# The Dynamic Imperative of the Maternal-Fetal Dialogue: Epigenetic Adaptability, Prenatal Programming, and the Ethics of Artificial Gestation

Cristina Brasi
*FBA-LAB*
via Caronti 5,
22026 Maslianico (CO), Italy.
cb@cristinabrasi.com

Filippo SanFilippo
*Department of Engineering Sciences,*
University of Agder,
Grimstad, Norway, 4879
filippo.sanfilippo@uia.no

Beatrice Seccomandi
FBA-LAB
via Caronti 5,
22026 Maslianico (CO), Italy
bea.seccomandi@gmail.com

***Abstract*— Contemporary developmental biology recognizes that the genome is not a static or deterministic code but functions as an adaptive device capable of dynamically responding to environmental demands through gene expression regulation. This responsive capacity is the foundation of phenotypic plasticity, essential for the survival and adaptation of offspring to the external world. Epigenetics, defined as the study of modifications that alter gene expression without changing the DNA sequence, is the primary molecular mechanism governing this flexibility. Epigenetic modifications, including DNA methylation, histone modifications, and non-coding RNAs (ncRNAs), are crucial for proper brain development, synaptic function, and neural circuit formation in the central nervous system. Epigenetics thus translates environmental eventual experiences into permanent or semi-permanent genetic instructions, enabling the organism to generate a biological response (such as that mediated by the neuroendocrine stress axis Hypothalamic-Pituitary-Adrenal, HPA) that aligns with the emotional state and surrounding environmental context. The central thesis of this discussion is that this tuning between biology and emotion is entirely mediated by the epigenetic configuration established during critical developmental periods, primarily gestation.**

***Keywords*— *artificial pregnancy, epigenetic adaptability, prenatal programming***

## I. INTRODUCTION

Essential, in order to understand the complex construct of personality, is the identification of what is defined as temperament. Temperament, from the Latin temperamentum, in modern usage denotes the component of affectivity, considered in psychology and hereditary biology as part of an individual's constitution and personality, from which emotionality, the quality, and the stability of affective tone depend. Even from this simple definition, it is clear how strong the impact is in terms of psychological stability and what influences it may have on behavior. To date, there is no single theory of temperament, but Bates's definition [1], in our view, is the one most capable of providing broad agreement. According to the author, "temperament consists of individual differences in behavioral tendencies that are rooted in biology, present from the beginning of life, and relatively stable across situations and over time" [1]. This designation of temperament makes it clear that it cannot be subject to substantial change. What we commonly refer to as disposition can be softened around the edges, can be understood and managed, but it can never be fundamentally altered. Currently, the study of temperament is linked to the study of attachment. The perspective is interactive, as the child's behavioral characteristics become intertwined with the mother's emotional state. In this way, the study of temperament takes on a relational meaning, creating a field of study capable of accounting for the dialectical process between development and environmental expectations [2].

## II. LITERATURE REVIEW

Temperament plays an essential role in understanding the architecture of human personality, representing the inherently biological and hereditary component that determines an individual's affectivity, emotional reactivity, and affective tone stability. Thomas and Chess's longitudinal model, though originally focused on biological innateness, was pioneering in recognizing that temperament is strongly modulated by prenatal influences and early experiences [3]. The New York Longitudinal Study was the largest and most important study ever conducted on personality; it began in 1956, with a sample of children from 84 families. The subjects were analyzed from

the age of 3 months up to adulthood. The NYLS is a cross-cultural study because it analyzed both children of Hispanic origin and children from lower social statuses. Data were also collected on a sample of children with mental retardation [4] [5] [6] [7] [8]. The authors' theoretical approach falls within an interactive perspective. For them, temperament, while fundamentally a personality construct resulting from innate brain traits, is also the result of prenatal influences on the fetus (thus introducing the first scientific data related to epigenetics), as well as the child's early experiences and developmental level. Thomas and Chess emphasize that, while heredity may play an important role in determining temperamental characteristics, these do not necessarily require a genetic basis [2]. In this way, the authors completely distance themselves from determinism. Thomas and Chess had important insights into concepts such as epigenetics, free will, and the possibility of breaking the chain of transgenerational transmission.

The term epigenetics was coined in the mid-1950s by C.H. Waddington [9] to describe the interactions between genetic factors and embryonic development. Epigenetic processes do not occur only during the development and cellular differentiation of embryonic life but also play an important role throughout adulthood, both as random expression and as a result of environmental influences [10]. It has been demonstrated that epigenetic mechanisms influence normal patterns of neurodevelopment and brain function and, consequently, the mechanisms involved in the "maldevelopment" implicated in certain psychiatric disorders. Supporting this hypothesis, there is evidence for the involvement of epigenetic mechanisms in neurogenesis, neuronal differentiation, cellular differentiation specification, and dendritic development [11]. Epigenetic modifications that occur during intrauterine life remain stable throughout life; however, it is now clear that these mechanisms are dynamically regulated and that epigenetic remodeling can occur during adulthood under the influence of environmental factors such as nutrition, drug use, exposure to chemical and physical substances, psychosocial factors, and psychotherapy. There is substantial scientific evidence supporting the epigenetic action of psychotherapies, so much so that they have earned the label "epigenetic drugs" [12]. It is known that psychotherapies modify brain circuits in the same way as psychotropic drugs, achieving therapeutic effects by improving the efficiency of information processing in malfunctioning brain circuits. Symptoms would thus be the phenotypic expression of molecular alterations on which pharmacological therapy and "talking therapy" act separately or in an integrated manner [12].

Contemporary neurobiological research has resolved the paradox of temperament stability. Although it is an innate disposition, its "moderate stability" over time does not imply genetic rigidity but rather the persistence of epigenetic markers that stabilize during sensitive periods of neurodevelopment. This persistence of epigenetic markers provides a "cellular memory" that establishes specific epigenetic vulnerability or resilience. The modifiability of temperament through learning and behavioural conditioning serves as a conceptual bridge linking the psychological construct to molecular analysis, confirming that epigenetics is the mechanism through which the environment can alter an inherited biological trait. If affectivity and emotional reactivity can be shaped by experiences, such modification must necessarily occur at the molecular level [13].

## III. METHODOLOGY

Gestation is a period of profound and intimate biochemical and physiological dialogue between mother and fetus, extending far beyond the simple transport of oxygen and nutrients. The maternal-fetal hormonal exchange is a crucial biological programming system for the formation of a healthy and adaptable individual. The placenta is the central organ of this system, acting as a complex endocrine gland and orchestrating bidirectional signals that influence fetal development while simultaneously regulating maternal and placental physiology. This fetal programming is not limited to the physical dimension but determines long-term resource management and psychological adaptation. Prenatal hormonal and nutritional exposure establishes molecular alterations with the potential for intergenerational transmission[13].

The placenta is not a static barrier but rather a dynamic filter essential for adaptability. Its most critical function in tuning the stress response is the regulation of fetal exposure to maternal glucocorticoids (cortisol). The enzyme 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2), expressed in the placenta, inactivates active glucocorticoids, offering partial protection to the foetus from excessive maternal stress hormones. However, this protection is dynamically regulated. Adverse conditions, such as maternal protein restriction or chronic stress, can overwhelm the barrier or lead to the downregulation of 11β-HSD2 expression, increasing fetal exposure. This excessive exposure reprograms the sensitivity of the fetal HPA axis, a neuroendocrine system fundamental for stress response, increasing the predisposition to neuropsychiatric and cardiometabolic disorders in adulthood. Exposure to glucocorticoids acts as a "predictive signal" of the postnatal environment, preparing the foetus for a challenging world through the development of a "thrifty phenotype" [13].

An example that helps us understand how epigenetics has subtle yet important nuances is the case of monozygosity. The

study of monochorionic twins represents a fundamental research model in the field of epigenetics. Since monozygotic twins share nearly all of their genetic heritage, any phenotypic differences that emerge between them can be attributed to variations in the environment, both prenatal and postnatal [14]. Epigenetic differences, such as DNA methylation patterns, are considered the primary mechanism through which these environmental influences translate into phenotypic discordances.

Even though they share the same uterus, the prenatal environment is not always identical for both twins, especially in the case of monochorionic twins who share a placenta. One of the conditions that creates marked prenatal discordance is twin-to-twin transfusion syndrome (TTTS), which occurs in 10–15% of monochorionic pregnancies. In this syndrome, the network of blood vessels within the placenta is not evenly distributed, causing an imbalance in blood exchange: one twin (the donor) receives less blood and nutrients, while the other (the recipient) receives an excess. This marked difference in hormonal and nutritional exposure in utero is reflected at the epigenetic level [15].

Studies have detected epigenetic discordances in key genes, such as the glucocorticoid receptor gene (NR3C1) and the protective placental enzyme gene HSD11B2, which are essential for regulating the stress response. TTTS has been specifically linked to epigenetic discordances, such as the hypomethylation of repetitive DNA elements like LINE-1 in donor twins, which correlates with developmental delays and organ dysfunction [14].

## IV. HYPOTHESIS

The optimal adaptability of the individual is achieved when there is a match between the "predicted" environment, programmed in utero through hormonal and epigenetic modulation, and the "real" postnatal environment. Pathology does not simply arise from deprivation but from the discrepancy, or mismatch, between the prenatal and subsequent environments. Research highlights that an artificial womb, providing a static, optimal environment devoid of natural hormonal fluctuations, stress, or circadian rhythms, would fail to deliver the necessary environmental instructions for proper functional tuning. [13]. A foetus programmed for extreme stability, once exposed to the unpredictability of the real world, would experience a catastrophic mismatch. The complete absence of dynamic, adaptive signals in the foetus would result in true “epigenetic misprogramming” [13], leaving the individual unprepared and vulnerable, unable to develop adaptive behavioural and social responses. The challenge in artificial gestation is therefore not the static provision of substances but the replication of the complex dynamic regulation that simultaneously acts as a protective barrier and an adaptive filter.

The interaction between environment and genome translates into a maladaptive phenotype through specific molecular signatures. Early stress, in particular, is known to permanently alter gene expression. A critical target in this process is the Glucocorticoid Receptor gene (NR3C1), fundamental for the regulation of the HPA axis [13]. Studies on human umbilical cord blood samples have demonstrated increased methylation of the NR3C1 gene in children born to mothers suffering from depression in the third trimester of pregnancy. This prenatal hypermethylation of NR3C1 has been shown to predict HPA axis dysregulation, manifested as altered cortisol reactivity to stress in infants as young as three months [16]. Similarly, maternal exposure to interpersonal violence (IPV) during gestation, but not before or after, has been associated with significantly higher levels of NR3C1 methylation in offspring [17]. These epigenetic alterations stabilize an inadequate or exaggerated stress reactivity throughout life, which is the biological basis of psychological vulnerability.

Another key epigenetic target of fundamental importance is Brain-Derived Neurotrophic Factor (BDNF), a protein essential for neuroplasticity, cellular differentiation, and synaptic function. Dysregulation of neuroplasticity, often mediated by epigenetic alterations affecting BDNF, is considered a primary pathogenic mechanism in numerous neuropsychiatric disorders, including major depressive disorder (MDD) and anxiety. Exposure to early-life stress (ELS) is correlated with hypermethylation of the BDNF gene promoter, compromising the brain's ability to remodel in response to experience [13]. BDNF methylation has been associated with maternal prenatal stress in extreme trauma contexts, such as war, with associations observed simultaneously in maternal blood, umbilical cord, and placental tissue, confirming BDNF as a central molecular target of trauma impact [18]. The differential methylation of key genes such as NR3C1 and BDNF constitutes the molecular signature through which the prenatal environment shapes the future coherence between biological and emotional responses [13]. If NR3C1 dysregulation sets an inadequate physiological tone, such as cortisol response, BDNF hypermethylation compromises the brain's intrinsic capacity to learn, integrate emotional experiences, and maintain the plasticity necessary for adaptation. These combined epigenetic modifications act to stabilize a maladaptive and vulnerable phenotype, predisposing the individual to a high psychiatric risk.

Fetal programming, essential for adaptability, depends not only on hormonal signalling but also on the sensory perception of the internal environment. Modern epigenetic research unequivocally establishes that human adaptability is not the result of a fixed genetic code but is mediated by a complex system of dynamic programming. Epigenetics is the molecular mechanism that translates the maternal-fetal dialogue into a psychophysiological phenotype capable of developing a biological response correctly correlated with the emotional response. This translation requires the molecular tuning of the HPA axis (via NR3C1) and neuroplasticity (via BDNF), integrated with the sensory synchronization provided by the multimodal stimuli of the maternal heartbeat and breathing [13].

The hypothesis of gestation in an artificial environment, even if technologically advanced, is configured as the deliberate and complete deprivation of this natural dialogue, both hormonal and sensory. If maternal stress and signals serve as "environmental instructions" for adaptive epigenetic programming, an artificial womb programmed for constant stability would induce "epigenetic misprogramming." Science has demonstrated that maternal mental health and stress permanently alter offspring; the deliberate removal of all maternal inputs (chemical, hormonal, sensory) represents the most extreme form of deprivation, with potentially more severe consequences than those observed in Early Life Stress conditions. The foetus would not receive the critical environmental signals, resulting in an individual profoundly vulnerable and unprepared to face the inevitable variations and stresses of the extrauterine world. The mismatch between the static gestational environment and the real world would be extreme, hindering the primary goal of evolution and development: adaptability [13].

## V. DISCUSSION

The creation of a human being in an environment scientifically insufficient for healthy psychological and physiological development raises a fundamental ethical dilemma. The long-term consequences of maladaptation, such as the cognitive disorders and neurodevelopmental deficits observed in preterm infants, impose a strong ethical imperative on the need to replicate prenatal dynamic inputs. The challenge for future gestational support technologies must not be limited to survival but must focus on replicating the entire dynamic communication system. This includes the complex hormonal modulation based also on fetal sex, the synchronization of circadian rhythms, and, above all, the simulation of multimodal sensory stimuli (voice, vibrations, physiological rhythmic variations). Research must be guided by the ethics of preventing fundamental mismatch, ensuring that the individual receives the epigenetic configuration necessary for coherence between their biological response and emotional experiences, thereby providing them with the adaptive resilience indispensable for extrauterine life environment. Prenatal tactile and auditory stimulation is fundamental in shaping postnatal sensitivity. Disruption of maternal circadian rhythms, for example, has been shown to cause hormonal and inflammatory abnormalities in rodent offspring, highlighting that biological synchronization is a crucial environmental input for epigenetic tuning. There are high-level scientific studies analyzing the effects of hearing the mother's heartbeat and breathing in the context of neurobiological development. A study published in the Proceedings of the National Academy of Sciences (PNAS) provided evidence of experience-dependent plasticity in the Auditory Cortex (AC) of preterm infants. Preterm infants exposed daily to authentic recordings of their mother's voice and heartbeat showed an auditory cortex more adaptively tuned to these sounds, replicating the uterine environment, compared to ambient noise. This evidence suggests that the maternal heartbeat and breathing are not passive background noises but essential inputs that actively direct neurodevelopment toward the demands of the postnatal environment [13].

The analysis of adaptability cannot ignore the multimodal and physical nature of maternal-fetal dialogue. A notable study compared the fetal physiological response, heart rate, and movement, to a passage spoken live by the mother versus a recording of the same passage after prolonged prenatal exposure. The results indicated a differentiated fetal heart rate response: minimal deceleration in response to live speech versus acceleration in response to the recorded format. This difference implies that the physiological tuning required for an adaptable being depends on the multimodal characteristics of physical interaction, such as body vibrations and subtle changes associated with the mother's physical presence, which are absent in recorded input [19]. The maternal heartbeat and breathing actually act as a physiological metronome that provides the sensory context to translate hormonal signals, such as cortisol, into specific neurological preparation. The absence of this dynamic physical dialogue in an artificial womb would constitute sensory deprivation, preventing proper physiological tuning and, consequently, coherence between biological and emotional responses, exacerbating the mismatch described earlier [13].

Despite the deep and lasting epigenetic imprint established during sensitive developmental periods, epigenetic mechanisms, unlike genetic mutations, are dynamically regulated and reversible. This reversibility is crucial because it

means that the psychological phenotype is not set in stone but is subject to continuous reprogramming dictated by environmental conditions and internal states. Various environmental factors, such as nutrition, lifestyle, and psychological states, translate into biological molecules through stress axis activation and immune activation, triggering epigenetic changes even in adulthood. This recognition provides the scientific rationale for the therapeutic efficacy of psychosocial interventions, suggesting that targeted interventions act as causal agents of biological reprogramming.

Neuroscience fully supports the concept that psychotherapy functions as a targeted genomic modulator, capable of correcting emotional and behavioural dysfunctions through epigenetic changes. Psychotherapy is recognized for modifying brain circuits, improving cerebral information processing, and promoting neuronal plasticity. Direct molecular evidence shows that patients who respond positively to therapy exhibit specific alterations in methylation status associated with a favorable clinical outcome. In particular, psychotherapy is able to correct the molecular signatures imprinted by Early Life Stress (ELS), acting on the modulation of stress and plasticity genes. BDNF, previously hypermethylated following early trauma, is a crucial epigenetic target. Studies have observed a decrease in BDNF methylation in individuals with disorders such as MDD and Borderline Personality Disorder (BPD) following psychotherapeutic treatment. This demethylation increases BDNF expression, restoring neuroplasticity and contributing to clinical remission [13].

Epigenetics plays a dual role: it is both a recorder of adverse experiences, creating vulnerability, and a reprogramming dial that offers reversibility. Psychotherapy, as a form of intensive environmental learning, exploits this epigenetic plasticity to physically rewrite the instructions imprinted by trauma, demonstrating the power of a dynamic environment, the therapeutic relationship, in recovering compromised adaptability. Understanding the molecular interaction between environment and genome is essential for guiding therapeutic selection. The efficacy of an intervention is ultimately a reflection of its ability to correct the underlying etiological mechanism. A prospective study that analyzed the interaction between baseline BDNF, childhood trauma, and response to SSRIs revealed a crucial distinction in patient stratification. High BDNF levels predicted remission in traumatized childhood patients treated without SSRIs, suggesting that for a predominantly epigenetic etiology, trauma-related, the environmental and behavioural intervention of psychotherapy might be the modality of choice. Conversely, high BDNF levels predicted remission in non-traumatized patients treated with SSRIs. This evidence pushes toward a personalized psychiatry model, where the identification of epigenetic biomarkers, such as BDNF or FKBP5 methylation, is essential for selecting the most precise therapeutic strategy, confirming that epigenetics is the key to reprogramming the imprints that define psychological adaptability [13]. The study of temperament therefore only makes sense if it is framed in terms of studying the degree and direction by which an individual can adapt and modify their behavior in accordance with the demands of the environment [2]. For example, by becoming aware of their own behavioral patterns, the individual, by making changes to their attitudes and behaviors, produces, as a consequence, modifications in the environment. This is because the changes in the individual result in the dynamics implemented by agents within the social environment losing their effectiveness, forcing those agents to themselves enact behavioral modifications in order to achieve the desired responses.

The same occurs in reverse: if, for instance, a child tries to get what they want through crying and screaming and the parents give in to this behavior, the child's behavior will be reinforced. However, if the parents ignore the behavior and instead focus on the child's emotional experience, the child will understand that such behavior is not functional in achieving their goal and will thus be compelled to adopt a new and different, more functional behavior. According to Thomas and Chess, it is the harmony between the individual's characteristics and the expectations of the environment (what is called the "Goodness of Fit") that ensures positive development. Risk factors are a function of the interaction between these two variables [20], [21], [22].

The interactions between fetus and mother are essential for creating a being with the adaptability needed to develop in a way that is consistent and appropriate to the environment in which they will live. Robotic gestation does not allow contact with the essential hormones for emotional interpretation, exposing the newborn to the risk of becoming an individual unable to recognize the emotional component that underlies all behavior.

The human brain responds to emotional stimuli by initiating specific actions that alter internal states, outward expressions, and the neural structures underlying cognition. These reactions help position the individual in an environment better suited for survival and overall well-being. Emotions signify a shift from a baseline state, marked by internal physiological changes that activate a range of responses. Their functions extend across physiological, motivational, cognitive, communicative, individual, and social dimensions. Beyond their regulatory role, emotions act as critical signals for communication and serve as social mediators. Through emotional socialization, children

acquire appropriate emotional behaviors from adults, who mold and guide these emotions in alignment with societal and cultural expectations. Emotional reactions are shaped by individual traits and cultural context. The amygdala, the brain's hub for processing emotions, is the first to react to stimuli. As a primitive and evolutionarily conserved structure, it retains its adaptive functions. Emotional responses, expressed through voluntary or involuntary motor actions, play a vital role in communication—both verbal and non-verbal. These responses, referred to as affective behavior, are significant because they influence every facet of human life, from psychological to physical well-being. Emotion regulation involves activating new emotional responses or modifying existing ones to align with behaviors deemed suitable for the environment. This process is supported by intricate neural networks that enable emotions to be managed through automatic cognitive mechanisms and deliberate, strategic processes. It is hypothesized that emotion regulation relies on a distributed neural network designed to modulate emotional states, rather than specific anatomical sites dedicated to individual emotional responses [23].

The creation of a human being in an environment scientifically insufficient for healthy psychological and physiological development raises a fundamental ethical dilemma. The long-term consequences of maladaptation, such as the cognitive disorders and neurodevelopmental deficits observed in preterm infants, impose a strong ethical imperative on the need to replicate prenatal dynamic inputs. The challenge for future gestational support technologies must not be limited to survival but must focus on replicating the entire dynamic communication system. This includes the complex hormonal modulation based also on fetal sex, the synchronization of circadian rhythms, and, above all, the simulation of multimodal sensory stimuli (voice, vibrations, physiological rhythmic variations). Research must be guided by the ethics of preventing fundamental mismatch, ensuring that the individual receives the epigenetic configuration necessary for coherence between their biological response and emotional experiences, thereby providing them with the adaptive resilience indispensable for extrauterine life.

On top of the ethical challenges reported above, artificial gestation poses several questions on the commodification of human life. By transforming pregnancy into a marketable service, this technology risks reducing the intrinsic value of life to a transactional exchange, governed by supply, demand, and competitive pricing. Hence, the pregnancy process will acquire characteristics typical of free markets, among which competition between suppliers, the point of the "right price" and consumer demand. Among these, it is particularly concerning the idea to provide a just market price for the creation of life, hence putting a monetary value on the experience itself. [24] Additionally, the lack of state regulation and the difficulty to have a world regulation on artificial gestation leads to further considerations. There is a possibility that, while a government may ban such practices, another one may be willing to adopt this type of technology, hence promoting a sort of "reproductive tourism" towards its country [25]. If coupled with potential state's policies on birth control, we could see how in states where limitations on births is active the usage of artificial pregnancies tools could lead to a bypass of demographic control policies, with maybe even the creation of black markets for the children and an impact on adoption numbers. On the other hand, in countries where there is a high push towards higher birth numbers, the use of artificial wombs could be obliged to increment natality, especially for couples with fertility issues, violating their free will. Another issue lies in the increase of inequality that this operation could lead to. The access to this type of technology may only be possible to wealthier people, hence aggravating social inequality in several states, due to costs relating to artificial pregnancy. Moreover, societal issues such as racism and gender inequality may be further highlighted by artificial pregnancies, as it is possible for parents to select a specific gender- and maybe discriminate against the other- and select traits that are more desirable for the children, favouring looks that undermine diversity [26]. Another ethical concern is due to the lack of knowledge on long term effects of artificial birth and given that the experiment subjects need to be human, there is a risk for a whole generation of children who may develop issues in the long run which we are not aware of currently [27]. Finally, the mental well-being of the child can also be impacted. Identity develops through relations and cultural context [28]. A child born by artificial gestation may feel alienated and different from others surrounding him, hence creating issues with their self-worth and their place in the world. Cases of bullying may also happen, with two scenarios being equally possible, with the children posing either as perpetrators (if perceived as "superior") or victims (if stigmatized as "artificial"). Considering the evolution from human–robot interaction (HRI) to collaboration (HRC) and ultimately teaming (HRT), epigenetics and artificial gestation are foregrounding human-centric requirements such as responsibility, user acceptance, transparency, and post-deployment oversight [29]–[32]. Complementary strands examine digital twins (DTs) of humans and robots as socio-technical instruments for monitoring, auditability, and risk management within HRT, arguing for "trust-by-design" practices and fit-for-purpose evidence regimes that could inform any safety case for artificial gestation technologies [30],

[32]. These works emphasise how legal and technical controls must be co-designed—linking validation, runtime assurance, and policy—to mitigate systemic vulnerability in human-centered robotics [33]. Finally, applied work on HRT controllers and multimodal feedback in emergency response illustrates how ethically framed design translates into concrete interface and control choices—an approach transferable to requirements for dynamic sensing, alarm thresholds, and human-in-the-loop governance in prenatal support systems [34].

## VI. CONCLUSIONS

Modern epigenetic research unequivocally establishes that human adaptability is not the result of a fixed genetic code but is mediated by a complex system of dynamic programming. Epigenetics is the molecular mechanism that translates the maternal-fetal dialogue into a psychophysiological phenotype capable of developing a biological response correctly correlated with the emotional response. This translation requires the molecular tuning of the HPA axis (via NR3C1) and neuroplasticity (via BDNF), integrated with the sensory synchronization provided by the multimodal stimuli of the maternal heartbeat and breathing.

The hypothesis of gestation in an artificial environment, even if technologically advanced, is configured as the deliberate and complete deprivation of this natural dialogue, both hormonal and sensory. If maternal stress and signals serve as "environmental instructions" for adaptive epigenetic programming, an artificial womb programmed for constant stability would induce "epigenetic misprogramming." Science has demonstrated that maternal mental health and stress permanently alter offspring; the deliberate removal of all maternal inputs (chemical, hormonal, sensory) represents the most extreme form of deprivation, with potentially more severe consequences than those observed in Early Life Stress conditions. The fetus would not receive the critical environmental signals, resulting in an individual profoundly vulnerable and unprepared to face the inevitable variations and stresses of the extrauterine world. The mismatch between the static gestational environment and the real world would be extreme, hindering the primary goal of evolution and development: adaptability.

## REFERENCES


[1] A. Adya, P. Bahl, J. Padhye, A. Wolman, and L. Zhou, “A multi-radio unification protocol for IEEE 802.11 wireless networks,” in Proc. IEEE 1st Int. Conf. Broadnets Netw. (BroadNets’04), Los Alamitos, CA, USA: IEEE, pp. 210–217, 2004.

[2] G. Attili, Alle basi della personalità. Teorie, metodi e ricerche sul temperamento. Firenze, Italia: Giunti, 1993.

[3] A. Thomas and S. Chess, “The New York longitudinal study: From infancy to early adult life,” in The Study of Temperament, Psychology Press, pp. 39–52, 2013.

[4] S. Chess and A. Thomas, “Temperamental individuality from childhood to adolescence,” J. Am. Acad. Child Psychiatry, vol. 16, no. 2, pp. 218–226, 1977.

[5] Y. Thomas et al., “Functional analysis of human T cell subsets defined by monoclonal antibodies. I. Collaborative TT interactions in the immunoregulation of B cell differentiation,” J. Immunol., vol. 125, no. 6, pp. 2402–2408, 1980.

[6] H. H. Goldsmith et al., “Roundtable: What is temperament? Four approaches,” Child Dev., vol. 58, no. 1, pp. 505–529, 1987.

[7] T. Partridge and J. V. Lerner, “A latent growth-curve approach to difficult temperament,” Infant Child Dev., vol. 16, no. 3, pp. 255–265, 2007.

[8] J. V. Lerner, “The role of temperament in psychosocial adaptation in early adolescence: A test of a ‘goodness of fit’ model,” J. Genet. Psychol., vol. 143, no. 2, pp. 149–157, 1983.

[9] D. Noble, “Conrad Waddington and the origin of epigenetics,” J. Exp. Biol., vol. 218, no. 6, pp. 816–818, 2015.

[10] M. Basso, S. Sleiman, and R. R. Ratan, “Looking above but not beyond the genome for therapeutics in neurology and psychiatry: epigenetic proteins and RNAs find a new focus,” Neurotherapeutics, vol. 10, no. 4, pp. 551–555, 2013.

[11] A. Iannitelli and M. Biondi, “Epigenetics in the therapy of psychiatric disorders,” Riv. Psichiatr., vol. 49, no. 1, p. 1, 2014.

[12] S. M. Stahl, “Psychotherapy as an Epigenetic ‘Drug’: Psychiatric Therapeutics Target Symptoms Linked to Malfunctioning Brain Circuits With Psychotherapy as Well as With Drugs,” J. Clin. Pharm. Ther., vol. 37, no. 3, pp. 249–253, 2012.

[13] P. D. Gluckman, M. A. Hanson, and A. S. Beedle, “Non-genomic transgenerational inheritance of disease risk,” BioEssays, vol. 29, no. 2, pp. 145–154, 2007.

[14] J. E. Castillo-Fernandez, T. Spector, and J. Bell, “Epigenetics of discordant monozygotic twins: implications for disease,” Genome Med., vol. 6, no. 7, p. 60, 2014.

[15] C. R. Lewis, H. A. Sowards, M. J. Huentelman, L. D. Doane, and K. Lemery-Chalfant, “Epigenetic differences in inflammation genes of monozygotic twins are related to parent-child emotional availability and health,” Brain Behav. Immun. Health, vol. 5, p. 100084, 2020.

[16] L. Cao, D. Laplante, and S. King, “Prenatal Maternal Stress and Epigenetics: Review of the Human Research,” Curr. Mol. Biol. Rep., vol. 2, 2016.

[17] M. Kundakovic, K. Gudsnuk, J. B. Herbstman, D. Tang, F. P. Perera, and F. A. Champagne, “DNA methylation of BDNF as a biomarker of early-life adversity,” Proc. Natl. Acad. Sci., vol. 112, no. 22, pp. 6807–6813, 2015.

[18] L. Provenzi et al., “Is Brain-derived neurotropic factor methylation involved in the association between prenatal stress and maternal postnatal anxiety during the COVID-19 pandemic?” Front. Psychiatry, vol. 13, p. 950455, 2022.

[19] L. Massoni, “Epigenetic and Mental Diseases: The Role of Psychotherapy,” Int. J. Transl. Med., vol. 4, no. 3, pp. 450–462, 2024.

[20] M. Rutter, “Temperament: Concepts, issues and problems,” in Ciba Found. Symp. 89—Temperamental Differences in Infants and Young Children, vol. 89, Chichester, UK: John Wiley & Sons, Ltd., 1982.

[21] P. Graham and J. Stevenson, “A twin study of genetic influences on behavioral deviance,” J. Am. Acad. Child Psychiatry, vol. 24, no. 1, pp. 33–41, 1985.

[22] W. B. Carey and S. C. McDevitt, “Stability and change in individual temperament diagnoses from infancy to early childhood,” J. Am. Acad. Child Psychiatry, vol. 17, no. 2, pp. 331–337, 1978.

[23] C. Brasi and C. Matteuzzi, “Defense of Ethical Behavior, Integrity, and Freedom of Thoughts,” in *Proc. 2024 Asian Conf. Commun. Netw. (ASIANComNet), Bangkok, Thailand, pp. 1–7, 2024.

[24] D. Hall, “‘Commodification of everything’ arguments in the social sciences: Variants, specification, evaluation, critique,” Environ. Plan. A: Econ. Space, vol. 55, no. 3, pp. 544–561, 2022.

[25] D. Spar, “Reproductive tourism and the regulatory map,” N. Engl. J. Med., vol. 352, no. 6, pp. 531–533, 2005.

[26] D. E. Roberts, “Race, gender, and genetic technologies: A new reproductive dystopia?” Signs: J. Women Cult. Soc., vol. 34, no. 4, pp. 783–804, 2009.

[27] C. Fethe, “Beyond voluntary consent: Hans Jonas on the moral requirements of human experimentation,” J. Med. Ethics, vol. 19, no. 2, pp. 99–103, 1993.

[28] D. B. Maehler e D. Hernández-Torrano, “Identity Development Research: A Systematic Review of Reviews,” Self Identity, pp. 1–36, 2025.

[29] F. Sanfilippo, M. H. Zafar, T. Wiley, and F. Zambetta, "From caged robots to high-fives in robotics: Exploring the paradigm shift from human–robot interaction to human–robot teaming in human–machine interfaces," Journal of Manufacturing Systems, vol. 78, pp. 1–25, 2025.

[30] E. F. Langås, M. H. Zafar, and F. Sanfilippo, "Harnessing digital twins for human–robot teaming in Industry 5.0: Exploring the ethical and philosophical implications," in Proc. IEEE Symp. Series on Computational Intelligence (SSCI), 2023.

[31] M. T. Hua, E. F. Langås, M. H. Zafar, and F. Sanfilippo, "From rigid to hybrid/soft robots: Exploration of ethical and philosophical aspects in shifting from caged robots to human-robot teaming," in Proc. IEEE Symp. Series on Computational Intelligence (SSCI), Dec. 2023.

[32] E.F. Langas, M.H. Zafar, and F. Sanfilippo “Exploring the synergy of human-robot teaming, digital twins, and machine learning in Industry 5.0: A step towards sustainable manufacturing” J. Intell. Manuf,2025.

[33] F. Sanfilippo and M. H. Zafar, "Human–robot teaming: A universal controller with multimodal feedback for emergency response robots," in Proc. Int. Conf. Robot. Autom. Eng. (ICRAE), 2024.

[34] A. S. S. Gonsholt, E. E. Greca, M. Haddad, M. H. Zafar, and F. Sanfilippo, "Enhanced human-robot teaming through attention multi convolutional neural network-based multi-modal sensor fusion for hand gesture recognition and orientation control," in Proc. 58th Hawaii Int. Conf. System Sci. (HICSS), Jan. 2025, pp. 590–599.