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The Constitution of the Human Embryo as Substantial Change

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This paper analyzes the transformation from the human zygote to the implanted embryo under the prism of substantial change. After a brief introduction, it vindicates the Aristotelian ideas of substance and accident, and those of substantial and accidental change. It then claims that the transformation from the multicelled zygote to the implanted embryo amounts to a substantial change. Pushing further, it contends that this substantial change cannot be explained following patterns of genetic reductionism, emergence, and self-organization, and proposes Gustavo Bueno's idea of anamorphosis as a means to encapsulate criticism against such positions.

Keywords: *anamorphosis, blastocyst, morula, pre-embryo, substantial change*

I. INTRODUCTION

At its core, this paper considers the transformation from the human zygote to the implanted embryo to be a substantial change.

In Section II, I will introduce the Aristotelian ideas of substance, accident, substantial change, and accidental change and will briefly discuss the scope and limits of their present-day validity. In Section III, I contend that the transformation from the early morula and blastocyst to the implanted embryo amounts to a substantial change, and I develop the idea that individual human organisms, such as implanted human embryos, are not substances that can be split or divided: somatic indivisibility is deemed to be a feature essential to such organisms, one not yet present in morulas and blastocysts. These two different kinds of individuality (that of the morula and the implanted embryo) strongly imply the existence of two different kinds of substances and, consequently, the occurrence of a substantial change.

In the final section, I will critically review certain ideas that have been put forward to account for that substantial change: genetic reductionism, emergence, and self-organization. To end, I will propose Gustavo Bueno's idea of anamorphosis as a way to synthetically encapsulate such criticism and will vindicate the value of negative knowledge.

Just as the ontological issues discussed in this paper may be used in tackling ethical problems relating to abortion, contraception, *in vitro* fertilization, pre-embryonic experimentation, and pre-implantation genetic diagnosis, the conclusions drawn herein may also be compatible with a wide range of differing, and even opposing, ethical approaches. Different conceptions of ethics and different ethical principles can lead to different practical conclusions, even when certain ontological foundations are shared. The study of the "conceptual geographies" (to use Engelhardt's terminology, 2011) of the ethical discussions surrounding those issues falls outside the scope of this article, but, as will prove obvious, the arguments provided here may be apropos to any ethics committed to defending the human individual.

I am also aware that the discussion of both the substantial change taking place in the continuous biological process of human embryogenesis and the criticism of the proposed models to understand that change raise questions of a philosophical (ontological) nature. Such questions cannot be directly deduced from the data provided by biological sciences, although these sciences remain indispensable. This paper is a philosophical essay that implies an ontological (and hence philosophical) interpretation of certain scientific facts relevant to human ontogeny. Owing to this philosophical status, I do not pretend to come to any apodictic scientific conclusion.

II. SUBSTANCE AND ACCIDENTS, SUBSTANTIAL CHANGE, AND ACCIDENTAL CHANGE

Throughout the history of philosophy and into the present day, the Aristotelian ideas of substance and accident have been the subject of much discussion.[1] In Aristotle's philosophy, the term *substance* (*ousia*) has two distinct, yet interconnected meanings: "primary substance" and substance in a "secondary sense." Substance is, chiefly, primary substance: the single specimen or individual (the single man or the single horse). Primary substance, the individual, is the subject of all predication and can never be predicated on anything (*Catt.* 2a 11–14; *An. Pr.* 43a 25–29). According to Aristotle, no definition or demonstration can be made of individual substances such as Socrates or Plato (*Met.* 1036a 5–8; 1039b 27–31). Substances in the secondary sense are the species and genus. Species are substances in a stronger sense than genus, because they are closer to the individual (*Catt.* 2b, 7–8). Substances in this secondary sense capture the universal common attributes of certain sets of individuals and thus define the essence of such individuals.

Aristotle's use of the same word (*ousia*) to refer to individuals (primary substances) and to universals (substances in a secondary sense) indicates his understanding of ontological and epistemological issues as inseparable, counter to Plato's attempt to disjoin the universal from the individual (*Met*. 1086 b5-13). This intimate interconnection between epistemology and ontology remains a characteristic of modern-day philosophy. Distinguishing primary substances (individuals) and substances in a secondary sense (a species and a genus) involves studying the differences and similarities between individuals as a means to determining which differences are accidental and which are essential. Accidents accompany the substance but can be absent without the substance losing its essence, since accidents are simply what happens (*accidere*) to the substance. Conversely, essential features must be present for a substance to be what it actually is.

Based on these distinctions, a substance can undergo two different kinds of change: accidental and substantial. An accidental change takes place when the substance is altered without disappearing or becoming a different substance: the subject of change is the substance that remains one and the same, even if some of its accidental properties are modified. However, a substantial change occurs when the substance disappears as such or when a new substance is generated. For Aristotle, the subject of substantial change is matter, and he illustrates substantial change through the genesis and annihilation of animals.

At this point, his doctrine of change requires reference to his hylomorphic theory. Without entering into a comprehensive discussion of Aristotle's ontology, a brief overview may prove instructive in this respect. Primary substances, Aristotle states, are a compound of matter and form. The matter of a given substance is that thing of which the substance is made, whereas the form is a complex set of qualities, whether accidental or essential. Essential properties are those a given substance needs in order to be the kind of substance it actually is. To the contrary, accidental properties can be lost or gained without the substance becoming a new kind of substance. As regards matter, the term is relative to a particular transformation since every substance is made out of others (there is no *creatio ex nihilo* in Aristotle's philosophy); for instance, a lump of bronze is the *matter* of the statue. Aristotle's theory of substance and substantial change leads us to this point.

The Aristotelian categories of individual and species are far from archaic ideas: currently, Linnaean taxonomy makes use of these categories, which are taken from Porphyry's theory of *praedicamenta*.[2] Darwinian and neo-Darwinian biology continue to use the same categories (individual and species) although, unlike Linnaeus, they state that species were not created separated from each other but are rather connected by phylogenetic relationships. For instance, it is common to consider that the *Homo sapiens* species, like many other animal species, can be characterized from a genetic, reproductive, morphological and chronological standpoint, and that there are operational criteria for deciding when a given organism is an individual of our species. Basic ontological assumptions dictate that every human organism is a special object, since no living being can exist in a disembodied state. In discussing "actually existing men,"[3] there also exists a substantial consensus surrounding the fact that a human organism is always endowed with somatic individuality, whereby each human is different from the others. That individuality affects humans' existence as primary substances (as different individual specimens), and it is an essential characteristic of humans as secondary substances in the Aristotelian sense since, apart from the Trinitarian mystery, each and every human organism is, without exception, endowed with individuality. Human individuals as primary substances can be subjected to myriad accidental changes while still remaining the selfsame substances. Nevertheless, individuality is not an accidental characteristic of human beings (such as size or skin color) but rather a necessary condition for our existence in a spatial and temporal framework. The notion of individual persistence is also an essential characteristic of human organisms, key to our making sense of the world. Human somatic individuality and its related dynamic stability are a *sine qua non* for speaking about a real, non-fictitious human being (to say nothing about an ethical or moral agent). Unlike George and Lee and unlike Morris, I fail to see how individuality and non-divisibility can be deemed to be accidental characteristics of actually existing human organisms (George and Lee, 2005, 92 and 94; Morris, 2012, 344–45).[4]

To the extent that there exist species and organisms endowed with certain essential features, since those individual organisms are not eternal, then the idea of a substantial change seems unavoidable. As living entities do not transubstantiate, substantial changes imply the annihilation of the preceding living substance and its reshaping into one or many substance(s) of a new kind. In sexual reproduction, when the two gametes fuse to form the zygote, the individual gametes disappear as such and are subsumed into a new structure, the two-cell zygote. Gametes are substances of one kind, and the zygote is a substance of another. As it is widely recognized, the formation of the zygote is not merely a change in degree but brings into being a new biological entity genetically different from the antecedent gametes. The two-cell zygote features a complete set of 46 chromosomes endowed with its own genetic variability and definite chromosomal sex (Kiessling and Anderson, 2003, 95–104; Brown, 2007, 602–603). George and Tollefsen (2008, 123) have extensively argued for the ontological significance of the constitution of the zygote. Smith and Brogaard (2003, 52–54) saw substantial change in the binary fusion of the gametes in the zygote.[5] The death of a living individual organism serves as another example: substantial change is here the organism's disintegration from a whole into its basic constituent parts, which entails the rupture of the dynamic equilibrium characterizing living entities. Regardless of the degree of scientific knowledge and technological control over those processes, there are reasons to believe that a substantial change is taking place: certain substances of a certain kind (the gametes, the living organism) are transformed (by fusion, by disintegration) into substances of a new kind (the zygote, the free molecules).

In any case, I admit that Aristotle's hylomorphic theory serves little towards providing an understanding of biological substantial changes. The origin of the hylomorphic theory was technical in nature, that is, it is closely linked to discussions of productions from a kind of craft or art (*technê*) such as sculpting, music, or medicine. This is shown in the transformations discussed by Aristotle, such as the sculptor. More generally, one might think of the Ancient doctrine of the divine demiurge, or divine artisan, who gives form to prior existing matter. The technical bent of Aristotle's hylomorphism advises against its application to biological organisms that have not been created by a demiurge according to a plan. Atheist assumptions acting in this paper imply that the *dator formarum* of biological transformations cannot be a personal intelligence; biologists commonly make this assumption when they remain in the immanence of their science. Nonetheless, hylomorphism's fall from favor in scientific biological contexts does not affect the necessity of speaking about individual organisms and about species, or the appropriateness of understanding certain changes (such as fertilization and death) as substantial changes, but only suggests that technical analogies must be used with caution in explaining certain substantial biological changes.

According to the two Aristotelian notions of substance, substantial change can also be understood in two different yet interconnected ways. First, in looking at primary substances as the subject of change, substantial change can be described as a process wherein one or several prior substances undergo a change resulting in one or several different individual substances. Second, in looking at secondary substances (species) as the subject of change, substantial change then refers to the process wherein one or several of the essential features of a given species fade away while certain different essential characteristics arise. Paralleling the intimate connection between primary and secondary substances in Aristotle, these two notions of substantial change could be seen as two different aspects of a single process.

III. THE TRANSFORMATION FROM THE ZYGOTE TO THE IMPLANTED EMBRYO AS A SUBSTANTIAL CHANGE

In what follows, I will apply the idea of substantial change to the transformation of the morula and blastocyst to the implanted embryo. I will contend that the individuality of the blastocyst is different from that of the implanted embryo: the former can lead to twins, whereas the latter cannot. This change can be considered a substantial change since it affects the type of individuality of the primary substances involved (the blastocyst and implanted embryo), and, at this point, it should be remembered that individuality is the chief characteristic defining primary substances. Approaching that change from the point of view of secondary substances reveals the somatic individuality of the implanted embryo (an individuality that includes its inherent impossibility of twinning) as an essential feature of what is usually considered a human biological organism, as different from other nonhuman organisms that can be split or undergo metamorphosis.

Thus, the attainment of somatic individuality affects the substance of the organism itself, both in the sense of primary substance (since primary substances are individuals) and secondary substance (since somatic indivisible individuality is one of the essential features of human organisms). Consequently, there is convincing evidence to regard the attainment of such somatic indivisible individuality as the litmus test for substantial change, as a signal for the genesis of a particular human organism. The main reason to support this claim is that human beings are substances of a certain kind, and, as such, they are necessarily endowed with a specific, characteristic somatic individuality. This somatic individuality is not completely reached until the possibilities of twinning and chimerism have been definitively discarded. Of course, other living entities have other kinds of biological individuality, which are sufficient for them, but that is not the issue here. To support my claim of the existence of a substantial change in the transformation from the zygote to the implanted embryo, I will follow, *inter alios,* Norman M. Ford, Jack Wilson, Barry Smith, and Berit Brogaard, and I will assume that in ontogenesis the individuality characterizing a human being has not been fully reached until the embryo is implanted in the uterus (Donceel, 1970; Mahoney, 1984; Anscombe, 1985; Ford, 1988; Shannon and Wolter, 1990; McCormick, 1991; Wilson, 1999; Smith and Brogaard, 2003; McMahan, 2007; Montague, 2011).

Monozygotic twins have the same DNA and are nevertheless different individual organisms, different individual objects, different individual substances, and, of course, different moral agents: we do not punish "one twin for what his brother-twin did," as Locke pointed out (Locke, [1690] 1997, II, XXVII, 21). In fact, recent studies even suggest that monozygotic twins' DNA is not exactly identical since a certain amount of epigenetic change is possible due to copy-number variation (Bruder et al., 2008). In my view, the idea of *doppelgängers*, hyper-identical twins, is contradictory since real monozygotic twins are two distinct functional individuals. Human individuals are not large, long-living, genetically homogeneous cloning organisms such as aspens, bamboo, bracken, or raspberries (Wilson, 1999, 88). As it is, nobody holds that genetically similar twins are a single somatic human individual with spatiotemporally disconnected parts. Two human twins are two different individual somatic organisms, and, therefore, their somatic individuality cannot arise prior to the moment of twinning. Even the staunchest advocates for locating the beginning of human life at fertilization must acknowledge that the genesis of the human individual is postponed in monozygotic twins.[6]

Tetragametic chimerism (when two zygotes with two different genetic identities fuse into a single somatic individual) also evidences the difference between somatic individuality and genetic identity. Relating to this are the controversial and well-known cases of Lydia Fairchild and Karen Keegan, whose cells are genetically heterogeneous (Yu et al., 2002). Although zygotes and blastocysts can bear chimerism, human individuals cannot be bonded to form a new human individual, since human individuals cannot be glued together or fused like clouds or water drops.

As stated, monozygotic twinning implies the existence of two different yet genetically identical somatic individuals. Tetragametic chimerism additionally implies the existence of somatic individuals who are not genetically homogeneous. These cases prove there is no biunique relationship between the zygote's genome and the somatic human individual. The possibility of artificially producing twins and chimeras at certain stages of zygote and morula development strongly suggests that zygotes, morulas, and human individuals are different kinds of substances, each bearing different constituent properties: the former two can undergo certain transformations such as splitting and fusing, twinning and chimerism, whereas the latter cannot. Regardless of whether these processes can take place spontaneously or be induced artificially, the point is that certain kind of substances can split and fuse while others cannot, which is an essential difference, even though most pre-embryos do not as a matter of fact divide or fuse. As Brown has stated, "[pre-embryos] cannot be stages in the life of human beings if they come into existence and go out of existence in ways that are incompatible with being human" (Brown, 2007, 610). Again, genetic identity alone does not suffice to account for a human being: as argued, the zygote's genetic identity predates the implanted embryo's somatic individuality while the somatic individual's death does not always correspond to genetic death, as occurs in brain-dead individuals who retain living somatic and reproductive cells.

Jason Morris holds as "unscientific and implausible" the idea whereby the original cell disappears at the moment of a cell's mitotic division (Morris, 2012, 347). The crux of his argument rests on the statement that "metabolism does not pause when an embryo twins. There is no cessation of biological function whatever" (344). However, in my view, what is at issue here is not the cessation of metabolism or other basic biological functions but the loss of that primitive individuality. The one-cell zygote does not die in the process of cleavage, although its previous individuality does indeed disappear. From a biological standpoint, differentiating between the mitosis and the death of an amoeba or activated egg is hardly problematic, since dead amoebas and zygotes are easily recognizable. As Brown posits, "an object can be destroyed and another object of the same matter could continue the space-time trajectory" (Brown, 2007, 592). Derek Parfit and Louis M. Guenin have also stressed this difference (Parfit, 1984, 262; Guenin, 2006, 483). Such is also the case for chimeric embryos, since the two original embryos disappear as such once they fuse.

Although the morula in these early stages is more than a featureless conglomeration of cells, the vast majority of embryologists recognizes that its cells are hardly integrated. Wilson compares the "insufficiently unified" morula to certain genetically identical but not causally integrated organisms such as the dandelion or the bacteria that make the blue in blue cheese, where physical connection does not entail functional integration (Wilson, 1999, 25, 85). Countering this claim of an absence of integration, George and Tollefsen have argued that the morula is not, like a bag of bottles, a disorganized aggregate but rather a unity with three main goals: to reach the uterus, to develop the structures necessary to make implantation possible, and to preserve its structural unity against various threats (George and Tollefsen, 2008, 151–52). Jason Morris, in a recent paper, has pointed out some significant weaknesses in George and Tollefsen's arguments. Rebutting the first goal, he remarks that "the embryo is passively moved toward the uterus by the cilia lining the walls of the oviduct" (Morris, 2012, 345). The second goal, in his view, is countered by the fact that unfertilized eggs can develop those structures up until the blastocyst stage if they are exposed to certain substances. Refuting the third goal, Morris goes on to state that if the sperm's entry point into the oocyte is responsible for the pre-embryo's structural organization (an issue which is subject to debate), then "differentiation would be attributed to the parents rather than to any new individual" (Morris, 2012, 346). Finally, Morris emphasizes that the mere coordination of the cells' development and cycle in the pre-embryo cannot serve as a criterion to identify a new individual organism, since similar coordination can also be seen everywhere between cells of different organisms.

Even if we acknowledge the morula is not a mere clump or cluster of dividing cells and is endowed with some kind of unity and individuality, its plasticity when artificially inducing twinning and chimerism provides essential information about the kind of *sui generis* individuality it has and about its loose internal functional integration. As already stated, human individuals are not substances that can be split or fused, and this is the main argument for believing that morulas and human individuals are different kinds of substances: the individuality of the aggregate-like structure of the early morula differs from the individuality of the implanted embryo and the fetus. Even if the process of twinning were understood as one twin forming from the other, the difference between these two kinds of substances, the morula and the individualized human body, remains (Lee and George, 2006; Howsepian, 2008; Napier, 2008; cf. McMahan, 2007, 177–8; and Montague, 2011). Morulas and blastocysts come into existence and disappear as such in ways unlike the way human individuals are supposed to persist. From an ontological point of view, persistence conditions are essential to human identity. Twinning and chimerism make a clear cut in the persistence conditions of the pregastrulation embryo, thus laying bare the implausibility of continuity theories.

As Ford has pointed out, "we need to discriminate between the development of a multicellular human individual and a mass of genetically human cells in a process of developing into a [one or several] multicellular human individual[s]" (Ford, 1988, 17). Michael Lockwood contends that twinning and chimerism bear out that "what we have, prior to the start of differentiation, is more properly regarded as the raw material out of which one or more organisms are to be constructed" (Lockwood, 1997, 43). Peter van Inwagen and Richard A. McCormick, among others, have also referred to the scant integration and interaction between the early embryo's blastomeres in order to emphasize its *sui generis* ontological status (van Inwagen, 1990; McCormick, 1991). Mark T. Brown states that "divisibility, fusibility and separability are indicators of the absence of the hierarchical integration of cells into tissues, tissues into organs, organs into organ systems, and organ systems into organisms that is the defining feature of animal life forms" (Brown, 2007, 615).

Furthermore, it is worth remembering that sperm, eggs, zygotes, morulas, and blastocysts can be frozen, cryopreserved, and later thawed, revived, and transferred. In some way, they share certain features with cryptobiotic tardigrades. Human individuals, however, cannot bear such extreme handling, and this also points to a substantial difference between the temporal discontinuity borne by the former and the latter's requisite temporal continuity.

The blastocyst's implantation in the uterus takes place during the second week. Although John L. Merritt and J. Lawrence Merritt II contend that "human life begins shortly after implantation of a blastocyst, on day eight after fertilization [...] when the mother begins nourishing the blastocyst with her life supporting, replenishing blood" (Merritt and Merritt, 2010, 2), committing to such a precise date is not necessary for the purposes of my argument. Suffice to say that, unlike the morula, the implanted embryo is a single heterogeneous entity with causally related parts (Lockwood, 1995). Twinning and chimerism are no longer possible at gastrulation, and the individual embryo's functioning would be impaired, were some of its parts removed. Therefore, the implanted embryo should be understood as a unique somatic organism, cohesive and self-integrated. It has reached the somatic numeric individuality, singularity, and distinctness particular to human organisms. The individual object referred to as the "implanted embryo" and the future individual human organism are as spatiotemporally continuous as human beings are. The implanted embryo is the same organism as the fetus and the child he or she grows and develops into (although they are not composed of the same cells due to the molecular turnover, which occurs on an ongoing basis; this turnover, though, also acts in adults at different ages). Substances such as the readers of this paper are not temporally discontinuous but persist continuously in existence until they cease to exist upon death, when their unity disintegrates. Twinning, chimerism, freezing, and cryopreservation involve a spatial and temporal discontinuity that characterizes human progenitor cells but cannot occur in human individuals. Ford argues that during gastrulation (day 14–19 postfertilization), the epiblast "ceases to be a cluster of more or less homogeneous cells to differentiate into a single multicellular, heterogeneous developing living human individual. [...] The appearance of one primitive streak signals that only one embryo proper and human individual has been formed and begun to exist" (Ford, 1988, 168, 172). Smith and Brogaard claim that human individuals exist no earlier than 16 days after fertilization: with gastrulation the cluster of cells of the late blastocyst is transformed into a single multicellular living individual that has a body axis. "Twinning is from this point no longer possible" (Smith and Brogaard, 2003, 63).

As above stated, the argument for the ontological difference herein defended between the morula and the implanted embryo rests, in large part, on the fact that human individuals cannot divide (as can blastomeres or the morula) or be generated by parthenogenesis. Human individuals lack the fractal, mereological structure of morulas. Avak A. Howsepian contends that this argument will lose its strength once the artificial cloning of adult humans becomes possible. The real possibility of achieving asexual human reproduction would open the door to a defense advocating the similarity between the canonical individual human organism (with heterogeneous parts) and the early morula (with homogeneous parts): the former can be cloned and the latter can be twinned (Howsepian, 1992, 502; 1997, 39). However, in my view, such an argument would be weakened by two significant circumstances. First, cloning an adult human from the nucleus of one of the somatic cells does not imply that the human individual divides him/herself into two parts capable of regeneration; second, since that nucleus must be introduced into an enucleated egg and transferred to the uterus of a woman, such a significant part of the physiology of sexual reproduction will remain necessary that the similarity between cloning and mitosis of the morula will nearly disappear.

Morris argues that the stages of development in human embryogenesis are merely arbitrary subjective artifacts inserted by biologists for the purposes of convenience. For him, they do not represent natural things, since the differences between accidental and non-accidental changes in human development are highly subjective.

> Where strict ontology would lead us to expect abrupt events leading to stark, qualitative changes, we see instead that reversible, modest, quantitative changes in gene expression alter the predispositions of cells and tissues to develop along different developmental paths. (Morris, 2012, 339)

Human development, in his view, can be easily, predictably, and reversibly manipulated by using quantitative, transient techniques (Morris, 2012, 343). Hence, "biology is therefore no aid in identifying substance changes that separate these stages" (Morris, 2012, 333). I suppose, though, that Morris finds biology of some use in differentiating human living organisms from corpses, or embryos from germinal cells: those differences are also subtle and can be easily manipulated, but, as far as we know, they are not reversible. It seems evident that quantitative, modest, and subtle interventions performed by physicians frequently make the difference between life and death. As any physician working in intensive-care units knows, an individual's death is occasionally the result of a subtle change. Equally subtle and modest "manipulations" are responsible for the differences between germinal cells and zygotes. The absence of reversibility in the changes under consideration herein strongly suggests that they are not merely subjective and can in fact be seen as "non-accidental" or "substantial changes." The progressive loss of cells' totipotency and pluripotency during embryogenesis is a proven fact. Even if, in a near future, specialized cells could be reprogrammed to be totipotent, it cannot be inferred from this hypothetical technological achievement that the change does not substantially affect the manipulated cells. In fact, at present we already exert technical and technological control over a wide range of substantial changes.

To conclude these mereological considerations, it is worth examining the relationship between the embryo and the gestational mother, for implantation marks the beginning of pregnancy as a maternal state (Grimes, 1997). Before implantation, the mother does not recognize the embryo as an independent organism, but, once attached to the uterus, the embryo must produce hormones and regulators of the immune response in order to inhibit the mother's reaction to reject it as an alien body. This can be seen as an immanent biological criterion for acknowledging the existence of a new independent organism different from the host. The difference between the genetic identity (of the zygote, morula, and blastocyst) and the somatic individuality of the implanted embryo has been shown even more evidently since *in vitro* fertilization technologies have enabled the separation of genetic and gestational parentage. These technologies have proved it possible to maintain the zygote, morula, and blastocyst beyond the womb. Notwithstanding recognition of its somatic individuality, the implanted embryo still forms a single unit together with the pregnant mother. The new whole under consideration exhibits an attributive structure because there are many asymmetric relationships between embryo and mother. During pregnancy, the interaction and cooperation between the two interwoven living individuals is constitutively essential for both the embryo and the mother: it is a condition for the formation of the embryo as a unique, developing somatic human organism, as well as a condition for the constitution of the mother as a gestational mother.

IV. THE IDEA OF *ANAMORPHOSIS* AS A CRITIQUE OF PHYSICAL AND CHEMICAL REDUCTIONISM, EMERGENCE, AND SELF-ORGANIZATION

In the previous section, I argued that the morula and implanted embryo are different kinds of substances, and, accordingly, we must acknowledge that a substantial change takes place during the 16 days after the first cleavage.

In that time, a group of initially unintegrated cells transforms into a multicellular individual human organism.

As stated in Section I above, the transformation of the gametes into the two-cell zygote also amounts to a substantial change. The vast majority of those denying that fertilization is the beginning of individual human life recognizes the substantial differences between the gametes and the zygote. The very nature of sexual reproduction, in which two distinct haploid gametes combine to yield a diploid structure that is clearly new and different from its precursors, makes the existence of a substantial change during human fertilization very apparent. It is obvious that the zygote, at least from a genetic standpoint, is a new substance compared to the forerunner gametes. This, I hold, is the main reason why discussing the mechanisms of substantial change as it relates to fertilization is not particularly pressing. However, as regards the transformation from the zygote to the implanted embryo, the supposed substantial change may pass unnoticed, masked by certain procedures that foment the process's continuity.

In what follows, I will critique the two most relevant strategies that could be proposed as a means to vindicate the ontological, substantial continuity between the zygote and the implanted embryo.

1. The first strategy argues that since it is possible to divide living organisms into their constituent parts, then it is also possible to provide an entire account of those organisms by understanding the relationships between those constituent parts.
2. The second strategy makes use of the ideas of emergence and self-organization.

According to first strategy, complex biological organisms are composed of tissues, and these are made of cells, and these of macromolecules, and these of atoms, and these of hadrons and leptons. However, the top-down analytic procedure assumes the prior existence of the organism as a whole since, by starting from particles and atoms and using the laws of physics alone, it is not possible to come to a bottom-up account of the constitution of a complex organism like a human embryo. As it is well known, Stanley Miller and Harold Urey formed certain basic organic monomers from some gases, such as methane, ammonia, and hydrogen, and further experimentation even saw the formation of peptides; nevertheless, the transformation of organic molecules into cells and living organisms (to say nothing about animals or humans) cannot be reductively explained from the laws of physics and chemistry: some biological processes, laws, and forces such as reproduction, evolution, and adaptation seem to be at work, and evidence strongly suggests they operate at higher structures as complex individual organisms and ecosystems. At any rate, acknowledging the limits of physics and chemistry in the reconstruction of complex organisms does not entail a vindication of nonmaterial factors such as "vital sparks," special "energy," "*vis essentialis*," "*élan vital*," or unidentified mystical guiding forces as per metaphysical vitalism. Of course, physical and chemical principles remain unchanged and continue to operate at the appropriate level, for the new biological relationships do not suspend the basic physical laws but make use of them, redirecting the physical and chemical forces in a special way.

The most salient project looking to reduce embryogenesis to its constituent parts is currently underway in molecular biology and genetics. Although classical preformationism (ovism, Malebranche, animalculism, Leibniz) is at present a historic relic, the invocation of genes as the sole agents controlling development has led to the idea that genetics could in principle fully explain all human embryonic development and that everything else in the cell and organism is prespecified (Lejeune, 1981; see also Annas, 1989). Certain geneticists have seen the genome as the essence of the living organism, its body plan, and the assembly instructions and toolkit for a ready-to-assemble individual. The metaphor of the genome as a computer program controlling, regulating, and activating the somatic structures has been in place for several decades (Keller, 2003, 136–7). As the pre-embryonic genome is not formed until the first cell division, it cannot trigger the sequence of events beginning with sperm penetration and ending with the first cleavage. Furthermore, the fertilized egg's genetic predeterminism has come under fire particularly for those organisms whose development depends largely on the embryonic environment and on the cells' local conditions and developmental history. In those cases, the same genome may lead to different phenotypes in different cellular contexts, including different development and physiological courses (Wolpert, 1994). Keller has convincingly argued against Rosenberg by positing that the embryo cannot be computed from the molecular structure of the fertilized egg (Rosenberg, 1997; Keller, 2003, 265–95). Partially erroneous is the claim that genes direct ontogeny, and misguiding is the comparison of the genome to a *program* ready to be run. As Robert says, "there is no straightforward 'unfolding' relation between genotype and phenotype" (Robert, 2004, 39): cases of pleiotropy (a gene affecting multiple structures) and polygeny (a trait affected by many genes) are ubiquitous. Kirschner, Gerhart, and Mitchison have stated

> that gene products function in multiple pathways and the pathways themselves are interconnected in networks, [so] it is obvious that there are many more possible outcomes than there are genes. The genotype, however deeply we analyze it, cannot be predictive of the actual phenotype, but can only provide knowledge of the universe of possible phenotypes. (2000, 87)

As such, a single human genetic identity can be shared by two somatically different individual organisms, as in monozygotic twinning. Moreover, evidence shows that acting on the organism at a higher level (by eliminating a group of cells during morphogenesis, for instance) may have a significant influence in the development of the embryo, whereas genetic redundancy can override the possible consequences of gene knockout (Brigandt, 2006, 2011). Against genetic predeterminism and reductionism, those results strongly suggest that structures higher than genes (such as cells or groups of cells) play an important role in ontogenesis. Consequently, subdisciplines such as cytology and embryology, which focus on higher level structures, cannot be reduced to genetics. Finally, the fact that a single somatic organism can carry several distinct genetic identities, as in chimerism, also suggests that the organism is not genetically predetermined from the very beginning. Robert summarizes his critique against genecentrism as follows:

> *contra* genetic informationism, genes do not contain all of the relevant specific information required for development, nor are genes uniquely informational; *contra* genetic animism, genes do not contain a *programme* for development [...]; and *contra* genetic primacy, although genes may be *primus inter pares* methodologically, ontogenetically the developing organism (including but not reducible to its genes) has pride of place. (Robert, 2004, 90)

According to second strategy, the idea of emergence has been widely used to gain an understanding of this type of process (Alexander, 1920; Broad, 1925). Taken from the Latin prefix *ex-* (meaning "out") and the verb *mergo* (meaning "to dip in" or "to sink"), in the vernacular the verb "to emerge" means "to move out of or away from something and become visible," as when the dolphin emerges from the sea. Nevertheless, certain other uses have betrayed this etymological meaning; the word "emergence" is also used to denote the process of coming into existence. For this reason, its use may be equivocal or ambiguous when it simultaneously denotes the process of a preexisting configuration becoming visible and the process of that configuration's coming into being. The potential conflation of these two concepts thus advises against using this idea to provide an understanding of the substantial change from the two-cell zygote to the implanted embryo.

The substantial change from the morula to the implanted embryo has been occasionally referred to by using the dubious expression of "self-organization" (Kirschner, Gerhart, and Mitchison, 2000), but I find this label inappropriate since such a reflexive formula conceals the selective evolutionary forces and external environmental pressures acting at different levels on the dynamics of the pre-embryo. Packing the cells into small groups, such symmetry-breaking processes cannot be disconnected from environmental circumstances, and the consequent morphogenesis (change in form) has been shown to be driven by certain genetic and somatic structures resulting from primordial evolutionary processes and forces. Geneticists frequently speak about the organism's "self-organization," "self-determination," and "self-assembly." However, all these reflexive formulas fall into a certain secular, residual, genetic essentialism. These metaphors and their related analogies ("genetic control," "genetic regulation," "genetic switches," "genetic activation") are a way to attribute agency to genes, a way to turn genes into the agents of embryogenesis. Mark T. Brown contends that "some form of genetic essentialism seems inevitable if the active potential of the human embryo is identified with the activation of a human genotype" (Brown, 2007, 603). Such a mandatory genetic essentialism does not mean, though, that the somatic individual and the phenotype are purely phenomenal and accidental. The "gene control hypothesis" forwards an ontologically misguided, *deus-in-machina* mechanism; as Jason S. Robert has insightfully stated, "genomes simply do not exist independent of the complex organisms of which they are but one part: organisms are not genomes writ large" (Robert, 2004, xii). Consequently, the change from the morula to the implanted embryo is hardly understood as merely "self-organization."

Current research has been complementing the aforementioned top-down reductive pathways and bottom-up "unfolding" methodologies with a more sideways contextual approach. Such "horizontal" determinants will be sought in the spatial and topological relationships and in the intracellular and extracellular medium in which the zygote, morula, and blastocyst develop. In the absence of a demiurge, all these adjustments occurring in ontogenesis become understood as an outcome to a long phylogenetic process such that an important part of the causal context characterizing that substantial change sinks to the depths of evolutionary history. The study of the evolution of embryonic development has led to the emergence of a new discipline called "evolutionary developmental biology" or "evo-devo," which looks at the developmental processes affecting evolutionary changes and into how development itself has evolved. Focusing their attention on the study of gene regulation and expression, evo-devo researchers ask how different species (even different orders and phyla) use the same genes during embryogenesis. Changes in gene regulation and expression seem to play a major role in evolution by providing a wide range of variation for natural selection to act on. Since many structures of human embryogenesis are shared with other different species, they can only be correctly understood in an evolutionary context. Among the evolutionary mechanisms affecting early embryonic development, Brian K. Hall has cited the processes of heterochrony and heterotopy (changes in the timing or positioning of developmental phases or parts), the transfer from maternal to zygotic genomic control, cell-to-cell interactions, cell differentiation, and cell migration (Hall, 2003). Nevertheless, genes should not be understood as the drivers of evolution but as the repertoire of possibilities, whose realization is ecologically driven (Carroll, 2005, 286). Jason S. Robert has proposed taking evo-devo even one step further: "organisms are more than epiphenomena of genomes, more even than epiphenomena of genomes in particular structured environments" (Robert, 2004, 129). To take development seriously means to adopt a developmental systems perspective, to take development as the basis of biological process and as the primary *explanandum* since "development is what distinguishes biological systems from other sorts of systems" (Robert, 2004, 34).

All those arguments claim that the implanted embryo (understood as a new human individual that itself is a developing organism) does not preexist in the genome, in the zygote, or in the early morula but is rather a new substance produced by the growing, transformation, recombination, restructuring, and reshaping of the primitive constituent parts, as well as the interaction both within them and with their changing environment at many hierarchical levels. Gustavo Bueno has proposed the philosophical idea of *anamorphosis* to refer to a process of forming a new whole (*morphosis*) that arises (*ana*-, up) from its constituent parts and is not the result of any planning demiurge (Bueno, 1994, 159–71).[7] This neologism encapsulates the apagogical recognition that preformationist, reductionist, and predeterminist explanations do not suffice to provide a full understanding of a given substantial change.

Granted, it could be argued that this new word adds nothing to knowledge sourced from the sciences (embryology, evolutionary disciplines, genetics, etc). Indeed, this is partially true, since philosophical ideas do not compete at the same level as positive scientific facts and concepts. Further, the purely critical nature of anamorphosis (against genecentrism, preformationism, reductionism, etc.) could lead some to view it suspiciously. However, the "negative knowledge" relating to anamorphosis is not the same as an "absence of knowledge," since negative knowledge has proved its great value in both science and philosophy. Some examples help illuminate this claim. From the second law of thermodynamics, the impossibility of a perpetual motion machine of the second kind can be derived. Here, the negative knowledge is that such a machine cannot be built, which is of chief interest to carry out improvements on the performance of real, effective engines. Yet another example is taken from geometry. A seminal theorem developed by Descartes, Euler, Legendre, and Cauchy states that only five regular polyhedrons are possible, the five platonic solids: tetrahedron, cube, octahedron, dodecahedron, and icosahedron. Consequently, the project of building a regular decahedron should be discarded. This abstract, geometrical, negative knowledge has significant technological consequences when designing computer chips in order to avoid crossing the conducting tracks linking the integrated circuits. The importance that denying spontaneous generation had in the constitution of biology as a modern science seems self-evident. Finally, in philosophy, the impossibility of laying metaphysics down as a science, as defended by Kant in his first *Critique*, can serve as an illustration of the value of negative knowledge. In fact, negative knowledge may serve as a powerful instrument to focus on relevant research strategies and programs.

The characterization of the substantial change from the multicelled zygote to the implanted embryo using the idea of anamorphosis, as illustrated above, implies the recognition that we still lack an exhaustive, scientific explanation of this process. Regardless of this limitation, the use of the idea of anamorphosis strongly recommends avoiding the methodologies of metaphysical preformationism and prevents us from overusing the ideas of reductionism and genetic predeterminism, and the obscure and mysterious patterns of self-organization and emergence.

NOTES

1. Significant examples of this discussion include Porphyry's theory of *praedicamenta*, the doctrine of universals (Roscellinus, Peter Abelard, William of Champeaux, Anselm of Canterbury, Ockham), the modern debate between rationalism and empiricism, and other theories dealing with the ontological status of general ideas, logic and mathematical concepts, and their relationship to individual bodies (Simmel's third kingdom, Popper's third world, etc.).

2. Porphyry developed the theory of *praedicamenta* in his commentary, *Isagoge*, on Aristotle's *Categories*.

3. The phrase "actually existing men" is taken from the phrase coined by Brezhnev referring to real-socialism. Brezhnev spoke of "actually existing socialism" as distinct from "utopian socialism" (Saint-Simon, Fourier, Owen, Proudhon, Kropotkin), insofar as the former exists in reality and the latter only on paper. Ontological assumptions acting in this paper require differentiating the real world from merely imagined possibilities that are incompatible with all we know about real biological organisms, including certain thought experiments proposed by armchair theoreticians about imaginary human beings who split like amoebas (Shoemaker, 1963; Prior, 1965–66; Wiggins, 1967; Parfit, 1971; Howsepian, 1992; Munthe, 2001), metamorphose like butterflies (Parfit, 1984, 203), transmogrify like Price's Martian dog (Price, 1977, 204–6), teleport and are transmitted by radio (Parfit, 1984, 199), have their brains transplanted (Olson, 1997; Munthe, 2001; Guenin, 2006, 488–9; Napìer, 2008), or reproduce parthenogenetically (Howsepian, 1992, 498–9). I am interested in human life as we know it: this paper's readers cannot divide or be divided like bacteria, amoebas, or flatworms. Cutting a human individual in half implies killing that individual, and if certain parts are removed or damaged, the organism will also die or at least find itself impaired. Likewise, the idea of the "metamorphosis or transmogrification of a primate" is as biologically contradictory as the idea of a square circle, geometrically, or the idea that an iron bar can float on water, physically. This paper's author and readers are not Camberwell Beauties, which metamorphose from caterpillar to chrysalis and subsequently to butterfly (cf. Parfit, 1984, 203). On one hand, it is clear that human beings cannot bear such great changes, and on the other hand, it is evident that a caterpillar that turns into a chrysalis and then a butterfly undergoes a substantial change, which affects its somatic individuality, despite its retaining genetic identity. Katleen Wilkes and Jack Wilson have judiciously located the limits of some of those so-called "thought experiments" at the point where they lose touch with reality (Wilkes, 1988, 1–49; Wilson, 1999, 9–16). As in Brezhnev's phrase, the ontological status of the "actually existing man" should be distinguished from that of imaginary, utopian humans.

4. Morris's argument that conjoined twins are "two people sharing a body" and that, consequently, human organisms are not necessarily individual (Morris, 2012, 344) would be met with a wave of disapproval from many biologists (to say nothing of philosophers). The assumptions I make in this article attribute the dramatic situation suffered by symmetric inseparable twins directly to the fact that two different persons share one single individual organism. The individuality of that singular organism should be deduced from the biological impossibility of separating the so-called "conjoined twins." Elsewhere, I have classified the various situations of dissociation between a human individual and human person, highlighting the cases where no canonical, one-to-one relationship exists between them (Alvargonzález, 2012, 378).

5. However, characterizing as a substantial change this fusion of two entities with two different sets of DNA (the gametes) into a single cell (the zygote) endowed with a new set of DNA is controversial because, as many researchers have shown, the merging of the new chromosomes (syngamy) does not take place until the two-cell stage (Mauron, 2004, 708; Brown, 2007, 607). In addition, biological research strongly suggests that, even when the new genotype is compiled, embryological development is still regulated by the ovular cytoplasm and maternal genes until the eight-cell stage (Brown, 2007, 607).

6. For instance, in their influential book *Embryo: A Defense of Human Life,* George and Tollefsen find themselves obliged to add a tagline along the lines of "excluding only cases of monozygotic twinning"

every time they declare that we began to exist at conception (George and Tollefsen, 2008, 55, 70, 81, 85, 108–10, 113, 115, 149).

7. I feel compelled to warn that, because Gustavo Bueno advocates the "at-fertilization" stance, he would probably disagree with the use I make here of his idea of anamorphosis (cf. Bueno, 2010a, 275–319; Bueno, 2010b; Alvargonzález, 2009, 2010a, 2010b).

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