anatomy is not dependent on messages from an individual's XX or XY sex chromosomes. In other words, each cell is not relying on the presence or absence of a Y chromosome in the local DNA to get signals for developing anatomical structures. In XY individuals, it's the presence of SRY that initiates the SOX9 latch to repress the WNT4 pathway, ultimately affecting all future signaling pathways. So it's not the Y chromosome, per se, that directly determines maleness. Rather, it's the inactivation of WNT4. If biologists genetically engineer the activation of WNT4 in XY mice, these mice develop as females that have ovaries that produce eggs. Additionally, if the gonads are removed from early rabbit embryos which results in no gonad-derived hormones (molecules) being sent to the rest of the body's cells, the embryos develop according to the female plan, regardless of whether the individual is XX or XY. This is because "…hormones from the testis are needed to overcome this inbuilt female bias" (Davies 2014, 154). We've briefly examined the typical XX or XY pathway and why there is an "inbuilt female bias," but scientists also now understand alternatives to these typical pathways.

Non-Typical Developmental Pathways

There are various ways the pathway to typical male or female phenotypes can be disrupted, including both genetic mutations and epigenetic modifications.[12] Without the ability to experiment on human embryos, identifying epigenetic modifications is difficult, but we can identify chromosomal abnormalities in humans that result in nontypical pathways.

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[12] We discuss four developmental pathways different from the typical male and female paths; see DeFranza 2015, 23-44, for a more expansive survey of non-typical pathways of sex development.

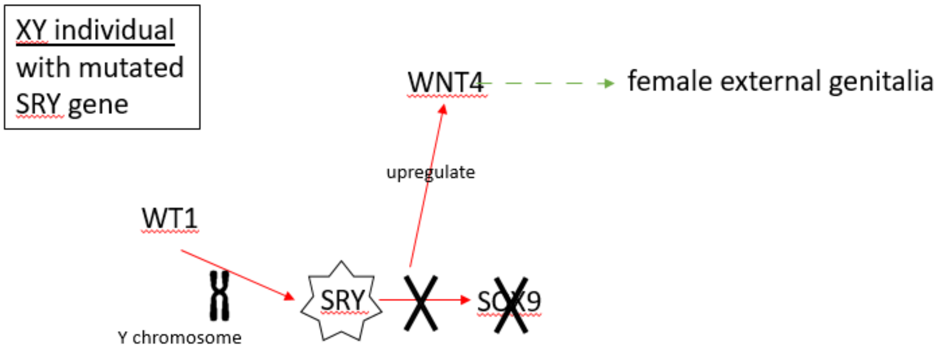

Figure 2: Disruption to the XY pathway by genetic disorder Swyer syndrome

Example 1: Swyer Syndrome. Swyer syndrome results from a mutation to the SRY gene on the Y chromosome (see Figure 2). Typically, the SRY gene on the Y chromosome leads to the formation of testis contributing to male differentiation. When the SRY gene is mutated, the SRY/SOX9 pathway is altered and terminates all subsequent cascading genetic and molecular events. Without SOX9 upregulation, the female signaling cascade (e.g. WNT4) is not repressed. As a result, the individual's differentiation follows the female pathway and develops typical female external genitalia even though the individual is XY. These individuals typically identify as female. Various genetic mutations can cause Swyer syndrome making it difficult to diagnose.

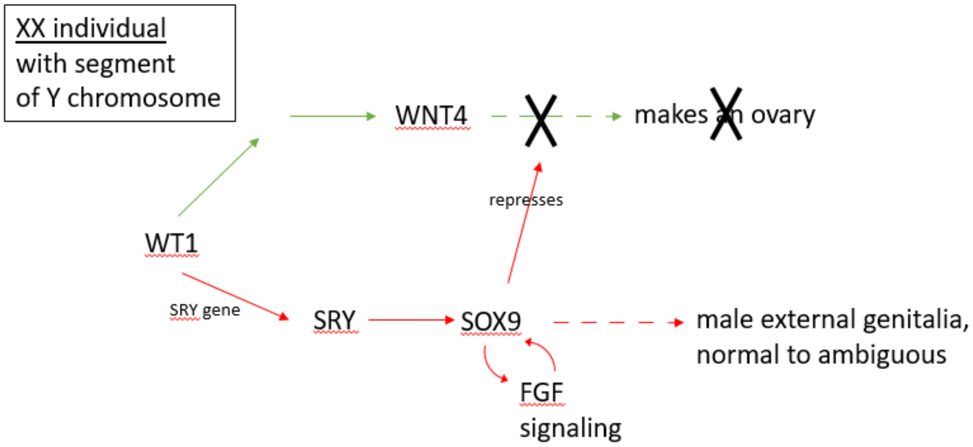

Figure 3: Disruption to the XX pathway by genetic disorder 46,XX male disorder of sex development

Example 2: 46,XX. The 46,XX male difference in sex development (DSD) appears in about 1 in 20,000 individuals who are born XX but present with a male phenotype (see Figure 3) (de la Chapelle 1981). Approximately 90% of these 46,XX testicular DSDs result from a segment of the Y chromosome containing the SRY gene moving to the X chromosome during cell division (Ashfaq et al. 2021). The presence of SRY on the X chromosome during development activates the SOX9-FGF signaling cascade repressing the WNT4 pathway which could lead to testis development. The majority of the 46,XX SRY positive individuals have typical male genitalia prior to puberty and are diagnosed following puberty based on infertility.

While these first two examples of non-typical developmental pathways involve the regulatory protein cascade leading to differentiation of the gonads (testes or ovaries), these next two examples affect the formation of internal and external genitalia by influencing hormone production after the gonads have differentiated.

Example 3: 5-alpha Reductase. 5-alpha reductase type 2 deficiency is a recessive intersex condition characterized by failed or incomplete development of the male external genitalia. 5-Alpha reductase is an enzyme responsible for the conversion of testosterone to its more active form, dihydrotestosterone (DHT). Recall that a sequence of hormonal events facilitates anatomical sex differentiation. During early development in typical males, DHT is responsible for triggering development of the male external genitalia (the penis, penile and cavernous urethra, Cowper's glands, prostate, and scrotum). A mutation in the 5-alpha reductase type 2 gene reduces the conversion of testosterone to DHT. The XY individuals with this mutation are born with ambiguous external genitalia: bilateral inguinal or labial masses consistent with testes, a labial-like scrotum, a blind vaginal pouch, and a clitoral-like phallus (Okiegwe and Kuohung 2014). Years later, as onset of puberty begins, the increase in testosterone production initiates masculine development: increased body muscle mass, deepening of the voice, enlargement of the phallus into a functional penis, testes descend into the scrotum, absence of breast development, and male patterns of hair growth can develop. Oftentimes these individuals are raised as female until they reach puberty, and then shift to identify as male.

Example 4: Congenital Adrenal Hyperplasia. Congenital Adrenal Hyperplasia (CAH) is a genetic condition resulting in impaired synthesis of adrenal gland hormones (Nikitina et al 2021). Typically the adrenal glands as well as the testes make androgens, a group of hormones in both males and females. Higher androgen levels usually lead to male-typical development in the womb, while low levels usually lead to female-typical development. CAH leads to high levels of androgen production in XX individuals. The excess androgen present during embryo development results in a virilization (or masculinization) of the external genitalia in utero. The clitoris may be large, the labia may be joined more like a scrotum, and the vagina may not be fully formed, or may be joined with the urethra. Virilization can result in uncertainty in sex assignment at birth; in some cases, the sex is initially designated as male on the basis of the appearance of the external genitalia (Khattab et al. 2017).

3. Contingent Sex Expression for Humans?

We have now surveyed six pathways for sex development among humans: two typical pathways (one each for XX and XY individuals) and four non-typical pathways (two each for XX and XY individuals). Given our understanding of contingency, sex expression for humans is contingent if, and only if, there are possible scenarios in which one's developmental pathway of sex determination differs from the pathway followed in the actual world. With our knowledge of typical and non-typical pathways outlined in the previous section, we can see that sex expression is indeed a contingent, and not essential, property of human beings. This is because for any possible developmental pathway of sex determination, there is a non-zero probability that an alternative developmental pathway could have been followed instead.

For example, let's suppose that the single cell zygote that became the philosopher Socrates followed a typical male pathway of sex development in the actual world. This means that the 3.2 billion nucleotide base pairs making up the DNA present in the zygote includes both X and Y chromosomes, later leading to the WT1 protein binding to a segment of the Y switching on the production of SRY protein. SRY switches on the SOX9 protein, creating the SOX9-FGF triggering loop which, as mentioned above, ensures the development of testes. But there are possible worlds in which the Socrates zygote–the very same zygote with the numerically identical chromosomal identity–follows a developmental pathway along which the SRY gene mutated during the germinal period of development. In that possible world, the Socrates embryo follows a female developmental pathway and develops female external genitalia even though Socrates is XY.

This result generalizes to other possible pathways for zygotes with DNA different from the Socrates zygote. This is because the sex determining developmental pathways that begin with a single cell zygote that eventually results in a multicellular organism with gonads involves many, many steps, each of which involves the replication of genetic material. Anytime genetic material is copied there is a non-zero probability that the resulting copy will not be an identical replica. That is, anytime genetic material is copied there is a non-zero probability that a mutation will occur. And if the mutation is of the right sort and occurs at the right time–

sufficiently early in development–in those worlds the result could be a sex determining developmental pathway different from the one followed in the actual world. XY humans following a typical developmental pathway become typical males, but only contingently so (as we saw with Socrates above). And XX humans following a typical developmental pathway become typical females, but only contingently so. For XX humans who are typically female in the actual world, there are possible worlds where they develop male, not female, genitalia.[13]

So far, we have only considered contingency as a function of both the logical and physical possibility of random mutations occurring at the relevant step along the pathway of sex determination. However, it certainly seems plausible that epigenetic factors, whether induced by environmental triggers or within a laboratory by scientists, could influence sex determination in humans as well. Recall that epigenetics involves changes to gene function without changing the DNA sequence. Laboratory experiments with mice show that epigenetic factors regulate the process of commitment to the male or female pathway (Stevant and Nef 2019, 355). Whether these mechanisms are precisely the same for humans is not yet established, although it seems reasonable to assume it is similar because of the relatedness between mice and humans (e.g. mammals).

For obvious ethical reasons, researchers will not perform the same sort of interventions on human embryos that they will perform on mice embryos. However, what this research on mice does demonstrate is the contingency of sex expression through experimental interventions on a relatively and relevantly similar mammal species. And while the possibility of the right sort of random genetic mutation or epigenetic effect is all that's needed to establish the contingency of sex determination, the theoretical possibility of intentional experimental intervention achieving what sometimes happens by chance adds emphasis to the contingency.

4. Philosophical and Theological Applications

Understanding the processes of sex determination in species like the blue headed wrasse and the red-eared slider turtle is useful for purposes of comparison to the developmental pathways of sex determination in humans. The obvious influence of environmental factors in determining sex for these species presents a helpful epistemic basis from which we can ask: is sex determination in humans contingent? We have seen that the answer is yes—the pathway of sex determination followed by human zygotes in the actual world is not the only possible pathway available to

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[13] As with the 46,XX condition discussed above.

them. This is not to say that human sex determination is contingent in the same ways that sex determination is contingent for fish and turtles. A female blue headed wrasse can transition from producing female gametes at one point in lifespan to producing male gametes at another point; this is not the case for humans. And a red-eared slider turtle egg can hatch either a typical pathway female or a typical pathway male, depending on the incubation temperature; a similar type of contingency is not the case for humans. That is, it does not seem possible for the numerically same human zygote to develop into either a typical pathway male or a typical pathway female. Thus, while there is contingency in sex determination in humans, that contingency does not get manifested in exactly the same ways as in other species. Nonetheless, we think that the observed contingency of sex determination in species including, but not limited to, humans, provides rich data for philosophical and theological reflection.

On "Male," "Female," and Fixed, Sexed Binaries

We have said at several points thus far that biologists–particularly those who work in the science of sex determination–tend to not think of "male" and "female," as fixed, universal, binary categories among species that reproduce sexually. They are not seen as fixed categories because there are numerous examples of species where individuals transition from male to female and vice versa. They are not deemed universal categories because there are individual members of sexually reproducing species who do not neatly fit into the typical male or female subsets of those species. And because they are not universal categories, they are not seen as exhaustive binary categories, either. For human beings, if one focuses exclusively on typical developmental pathways for XX and XY individuals, one might be tempted to think that there *is* a sense in which "female" and "male" would be exhaustive binary terms–provided "female" is shorthand for "typically produces large gametes," and "male" as shorthand for "typically produces small gametes." But as we have seen, the typical paths are not the only developmental paths available for sex determination in humans.

This complex and varied biological landscape undermines any tacit or explicit appeal to biology as the basis for a kind of gender-essentialism based on alleged facts about biological sex. On a strong essentialist view, sex is seen to be (a) universal (every human has a sex), (b) binary (every human is either male or female), and (c) immutable (one's biological sex is deemed to be an essential property of persons and as such, the ideas of sex transition or the contingency of sex determination are viewed as category mistakes). Strong essentialists also endorse a tight, normative link between sex traits and gender identity which includes the roles, behaviors, and social spaces occupied by men and women. On the strong essentialist view, gender identity is also deemed to be universal (every human is gendered), binary (every human is either a man or a woman), immutable (part of one's essential male or female nature), with the additional claim that gender identity is (d) biological (necessarily connected to facts about biological sex).[14] Philosopher Robin Dembroff addresses this move in what they call the *identity view,* according to which "gender is *identical* to sex, where sex is taken to be determined by one's reproductive features" (Dembroff 2018). Dembroff discusses the following argument for the identity view, according to which nonbinary genders are impossible:

(1) Someone's gender is identical to their set of reproductive features.
(2) There are only two possible sets of reproductive features.
(3) So it is impossible for someone to have a nonbinary gender.

Dembroff points out that as an argument against nonbinary gender identity, the argument fails in two respects. First, premise (2) is demonstrably false (as our extensive discussion of multiple non-typical pathways of sex development shows). Second, the argument equivocates on "gender." The sense of "gender" employed in (1) refers to reproductive features, whereas the sense of "gender" employed in (3) refers to social identity.

We discuss Dembroff's interesting article in order to show how the assumption of premises (1) and (2)—key components of the identity view–can be used to support spurious conclusions about gender.

Consider a philosophical argument one might advance for gender essentialism according to which gender is an essential, biologically based binary property of human beings. The following argument for gender essentialism mixes some biology with assumptions stemming from the identity view. Starting with a biological premise, the argument goes as follows:

(4) Human reproduction requires clear, distinct, complementary, and binary biological roles for males and females.

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[14] The preceding paragraph is a composite of gender essentialist views that are found across theological traditions, including Catholic, Orthodox, and Evangelical theologies. See, for example, Catholic strains of gender essentialism are presented in (Congregation for Catholic Education 2019) and critiqued in (Ulishney 2023); Orthodox gender essentialism presented and critiqued in (Rich 2023); Evangelical essentialism presented and critiqued in (Nordling 2011).

(5) If reproduction requires clear, distinct, complementary, and binary biological roles for males and females, then human society requires clear, distinct, complementary, and binary gendered social roles for males and females.
(6) All humans are either male or female.
(7) Therefore, all humans fit into clear, distinct, complementary and binary gendered social roles.

Or, one could up the theological ante and offer the following argument:

(8) According to scripture and tradition, males and females have clear, distinct, complementary, and binary gendered social roles.
(9) According to scripture and biology, all humans are either male or female.
(7) Therefore, all humans fit into clear, distinct, complementary, and binary gendered social roles.

Notice that the theological argument as stated doesn't logically entail patriarchy, but is often operationalized in ways that define the "complementary roles" within a hierarchy where social power is reserved for males.

However, there are good philosophical, theological, and biological reasons for rejecting these arguments. Even if one were to grant premise (4), according to which human reproduction requires distinct and complementary biological contributions from males and females, that by itself is no reason to think (5) is true. That is, there is no reason to think that the biological requirements for species propagation necessitate distinct and complementary gendered social roles. Put another way, there is no logical contradiction in the claim that biological reproduction within our species can flourish in a variety of different social arrangements. Beyond mere logical considerations, both experience and social science confirm that multiple social arrangements pertaining to gender–including nonbinary treatments of gender–can support our species (Hartke 2018). Premise (5), therefore, should be rejected.

Biologists will reject both (6) and (9). Claire Ainsworth (Ainsworth 2015, 288) puts it this way:

> [D]octors have long known that some people straddle the boundary [between female and male] – their sex chromosomes say one thing, but their gonads (ovaries or testes) or sexual anatomy say another … What's more, new technologies in DNA sequencing and cell biology are revealing that almost everyone is, to varying

> degrees, a patchwork of genetically distinct cells, some with a sex that might not match that of the rest of their body.

Recall that at the outset we specified a non-hierarchical, domain specific version of the Wesleyan Quadrilateral. As such, questions about the biological features of male and female members of the species, as well as the way the distribution of those features are present in the population, are scientific and empirical questions. The epistemologically salient authority here is biology, not biblical texts.

The Naturalness of Sex Transition

One assumption that is sometimes made in theological treatments of sex determination and how biological facts may relate to our understanding of human persons, is the assumption that universally in nature, sex is biologically hardwired and fixed. As a result, the idea of transitioning from one sex to another is deemed to be something imposed on, and contrary to, "natural" categories of sex expression.

But that is simply not true. Sex transition is a commonplace, naturally occurring phenomenon among many species that reproduce sexually. For species like the blue headed wrasse, IP females being able to transition to TP males is crucial for the species' capacity to survive and reproduce. For many, the naturalness of sex transition is disorienting and re-orienting. Anecdotally, each of the authors of this paper have had experiences discussing examples of sex transition in nature with audiences who are encountering this information for the first time. A common audience response is a bit of initial skepticism and incredulity, followed by amazement, followed by an immediate and palpable paradigm shift about what they thought was biologically possible. While this response is interesting sociologically and psychologically, we offer some philosophical reflections to unpack, understand, and help navigate the conceptual and existential territory.

As evolved, psychological beings, humans have developed a variety of cognitive strategies to create and protect a (somewhat) coherent narrative for interpreting and explaining the past and present, as well as for predicting the future. New information that easily fits with our background knowledge, helps bind us to others important to us, and centers one's own role in displaying the values one holds, will quickly be incorporated into one's explanatory story. Conversely, information that contradicts assumed background knowledge or might put one at odds with one's in-group, tends to take more time in order to be accepted, if accepted at all. As such, it's easy to see why for those who assumed that sex is biologically fixed as an essential property of individuals may feel some dizzying cognitive dissonance when presented with examples like the blue headed wrasse or red-eared slider turtle. Reflective individuals encountering this information might find themselves asking, "*If I were wrong about this, what else could I be wrong about?*" A related and more specific question that might arise when acknowledging that sex transition is a commonplace, natural phenomenon, is "*How should the naturalness of sex transition for some species impact how one thinks about sex transition and transgender experience among humans?*"

Transgender theologian and educator Austen Hartke addresses this question in his *Transforming: The Bible & the Lives of Transgender Christians.* After discussing biologically diverse practices of sex determination in nature, including sex transition of female to male in the blueheaded wrasse, Hartke goes on to consider what this might mean for understanding transgender people.

> Of course humans are not fish, and transgender people don't have the option to change the kinds of gametes their bodies produce, but scientists are beginning to suspect that the diversity we see in sex and gender in humans may also be beneficial for our species….Parents raising a child often benefit from having a third person around to help out, and that third person will be most available to help if they don't have children of their own. (Hartke 2018, 41–42)

Hartke goes on to apply a version of E.O. Wilson's kin-selection hypothesis to transgender people:

> These same benefits [of kin altruism] now appear to apply to transgender people and their families within cultures that support and affirm trans folks. Several studies done with the fa'afafine–the third-gender-identified people of Samoa–bear out what the kin-selection hypothesis first suggested: that transgender people who are accepted in their families are more willing to invest in their nieces and nephews than other cisgender relations. This in turn means that families that include and accept their transgender children and siblings are more likely to thrive together. (Hartke 2018, 42)

To be clear, Hartke is not arguing that transgender people merely have instrumental value as humans in virtue of their capacity to contribute to the reproductive fitness of wider populations. Rather, given that sex transition is a commonplace, naturally occurring phenomenon among many species that reproduce sexually, Hartke provides one model for thinking through how sex difference among human populations can fit within a wider biological and evolutionary context–a model which can alleviate some of the cognitive dissonance people may experience when contemplating various examples of sex transition and difference.

It is an interesting empirical question whether coming to understand that naturalness of sex transition in non-human species prepares people, psychologically, to be more accepting and supportive of sex transition in humans. If that is indeed the case, then disseminating information about the science of sex determination could open up theological spaces in ways similar to what has happened when data from other sciences seeped into the theological mainstream. For example, theological models that assumed or entailed a young universe required revision in light of big bang cosmology. Similarly, taking seriously humanity's evolutionary backstory has opened up space for new theological reflection concerning human nature and concepts like original sin. Alongside archaeological discoveries and developments in biblical studies, these and other examples of science-informed theology opened up new ways of reading biblical texts–ways that refresh and contextualize theology for our times.

Parallel Paths and the Contingency of Sex Expression

Imagine a footbridge along a path that runs east to west as far as the eye can see. Both the bridge and the path are narrow, with room enough only for one person to walk single file. In fact, the path is so narrow that there's no way to turn around once you start walking. Now, suppose that the only way onto the path is to be dropped onto the bridge from above. If you land on the bridge facing east, you can only walk to the east, and if you land on the bridge facing west, you're only walking west if you're walking at all.

If "walking east" represents following a typical male pathway, and "walking west" represents following a typical female pathway, then this thought experiment illustrates how some people think about our sexed bodies and developmental pathways. Some think that nature drops you onto the bridge facing one way or the other, and once the direction is set there are no other available pathways–in the actual world or any other possible world. On this view, you either walk the male path or the female path–those are the only options available and there are no other options available once the direction is set.

Now, instead of the footbridge on the east/west path, imagine a single lane roadway with a definite starting point in a parking lot. If you were to travel along this road after getting dropped into the parking lot, you'd soon come to a fork in the road. The left fork becomes something like a highway with wide, smooth lanes along which it is easy to travel. The right fork becomes a road that runs parallel to the highway for its entire length. There are off-ramps that look like they may have connected to the two roads at one time, but now it appears that each off-ramp has a barricade that prevents moving back and forth from the highway to the parallel road. It turns out that most people take the highway when they reach the fork and never leave it, although the parallel road is there all the time.

The interstate/parallel road analogy is a much better illustration of sex development for human beings than the footbridge analogy because it more accurately represents what we've come to understand about the science of sex determination. No analogy is perfect, but suppose the "interstate fork" represents following a typical pathway of sex determination. If you get on the "typical path highway" in an XY chromosome "vehicle," your journey is of the typical male type. But even if you're on the typical male highway, the "parallel road"—in this case, representing a path of female development–never goes away. Similarly, if you get on the "typical path highway" in an XX chromosome "vehicle," your journey is of the typical female type. But both the highway and the parallel road run side-by-side all along life's journey.

What the "parallel road" illustration highlights is that although human sex development follows a particular pathway of expression, individuals posses the genetic potential, in the right circumstances, to express sex differently from how one is actually expressing sex. In this way–possessing the capability to, in the right circumstances, express sex differently from how one is actually expressing sex–humans are like the female blue headed wrasse. Both typical pathway humans and typical pathway female blue headed wrasse possess "parallel roads" of sex expression. However, in humans, the "off-ramps'' from the "highway" to the "parallel road" are mostly blocked, whereas in the wrasse, certain circumstances will trigger the female wrasse to leave the typical path highway and move over to the parallel road–in that case, becoming a TP male.

One final nuance. So far in the parallel road analogy we've been looking at individuals who, when they come to that early fork in the road, take the left fork down the typical path highway. But the contingency and variability of sex expression in humans means that the very same individual who follows a typical path in the actual world could have followed the parallel path of sex determination had things gone differently early in development. This means that for any typical pathway male in the actual world, there are possible worlds in which that same individual follows the parallel path that is part of their genetic makeup–in those worlds they express sex in non-typical ways–ways that reflect certain characteristics one would find in typical females. Similarly, for any typical pathway female in the actual world, there are possible worlds in which that same individual follows the parallel path that is part of their genetic makeup–in those worlds, they express sex in non-typical ways–ways that reflect certain characteristics one would find in typical males. The ongoing presence of parallel pathways of sex development and the contingency involved in whether one follows the typical path or its parallel alternative, has the following consequences for thinking through the nature of human persons.

First, similar to the discussion in the previous section, it is an interesting and testable empirical question whether coming to understand the ongoing presence of parallel pathways of sex development and the contingency of sex determination would prepare people, psychologically, to accept sex transition in humans. It does seem that, philosophically, the ongoing presence of parallel paths should undermine resistance to human sex transition based on a mistaken concept of humans possessing a fixed, sexed nature. Instead of thinking that people who undergo medical or surgical interventions to facilitate sex transition are "going against their biological nature," a better way to understand their actions would be to see them as building or repairing the ramps from one path to the other–both of which are part of one's human nature.

Moreover, the ongoing presence of parallel paths is fertile ground for theological reflection. Each human person–a creature who bears God's image–has in their embodied nature the capacity to express traits associated with both males and females. The typical path of sex development is not the only pathway available–especially before coming to the developmental "fork in the road." Biological factors of sex difference can be seen not as differences in kind, but rather of degree. This has negative implications for theologically motivated gender essentialism where one's particular pattern of sex expression is seen as an essential, fixed part of who they are.

Conclusion

For many species that reproduce sexually, how sex is expressed at different points across lifespan is highly contingent and dependent on various environmental factors. It turns out that that while human sex determination is not susceptible to environmental cues to the same degree we see in other species, there is sufficient contingent variability among the pathways of human sex development to undermine simple fixed biological categories of male and female. This opens up rich theological spaces for science-informed reflection on being "male" and "female", responses to sexual difference, and differing models for understanding sex transition in humans.[15]

Bibliography

Ainsworth, Claire. 2015. "Sex Redefined." *Nature* 518: 288–291. https://doi.org/10.1038/518288a.

Ashfaq, Sara, Ahmed Siddiqui, Waqas Shafiq, and Umal Azmat. 2021. "A Rare Presentation of Disorder of Sex Development." Cureus 13, no. 1. https://doi.org/10.7759/cureus.12782.

Capel, Blanche, Ceri Weber, Yingjie Zhou, Jong Gwan Lee, Loren L. Looger, Guoying Qian, and Chutian Ge. 2020. "Temperature-Dependent Sex Determination is Mediated by pSTAT3 Repression of Kdm6b." Science 368, no. 6488: 303–306. https://doi.org/10.1126/science.aaz4165.

Carey, Nessa. 2012. *The epigenetics revolution: How modern biology is rewriting our understanding of genetics, disease, and inheritance*. New York City: Columbia University Press.

Congregation for Catholic Education. 2019. "Male and Female He Created Them: Towards a Path of Dialogue on the Question of Gender Theory in Education." URL: http://www.educatio.va/content/dam/cec/Documenti/19_0997_INGLESE.pdf.

Davies, Jamie A. 2014. *Life unfolding: How the human body creates itself*. Oxford: Oxford University Press.

DeFranza, Megan K. 2015. *Sex Difference in Christian Theology*. Grand Rapids, MI: Eerdmans.

De la Chapelle, Albert. 1981. "The etiology of maleness in XX men" *Human Genetics* 58, no. 1: 105–116. https://doi.org/10.1007/BF00284157.

Dembroff, Robin, 2018. "Why Be NonBinary?" Aeon, October 30. URL: https://aeon.co/essays/nonbinary-identity-is-a-radical-stance-against-gender-segregation.

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DuBois, L. Z., & H. Shattuck-Heidorn. 2021. “Challenging the binary: Gender/sex and the bio-logics of normalcy.” *American Journal of Human Biology*, 33(5), e23623. https://doi.org/10.1002/ajhb.23623.

Eliot, L., Ahmed, A., Khan, H. & Patel, J. 2021. “Dump the “dimorphism”: Comprehensive synthesis of human brain studies reveals few male-female differences beyond size.” *Neuroscience & Biobehavioral Reviews*, 125, 667–697. https://doi.org/10.1016/j.neubiorev.2021.02.026.

Fausto-Sterling, Anne. 2020. *Sexing the Body: Gender Politics and the Construction of Sexuality.* 2nd ed. New York: Basic Books.

Gahl, William. 2022. “Histone,” National Institute of Health, accessed February 25. URL: https://www.genome.gov/genetics-glossary/histone.

Garcia-Moreno, S. Alexandra, Michael P. Plebanek, and Blanche Capel. 2018. “Epigenetic Regulation of Male Fate Commitment From an Initially Bipotential System.” *Molecular and Cellular Endocrinology* 468: 19–30. https://doi.org/10.1016/j.mce.2018.01.009.

Hartke, Austen. 2018. *Transforming: The Bible and the Lives of Transgender Christians*. Louisville, KY: Westminster John Knox.

Joel, D. 2012. “Genetic-gonadal-genitals sex (3G-sex) and the misconception of brain and gender, or, why 3G-males and 3G-females have intersex brain and intersex gender.” *Biology of sex differences*, 3(1), 1–6. https://doi.org/10.1186/2042-6410-3-27.

Joel, D., Berman, Z., Tavor, I., Wexler, N., Gaber, O., Stein, Y., Shefi, N., Pool, J., Urchs, S., Margulies, D.S., Liem, F., Hänggi, J., Jänckef, L. & Assaf, Y. 2015. “Sex beyond the genitalia: The human brain mosaic.” *Proceedings of the National Academy of Sciences*, 112(50): 5468–15473. https://doi.org/10.1073/pnas.1509654112.

Joel, D. 2021. “Beyond the binary: Rethinking sex and the brain.” *Neuroscience and Biobehavioral Reviews*, 122: 165–175. https://doi.org/10.1016/j.neubiorev.2020.11.018.

Khattab, Ahmed *et al*. 2017. “Clinical, genetic, and structural basis of congenital adrenal hyperplasia due to 11β-hydroxylase deficiency.” *Proceedings of the National Academy of Sciences*, 114(10), E1933–E1940. https://doi.org/10.1073/pnas.1621082114.

Lamm, Melissa S., Hui Liu, Neil J. Gemmell, and John R. Godwin. 2015. “The Need for Speed: Neuroendocrine Regulation of Socially-Controlled Sex Change.” Integrative and Comparative Biology 55, no. 2: 307–322. https://doi.org/10.1093/icb/icv041.

LaPorte, Joseph, 2022. “Rigid Designators,” *The Stanford Encyclopedia of Philosophy*, edited by Edward N. Zalta. URL: https://plato.stanford.edu/entries/rigid-designators/.

Loewe, Laurence. 2022. "Genetic Mutation," *Nature Education*, accessed February 25. URL: https://www.nature.com/scitable/topicpage/genetic-mutation-1127/.

Maney, D. L. 2014. "Just like a circus: the public consumption of sex differences." *Ethical issues in behavioral neuroscience*: 279–296. https://doi.org/10.1007/7854_2014_339.

Menzel, Christopher, 2021. "Possible Worlds," *The Stanford Encyclopedia of Philosophy*, edited by Edward N. Zalta. URL : https://plato.stanford.edu/archives/fall2021/entries/possible-worlds/.

Nikitina, I.L., E.K. Kudryashova, I.A. Kelmanson. 2021. "Prenatal Androgen Exposure and Gender Behavior in Disorders of Sex Development." *Sexologies* (May 11, 2021).

Nordling, Cherrith Fee. 2010. "Gender." In *The Oxford Handbook of Evangelical Theology* edited by Gerald R. McDermott. Oxford: Oxford University Press.

Okeigwe, Ijeoma and Wendy Kuohung. 2014. "5-Alpha reductase deficiency." *Current Opinion in Endocrinology & Diabetes and Obesity* 21, no. 6: 483–487. https://doi.org/10.1097/MED.0000000000000116.

Rich, Bryce E. 2023. *Gender Essentialism and Orthodoxy: Beyond Male and Female*. New York: Fordham University Press.

Rippon, G., Eliot, L., Genon, S., & Joel, D. 2021. "How hype and hyperbole distort the neuroscience of sex differences." *PLoS biology*, 19(5), e3001253. https://doi.org/10.1371/journal.pbio.3001253.

Stévant, Isabelle and Serge Nef. 2019. "Genetic control of gonadal sex determination and development." *Trends in Genetics* 35, no. 5: 346–358. https://doi.org/10.1016/j.tig.2019.02.004.

Schnebly, Risa Aria, 2021. "Sex Determination in Humans." *Embryo Project Encyclopedia* URL: http://embryo.asu.edu/handle/10776/13286.

Shattuck-Heidorn, H., Danielsen, A. C., Gompers, A., Bruch, J. D., Zhao, H., Boulicault, M., Marsella, J. & Richardson, S. S. 2021. "A finding of sex similarities rather than differences in COVID-19 outcomes." *Nature*, 597(7877): E7–E9. https://doi.org/10.1038/s41586-021-03644-7.

Ulishney, Meghan Lougmane. 2023. *Original Sin and the Evolution of Sexual Difference*. Oxford: Oxford University Press.