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Asymmetric developmental bifurcations in polarized environments: a new class of human variants, which may include autism

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Inspired by discrete stable alternative states that often coexist with the dominant phenotypes of a species, we propose that asymmetric developmental bifurcations (ADB) may provide a biological framework for grouping autism together with some human alternative organizations rather than with disorders or diseases. These include minority embryological or obstetrical variants, such as twinning and breech presentation, as well as minority information processing variants, such as left-handedness and importantly prototypical autism. Four common contextual, developmental, adaptive, and mechanistic features unify these alternative conditions as ADBs: 1) ADBs occur in a dynamic system formed by an individual and his environment with two polarized stable solutions. 2) The bifurcation occurs in a critical period of development and is significantly shorter than the stable states that precede and follow it. 3) While the frequent branch of the ADB optimizes evolutionary success, its rare branch has an adaptive cost, which is still compatible with survival. 4) Both rare and frequent branches of the ADB are human possibilities, favoured without major/deleterious changes by familial and/or sexual predispositions. Framing autism as a categorical, alternative phenotypic prototype in a polarized choice between social bias and its absence, elucidates autism's recurrent divergence within the species, its developmental and information processing characteristics, and its adaptive challenges.

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BACKGROUND

In the context of evolutionary theory, living organisms typically exhibit relatively stable phenotypes during hundreds of years despite constant, but minor, variations across multiple traits. Large evolutionary changes occur over longer periods through the alignment or misalignment of these variations with unpredictable environmental changes. On the time scale of a single individual's life, several states of alternating equilibrium can compete with the dominant state of the individual. Some of them belong to the heritage of the species (anger, anxiety) but become pathological and psychiatric when extreme. However, a unique form of alignment between variations of living organisms and their environment occurs when a species simultaneously presents two stable, sometime lifelong alternative possibilities, each resulting in largely distinct phenotypical states coexisting within the same species, albeit at an asymmetric prevalence. In animals, situations have thus been identified where a continuously distributed genetic liability produces two contrasting adult morphological, physiological, or behavioural phenotypes, stably but asymmetrically represented within the species. This is the case, for instance, of the coexistence of long-winged and flightless forms of certain female locusts [1]. The orientation toward one or the other of these alternative states satisfies randomly distributed genetic factors evolving in a constrained environmental system [2].

In humans, alternative stable states can also exist, although they are not typically described as such. One of the most obvious examples is hand dominance, being left-handed rather than right-handed. Other "developmental", stable alternatives are mostly observed during the embryonic development, such as twin pregnancies rather than single, or presenting in the breech rather than cephalic position at birth. Each of these variants has been extensively studied in regard to their internal and external liabilities, their predisposing factors and evolutionary persistence, despite their adaptive challenges. However, they have not been conceptualized through their common properties as *alternative developmental stable states*.

This article builds upon these existing separate accounts to introduce a coherent new perspective on autism as a human developmental possibility, namely as an *asymmetric developmental bifurcation (ADB)*. We argue that unifying these different phenotypical longitudinal variations, beside the interest of conceptualizing them as "natural" human possibilities within

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human evolutionary changes, shed light on the biological, evolutionary and societal status of autism. Critically, it may account for the particularities and resemblance of autistic children in their prototypical form, for which continuous models of liability fail [3]. While societal progress, particularly the neurodiversity movement, has increasingly questioned the categorization of autism as a disorder, it remains to elucidate if and how it differs from a disease. By comparing autism to other alternative states in the biology of the human species, we can potentially enhance both their societal standing and the scientific inquiry into them.

One way to model alternative psychological states is to consider them as attractors of a dynamical system. The application of dynamic systems to the modelling of variations in a cognitive or psychiatric state generated two streams of research. The most established focuses on the notion of bifurcation in the formation of an organism: a phenotype is a consequence of the development that precedes it, at the moment where it appears as distinct. It finds fruitful applications in the modelling of organogenesis in embryology, in relation to evolutionary constraints [4]. These authors convincingly established how continuous genetic variation can generate discontinuous phenotypes through the mechanics of a "developmental program". The other, more recent stream, applies at the neurobiological level the notion of attractor and return to equilibrium after perturbation of a system [5]. It concludes that itinerancy between attractor states in neural systems explains how discrete states can emerge and persist through neural dynamics. This modelling can be extended to psychiatric destabilization at large (e.g., mood fluctuations, panic attacks; for a review of psychiatric applications, and to suggest types of data collection or intervention in this framework, see [6, 7]). Dynamic conceptualization provides a coherent understanding of the interactive and multicausal nature of developmental transformations and manifestations (e.g., see Smith & Thelen, 2003 [8] for a developmental application of dynamic systems theory). Overall, dynamical systems theory offers psychiatry a framework to understand mental illness as a temporal, physiological phenomenon with identifiable parameters, transitions, and patterns, moving beyond static disease models [9].

Our approach is primarily inspired by the first, embryological biological application of the dynamical system framework, applied to a condition considered partly neurodevelopmental and partly psychiatric: autism. It is based on a non-trivial analogy between postnatal developmental programs in the context of which the autistic phenotype develops, and the sequence of morphological development organizing the transformation of the foetus. This trend of research relies on applying developmental bifurcation modelling on the succession of stable normative states, and the occurrence of distinct and rare alternatives psychological organizations on a large time scale. We hereby hypothesize that certain developmental discontinuities, *asymmetric developmental bifurcations*, are characterized by the 4 following properties:

System polarization

Asymmetric developmental bifurcation occurs in an inexorably evolving dynamic system composed of the developing individual and its living and informational environment. At various time points, its development is channelled into states compatible with its biological constraints, according to dichotomous poles of its environment. ADBs occur when a dominant and an alternative state are the only two possible solutions of the system.

Non-linear temporal parameters

ADB evolution contrasts bifurcation point and stable states. The bifurcation decision occurs in a critical period of development and is significantly shorter than the stable states that precede and follow it. Those are stable under minor perturbations, resulting in their long-term irreversibility to external intervention or random events, while intermediate states are unstable.

Asymmetrical prevalence

The common and rare states of an ADB differ in their respective prevalence and adaptive properties. Common states circularly optimize evolutionary success. Rare states have an adaptive cost, but are still compatible with survival.

Inclusion among possibilities of the species

The rare outcome branches of an ADB occur at a basic, constant rate in the human species. When chosen, they are favoured by familial and/or sex-linked predispositions without major/deleterious modifications. Mechanic or genetic changes of typical development may act as predisposing factors, not as causal factors.

These four properties (see Mottron, 2024 [10] for a detailed account) will be presented for a canonical ADB, breech presentation, then twins and left-handedness, before exposing how they can shed light on several crucial aspects of the development and characteristics of autism.

Breech presentation as a canonical asymmetric developmental bifurcation

System polarization. At the end of pregnancy, the dominant position of the human fetus is head down, with the nose facing the mother's sacrum [11]. Human anatomy, head-to-body size ratio, and the timeline of pregnancy impose two polarized solutions to the fetal position after the period during which the fetus "floats" in the uterine cavity, one of which is heavily favoured by evolution [12]. If the fetus remains positioned head-up when it becomes too bulky to turn around, it will stay in this position until delivery unless external manoeuvres are performed, resulting in a breech delivery. Breech presentation is typically categorical, with two major subtypes: complete breech (with feet touching the bottom, 35.8%) and frank breech (with feet touching the head, 64.2%) [13]. It is also stable: spontaneous version is rare, and spontaneous reversion after an external cephalic version is common [14].

Non-linear temporal parameters. The bifurcation between cephalic and breech presentation occurs at a critical moment in fetal development, determined by the gradual change in the size relationship between the developing fetus and its uterine environment. It becomes irreversible around the 25th week of gestation [15]. The prevalence of breech presentations decreases tenfold between gestational weeks 24–25 and term pregnancies, and the likelihood of a spontaneous reversal due to its movements in the uterine cavity and its own kicking radically diminishes [16].

Asymmetrical prevalence. Breech presentation occurs in 3–5% of pregnancies with minimal variation in prevalence over historical eras and across all ethnic groups, and never becomes the majority [17]. It results in a partial, unpredictable compatibility with survival, being historically a significant cause of fetal or maternal death and serious perinatal injuries still around 1% [18, 19] in vaginal deliveries of breech presentations. These adverse outcomes are now largely prevented by the routine practice of caesarean sections [20], external cephalic version [21] and improved aseptic precautions. In most cases, the baby is now born without problems and shows no long-term effects [22].

BD as a possibility of human pregnancy. In most breech presentations and deliveries, neither the child nor the mother has diseases, genetic anomalies, or malformative anomalies. Neither have they experienced any particularly traumatic, infectious, or metabolic incidents during pregnancy or delivery. Breech presentation is more common in children of parents delivered in breech presentations (OR = 2.2) [23]. Its multiple predisposing factors, such as a fetus being too small or too large

for the gestational age, a uterus that is too small, too large, too rigid or too flexible, or a woman of small stature, are frequently familial, acting alone or in conjunction with other contributing elements such as prematurity, being a female fetus, and random events[15, 24],.These factors are most frequently dimensional (*e.g.*, older maternal age, low gestational age, low birth weight), but also categorical, yet non-pathological per se (*e.g.*, nulliparity, female fetus). More rarely, breech deliveries are associated with identified genetic anomalies (*e.g.*, teratogenic mutations, copy number variations in the child) or heterogeneous embryological defects (25:6,5, 26:11,7%), uterine malformations, or obstetrical events (*e.g.*, abnormal placenta implantation, or any other incident occurring during pregnancy or close to delivery) [25, 26].

Twin pregnancy

System polarization. Twinning subtypes and twinning itself are determined by divergent possibilities of the same mechanisms regulating typical human reproduction. The majority of human pregnancies are uniparous mono chorionic (one placenta) and mono amniotic (one amniotic sac), but a bifurcation is possible at the time of fertilization and in the days following it towards rarer form of twin pregnancies. While the number of fetuses is, in absolute, an ordinal trait, there is a *de facto* polarization of the types of possible twin pregnancies. They are compatible with a pregnancy carried to term, at least for some of them.

Non-linear temporal parameters. The developmental program of cellular and hormonal events involved in twinning, whatever its subtype, follows a unidirectional, irreversible sequence. The bifurcation of the reproductive system towards one or other of the types of pregnancy is an event counted in days. Its duration depends on the type of twin pregnancy, each of which involves a distinct synchrony between single or multiple ovulations on the one hand, and fertilization by one or more spermatozoa and the division of the zygote on the other. In dizygotic pregnancy, this event is prepared during the follicular period of two weeks by the maturation and release of two follicles, but the critical moment remains that of their simultaneous fertilization by two spermatozoa. In the case of monozygotic pregnancy, the division of the zygote occurs between the 1st and 13th days after fertilization [27], giving rise to a bichorial diamniotic (>3 days), monochorial twin pregnancy diamniotic (3–6 days) or very rarely monochorial monoamniotic (7–13 days), but the division itself, whenever it occurs, is a matter of hours.

Asymmetrical prevalence. Twin pregnancy occurs in less than 2% of pregnancies, consistent over the past century [28] for dizygotic twins, with around 3-4 dizygotic for one monozygotic. Monochorionic monoamniotic twins are very rare (1% of monozygotic pregnancies). Twin pregnancy can lead to very severe consequences for unborn children (extreme prematurity, fetal death cord entanglement, extreme prematurity, perinatal mortality, malformations, transfuser-transfused syndrome [27]. The survival rate of at least one twin was still lower than that of singleton pregnancies in 1950 [29]. However, twin pregnancy is compatible with the birth of a normal individual, without any adaptive disability.

Twinship as a possibility of human pregnancy. The factors that favour multiparous pregnancies are non-pathological dimensional and ethnic in nature and add to family predisposition. The risk doubles between the ages of 20 and 40. At a constant number of pregnancies, twice as many twins are born in Africa than in Europe, and three times more than in Asia. Hormonal treatments for subfertility and in vitro fertilization multiply them by a factor of 15. Beyond ethnicity, the predisposition to having twin pregnancies runs in families. The risk ratio of twin offspring for a twin parent is 2.49 [30]. Common variants make up a polygenic score that favours twin pregnancy in combination with chance (which also controls the survival rate) and other kinds of traits. It is shared by both parents [31]. A slight excess of males is observed in both mono and dizygotic twins [32].

Left-handedness

System polarization. Manual lateralization is largely dichotomous. The lateralization of eye, foot, hand, and language are most often, but not constantly, associated with each other, with a clear dominance for a lateralization of the hand on the right processed by the opposite hemisphere of the brain, and of language on the left hemisphere [33]. Handedness can be task-specific (*e.g.*, between hand and foot), justifying the category of "mixed handedness", but the dichotomy remains explanatory between left-handers (2.4% strong, 9.1% mixed) and right-handers (56% strong, 29% mixed). Ambidexterity is rarer (3.3%[34],) and may represent an independent and rare outcome, differing by the common variants predisposing to it [35]. However, lateralization is fragmented into hand performance and hand preference, into different functions (*e.g.*, eye, hand, foot) and tasks (writing, throwing) components.

Non-linear temporal parameters. The orientation towards a rare lateralization would take place during intrauterine life [36], since the fetuses already suck their right thumb in the majority. The unstable period between the two branches of the bifurcation consists in come-and-go dominance alternative, following a dynamic system progression until stabilization at an equilibrium, stable state [37]. Hand preference can be reliably detected from 6-months onwards [38] but is only stabilized around 6 years [39]. For cerebral lateralization of language, it continues after adolescence [40].

Asymmetrical prevalence. There is no human group where left-handed people are in the majority [41]. The prevalence of left-handedness is estimated at 10.6% [42] therefore at least three times more than breech birth, 5 times more than twin birth and ten times more than prototypical autism. Right-brain dominance for language increases with the degree of left-handedness [43]. Ethnic [44] and historical [45] differences in handedness are relatively stable, in the range of a few percent. The term "left-handedness" is largely negatively connoted in multiple civilizations and "correction" of left-handedness was the norm in the first half of the 20th century, at least for writing [46]. "Converted" left handeds for writing are rare (*e.g.*, 9.5%[47],) and still use their left hands for other tasks [48].

Left-handedness as a possibility of human brain organization. Despite the importance of the functional brain modifications causal or consecutive to left-handedness [49], it is not pathological. Several dimensional characteristic values increase the probability of being left-handed. Decreased gestational age and/or birth weight increases its prevalence, which exceeds 20% in prematurity. This increase is not associated with identifiable neurological lesions, however [50]. Left-handedness obeys a consensual family predisposition [51, 52], despite some heterogeneity in measurement and targeted groups [53]. The polygenic disposition to left-handedness implies the non-pathological polymorphism of several dozen loci [35, 49]. This acts in conjunction with a male predisposition [42]. Left-handedness prevalence has increased during evolution [54]. It is now stable in the human species on a historical scale, but presents minimal differences in prevalence between ethnic groups [55], normative cultural pressure [56], and over time [57]. Critically, as is the case for autism, monozygotic twins are frequently discordant for laterality [58]: the genetic constraints on lateralization leave the possibility of a polarized, possibly random, post-conception alternative.

Prototypical autism as an asymmetric developmental bifurcation of information processing

The existence of children who exhibit distinct, albeit very similar behavioural features at the same age was the basis for the initial categorical recognition of autism [59] and remains that of its accelerated, worldwide detection by experts [60]. This form is identified (with certain nuances) as "frank" [61], or prototypical, but does not conceptually or clinically overlap with ''severe" autism. It is narrower than the DSM 5 [62] and the ICD-11 [63] autism spectrum criteria. Prototypical autism [62] refers to a highly homogeneous autistic phenotype that typically emerges during the second year of life. It is characterized by a developmental plateau or a socio-communicative regression, alongside the recognizable onset of specific signs. This presentation occurs in the absence of any identifiable neurological or genetic condition that could explain the phenotype and is recognized with a high degree of clinical certainty. It excludes borderline presentations such as the former pervasive developmental disorder not otherwise specified (PDD-NOS) or the "Asperger" phenotype described in the DSM-IV. In the following, "autism" refers to prototypical autism.

System polarization. We call "social" what, in the world surrounding an individual, belongs to its human conspecifics, and "non-social" the physical, structural, informational and perceptual properties of this surrounding world. Information surrounding the typical child, in his first years, is temporally and/or spatially related to the presence of his caregivers, conditioning its processing and further integration in a certain relation to these caregivers. The social bias in the processing of information (*e.g.*, joint attention) is the subjective integration of this relationship in the construction of one's cognitive and emotional life [64]. Typically, the processing of environmental information is influenced by the consideration of others as intentional agents, particularly in situations requiring joint attention or in symbolic play where a fictive other is assumed. Processing information in terms of social bias or its absence is not simply a matter of dividing one's surrounding world it into its social and non-social elements. Rather, it reflects a mode of processing, in which the social value attributed to a given content radically shapes the way it is perceived and interpreted. We define "social bias" as the processing of information in reference to a conspecific, whether real or symbolically assumed, in guiding behaviour or reasoning. Humans can indeed treat social information (a face, a voice, a movement) without social bias, for example, as a physical, perceptual property. Conversely, they can treat an a priori non-social element of the world (*e.g.*, a physical, perceptual, or informational property) as symbolically inseparable from its social or human-related character, as when a voice is treated as speech rather than noise, or when an object is interpreted as a representation of a human in pretend play. What we call *social bias* is therefore the treatment of an information (which itself can be "human" or "non-human") in a certain relation to the conspecific, and *absence of social bias* refers to its processing independently of such a relation.

The polarization that allows our integration of autism into ASB is the contrast between social bias and the possibility of doing without it, in the sense that, during childhood, autism follows a non-socially biased path in processing its surrounding world [65]. While the information within a child's environment is typically interpreted through this *social bias*, it can alternatively be processed based solely on its physical or informational properties[1]. This social/non-social polarization of the child's orientation towards his environment can be applied to his entire animate, inanimate and linguistic umwelt [66].

The behavioural data supporting this reinterpretation of autism as a rare bifurcation toward the processing of information without social bias, in the polarized *social bias*/*no social bias* system, is the bipolarity of autistic signs between signs of area A (deficit in social interaction) and area B (presence of non-social, "repetitive" signs), in the DSM 5 (for a detailed treatment, see [62]). The distribution of autistic signs in the DSM 5 is polarized between 3 "A" signs: A1: deficit in social reciprocity; A2: deficit in non-verbal behaviours, as socially oriented facial expressions; A3: deficit in establishing and maintaining relations and 4 "B" signs: B1: stereotyped movements or speech, B2: intolerance to change, B3: intense fixed interests; B4: atypical sensory-based behaviours. Autistic "A" signs are both *social* and *negative*: they manifest the absence of a behaviour directed toward or with conspecifics that typical individual does (*e.g.*, joint attention). Autistic "B" signs are both *non-social* and *positive*: they are behaviours toward physical, structural or informational aspects of the word that only autistic children produce to this extent (*e.g.*, prolonged fixation of rotating objects).

The dichotomy is taken as evidence for both the polarization of the possible processing of environmental information by the child and the orientation toward autism in this bifurcation, as manifested by its defining signs. This polarization goes beyond the tautological rewording of social "A" signs and repetitive "B" signs of autism as social and non-social signs. It accounts for their *relation* and their simultaneous, overt appearance during development. In this context, we reinterpret the 3 "social" signs of autism in the DSM 5 (reduction or atypicality of socio-emotional reciprocity, non-verbal aspects toward *congeners* and long-term *social* relationships) as the processing of (and interest for) environmental information that disregards the typical *social bias*. This absence of hierarchical role and importance of conspecifics, results in a reorientation of the largest part of motivational and processing resource toward a recurrent, but above all increased, interest in non-social aspects (physical, causative, mechanistic) of the universe around him. The four "repetitive" signs in the DSM-5 (repetitive movements and use of *objects*, intolerance to overall *environmental* changes, intense interests in specific categories of *objects or information*, and general "*sensory*" aspects) result from interest in, reactivity to, and processing of information without *social bias*; the information is not analysed as cooperative or socially relevant.

Empirically, this is manifested by superior performance, role and autonomy of perception [67–69] (e.g., Mottron et al, 2007 [70], Ozonoff et al. [71]), the absence of superiority of social orientation indices -such as the adult's gaze on non-social cues like arrows, to direct the child's attention [72], the spontaneous and preferential orientation preference toward inanimate and non-social complex information [73], the prolonged neural encoding of visual information [74]. Alterations in brain processing hierarchy that may favour externally oriented perceptual processing compared to socio-cognitive processing, have been demonstrated by three different groups [75–79]. This bifurcation toward a disregard for social bias in a polarized possibility of information processing finds its clearest example in language, which can also be perceived and used to communicate with someone, or be treated as a pure form, as a mental object [80]. In the absence of a social bias for language processing, it is then reduced to a formal system with rules and regularities. The non-social learning of language [81] therefore finds a similar origin. Overall, the autistic toddler preferentially orients itself and processes non-social informational/ not socially biased aspects of this environment [82].

Non-linear temporal parameters. The autistic bifurcation would be the gradual, then accelerated and momentarily irreversible transition, reorienting a hierarchized relationship with the world obeying a *social bias*, toward a processing of information

[1]This is inspired from René Thom's opposition between the "pregnance" of a form, its species-related biological effects, and the "salience" of its physical and informational properties (66.Wildgen W. Thom's theory of „saillance"and „prégnance" and modern evolutionary linguistics. In: Wildgen W, Per Aage Be, editors. Semiosis and catastrophes. Bern: Peter Lang; 2010. p. 9-19.

independently of this bias. Before autism in its most prototypical form is clinically detectable, around the 4th trimester of life, "sib-pairs" studies of siblings of autistic children show discreet indications of prolonged treatment of non-social aspects of environment [71] and less interest in or reaction to peers or parents [83, 84] from the end of the first year. Quite abruptly around 18–22 months [85], spontaneous orientation and reception of the social concomitants of the information present in his environment reduce drastically. The reactivity, constant in the typical child, to the visual and auditory addresses that other humans send them, as well as socially oriented initiatives will regress [85, 86], representing frequently the first red flag for an autism diagnosis in parents and professionals. This regression is often concomitant with a loss of oral language, or an absence of its development which can last several years [87]. The child will then favour non-communicative aspects of language [81] particularly written language, over the oral language carried by the conspecific [88, 89].

Following the fourth-semester critical points where distinct and recognizable signs abruptly manifest, the prototypical autistic phenotype remains stable in the first years. In contrast, it can lead to unpredictable and considerable modifications during school years and later on. The modifications of an autistic phenotype consecutive to intervention do not fundamentally alter the child's trajectory [90]. The transactional [91] nature of autistic signs, -each sign happens in a dyadic child-peers relation, associating the child and his or her social life context-, makes the signs modifiable by the way in which they are received. However, the modifications obtained are minimal [70], even if they can fall below a conventional diagnostic threshold [92]. Autism once installed resists attempts to reverse it. Attempts to prevent it before its onset in children at risk [93] have not shown their capacity to profoundly influence the autistic developmental trajectory.

Asymmetrical prevalence. The prevalence of autism, even if we stretch the diagnostic criteria, remains below 5%. The median of prevalence studies is around 1% [94], therefore in the same orders of magnitude as the other bifurcations, with the exception of left-handedness. This prevalence remains relatively constant over time if we stick to prototypical autism [95]. It, however, increases considerably when prototypicality of the presentation is not considered [96, 97]. Higher prevalence reported in US can be explained by the combination of service-based subject ascertainment, minimal specificity of instruments in clinical settings [98], social pressure to obtain a diagnosis [99], inclusion of diagnosis in adulthood without any notable signs during development [100], and the absence of differential diagnosis with varied conditions whose predominant symptoms are of psychiatric nature [101].

Autism, even in the most favourable outcome, always has an adaptive cost: despite notable exceptions autistic lives are, overall, more difficult, less successful, more at risk of physical issues, shorter and more challenging than those of the typical population [102]. This cost can extend over a lifetime, with the autistic person remaining dependent on those around them for their access to autonomy and sometimes even for their survival. The adaptive prognosis of people identified as on the "autism spectrum", however, depends on the more or less conservative way in which their diagnosis is operationalized. Even when restricted to autistic people without an associated neurodevelopmental condition, but who present a frank picture at preschool age [103], autism can lead to diametrically opposed adaptive prognoses from the same level of severity, prototypicality and clinical certainty, without a reliable predictor [104]. The notion of optimal outcome [105] indicates that 10–30% of previously diagnosed autistic children no longer meet the criteria for ASD at adolescence. The tendency for adaptive and communicative improvement is dominantly found, while a minority but highly variable portion present major behavioural problems, and/or a state of almost complete dependence on those around them [106]. This same gap is found in the language prognosis: around a tenth of them remain functionally non-verbal, compared to a tenth who progress towards perfect language. The majority evolves towards a more or less functional language [107].

Autism as a human possibility. There are currently no established biomarkers for autism [108]. An extensive meta-analysis of the biochemical (374 studies), brain imaging (203 studies), neurophysiological (133 studies), neuropsychological (65 studies) or genome-wide associations (5 studies) studies, did not find any biomarker that can have a sensitivity and specificity beyond 80% in two independent studies [109]. Whether at the genetic or anatomical brain imaging level, we identify deleterious, possibly causative mutation or neurodevelopmental events, in less than 10% of autistic individuals as currently defined, and these differ from one comorbid syndrome to another [110]. Neuroimaging subtyping studies have, furthermore, pointed to marked variations in structural as well as functional imaging phenotypes across individuals [111, 112] idiosyncratic to each individual [113] but overall compatible with disappearance of the social bias and enhanced perceptual functioning models [67]. The reversal of processing hierarchies [76, 77] has been put forward as a unifying principle across findings in neuroimaging and cognition [114]. It implies a reorganisation of an otherwise intact information processing and motivational system, rather that the cascadic consequence of a deleterious neurogenetic event.

Familial predisposition is one of the most established aspects in the neuroscience of autism. A family that has had an autistic child is more than 20 times more likely that its next child will also be autistic. If it has 2 autistic children, they are almost 40 times more likely than in the general population [115]. Family predisposition can be mediated by the level of education of the parents [116]. Monozygotic twins are more often concordant than discordant for autism, but this concordance but does not exceed two-thirds [117, 118], as is the case for laterality. Concordance does not imply severity, a notion that associates adaptive challenges and prototypicality of presentation [119]. The expression of this condition can thus differ even in identical twins and go as far as a frank discordance. The median male:female ratio of autism [94] is around 4/1, but lower values (3/1) are reported as well [120], circularly dependent on the accepted prototypicality of the feminine phenotype. Harmonious macrocephaly is not a biomarker strictly speaking, since it does not concern the entire autistic population, and is unequally distributed between autistic men and women. It can be classified as a risk factor, but still aggregates to the most prototypical presentations [103].

DISCUSSION

At least four non-pathological embryological (Twinship, Breech presentation) and information processing (Left Handedness, Autism) stable alternative states of the human species share several remarkable contextual, temporal, prevalence, and evolutionary characteristics. Each of them heuristically benefits from their inclusion in a common concept, ADBs. For autism, this model has considerable explanatory power for the nature, association and polarization of autistic signs, their abrupt chronology of appearance, the lack of reliable circumscribed causal mechanisms beyond familial predisposition, and its post conception roots, attested by the frequent discordance for autism of monozygotic twins. We will now discuss certain theoretical consequences and empirical perspectives of this conceptualization, limiting ourselves to those concerning autism.

Contribution to the dimensional-categorical alternative in autism science

The scientific community has gradually moved from a categorical definition of autism to that of a spectrum encompassing less

reliably defined and homogeneous presentations. Autistic individuals thus identified lose their phenotypic link with the initial description, with major consequences on the production of knowledge [121]. It founds an apparent legitimacy in the contemporaneous movement toward de-reifying psychiatric categories [122], questioning their status as "natural categories". However, treating all clinical entities in the same way, and particularly by favouring dimensional descriptions by autistic "traits"[123], is at risk of missing situations where phenotypic and temporal discontinuity is a central element of the variation under study. There may be "kinds of kinds" differentiating the statuses and delineation of human variations either biological or psychological [124]. This justifies re-entering discontinuous states and trajectories into our understanding of the cause of some variations [125] as well as their persistence as a species possibility.

The integration of prototypical autism into the ADB framework suggests that the *kind* of developmental discontinuity that delineates it from non-prototypical forms, as well as from other conditions considered psychiatric, may not be generalizable or even informative for psychiatric entities outside autism, while it is shared with a few other non-psychiatric stable alternative states. It argues for a categorically defined atypical development. A developmental bifurcation leads to a stable and prototypical form, influenced by an irreversible developmental program (i.e., a non-social bias). The prototypical forms can be divided into subgroups, such as with or without language delay. These subgroups can be conceptualized as possible outcomes of the same initial bifurcation, much like the different types of breech presentation at birth. Although distinct, these alternative presentations are also strongly constrained by the specific context and timing of their occurrence, just as breech presentation itself is. Beside objective similarity within members of the same ADB, the notion of prototype circumscribes the group of signs that actually generate clinical certainty [126]. It maintains flexible categorical modelling in situations where the notion of traits does not allow for it [127]. Mechanistically, this distinguishes predisposing factors or the preclinical phase from the elementary components of a stable, homogeneous, phenotypic form. Predisposing familial factors precipitate the development in an alternative stable state, the prototype, whereas "traits" blur the boundary between the prototype and its similar phenotypes. In autism, ADBs integrate the dynamic influence of familial traits at a critical stage of the developmental program, resulting in a prototypical phenotype, while also allowing its modulation into diverse developmental outcomes that may diverge from this prototypical form by preschool age.

Contribution of ADB to the role of genetic load in the occurrence of prototypical autism

The role of genetic load in the development of autism is one of the field's most well-established scientific findings [128–131]. This is demonstrated by a concordance rate in siblings that is between 20 and 40 times higher than the prevalence of autism in the general population. There is also a concordance rate in monozygotic twins around twice as high as the concordance rate in dizygotic twins [118]. Although genetic load is the leading contributing factor in the occurrence of autism, its positive predictive value remains modest [132]. Notably, when concordance is present in monozygotic twins, it does not extend to the severity of the phenotype [119]. In line with a given genetic load, the factors that determine the more or less prototypical form of autism in concordant siblings remain unknown and could be random [117, 133]. Genetic load shapes the developmental landscape individually, giving rise to both prototypical autistic individuals and other conditions, such as non-autistic language delay [134], which is most frequently associated with autism in siblings. The same genetic load that enables a phenotype to cross the diagnostic threshold also allows for substantial inter-individual variation in phenotypic severity, further complicating the interpretation of genetic contributions. Critically, diagnostic concordance in monozygotic twins is only 48–88% [135]. Overall, triggering a bifurcation may depend on genetic and environmental factors, but stochasticity may also render these events partially unpredictable.

Contribution of ADB to the heterogeneity of the autism spectrum

ADB's empirical "common ground" therefore does not apply to the entire spectrum as defined in the DSM-5. The ADB model predicts that the distribution and grouping of prototypical autistic signs are distinct from what is observed in the broader current conception of the spectrum. It helps to clarify the boundaries with related forms, such as unaffected family members, broader neurodevelopmental disorders, individuals who meet DSM-5 autism criteria but are associated with deleterious mutations or pre- and perinatal events, a large proportion of people who self-identify as autistic, and, a fortiori, variability within typical development.

Prototypical autism to which this model applies, does not overlap with "profound autism" which is based on the intensity of support needed rather than on a shared developmental etiology [136] and behavioral phenotype, but does not exclude that prototypical autistic may display "profound" features. Elevated support needs, or "severity," may result from factors as diverse as the direct impact of autistic behaviors or symptoms, behavioral challenges, co-occurring intellectual disability, or from their combination [137]. These aspects, which result in an intrinsically heterogeneous "severe" clinical category, lie outside the explanatory scope of the ADB model. Neither is the ADB model intended to explain the autistic phenotype observed in individuals with associated high-penetrance variants (e.g., 16p11.2 CNVs, NRXN1, CHD8). High-penetrance variants are involved in a proportion of cases of syndromic autism, alongside environmental factors, such as exposure to valproic acid, and prenatal and perinatal factors, such as prematurity. These situations may offer insight into multiple neurogenetic mechanisms [138], but their contribution to familial, prototypical autism is not straightforward. By distancing itself from variant-associated conditions or causal biomarkers, this model contributes separating prototypical autism from syndromic autism [110], to the opposite of "convergence" models [139].

The ADB model does not exclude the possibility of identifiable "triggers" for the occurrence of a bifurcation, but it accounts from the evidence that autism most frequently occur without them. The explanatory scope of the bifurcation model remains restricted to developmental trajectories involving regressive/plateaued development or behavioral discontinuities. While regressive autism has been estimated to account for approximately one-third of frank autistic phenotypes, its prevalence increases substantially in prospective sibling cohorts. In these cohorts, socio-communicative regression has been reported in over 80% of cases [85], and the bifurcation framework may apply to an even greater proportion if broader behavioral discontinuities are considered.

This model therefore is grounded on a reconceptualization of the notion of "cause" of autism, which sources in the role of predisposing factors in other ADBs and in their mutual relationships. Concordantly, there is an intriguing co-occurrence among ADB, with an over-representation of left-handedness in the other bifurcations, particularly in autism (OR = 2.49) [140] and to a lesser extent in twins (OR = 1.40) [58] and in boys born breech [141] but also in other neurodevelopmental conditions [142]. There is also a possible co-occurrence of breech presentation [143] with twinning as well as with autism [144, 145].The inter-relation of two contrasting phenotypes (e.g. being right vs left-handed; being autistic, vs. following a typical developmental course), within a continuously distributed genetic liability, may ultimately be better

understood through a meta-level perspective on developmental bifurcation processes. These observations suggest that a framework based on dynamic systems theory may provide a valuable conceptual tool for understanding the co-development of specific neurodevelopmental conditions or traits without reducing their comprehension to "biological", deficit-based, causal mechanisms.

Demonstrating that the current heterogeneous autism spectrum contains (and masks the identification of) a prototypical cluster of highly similar children, with the greatest clinical diagnostic certainty for clinicians to whom the model can be applied, is a prerequisite for its validity [103]. Identifying and clustering prototypical autism, which cannot be accounted for by dimensional models, requires an inventory of signs at a much greater qualitative level of precision than their current description as "repetitive behaviours" in the DSM-5 (e.g., "prolonged inspection of three-dimensional objects" instead of DSM-5's "Highly restricted, fixated interests that are abnormal in intensity or focus"). Such qualitative precision in the description of signs will allow us to demonstrate that in prototypical autism, these signs: consistently appear together, a prerequisite for defining nosographic entities [146]; are observed at an exceptionally high level of similarity [62]; and share a discontinuous developmental course, with no visible signs in the first year, followed by progressive then sudden alterations in the second year, then a plateau of stable signs, and most frequently, a tendency toward normalization.

Contribution of ADB to psychiatry

In this model, the bipolarization of the context is a condition for the stability of the dominant and rare form of the bifurcation, constraining possible "choices" of the developmental program. In the field of psychological and psychiatric conditions, this does not apply to situations where the variable is clearly dimensional in nature (*e.g.*, ADHD, temperamental variants), continuous and progressive (*e.g.*, personality disorders), fluctuating and unstable (*e.g.*, schizophrenia), predominantly related to an objective modification (*e.g.*, specific or pleiotropic effects of a rare deleterious mutation), or poorly compatible with survival. In the case of autism, the ADB model radically separates an asymmetric bifurcation from dimensional phenotypic variation resulting from common variants in other domains (*e.g.*, "big five" personality variations), from rare genetic variants, and from most "psychiatric" entities. This separation is not consensual [147, 148] and is the subject of a lively debate on the more or less strict delineation of the "autism spectrum" [110], in which ADB can play a critical role. The notion of asymmetric bifurcation isolates a mode of causality and a type of polarized variation within the nowadays considered "neurodiverse", as well as within the autism spectrum, and even more so from conditions considered "psychiatric variations" [149]. In contrast to the "ableist" movement, the reinterpretation of autism within the ADB framework restores a biological status to certain components of neurodiversity. It unapologetically objectifies their adaptive issues, allowing for the ethical content of neurodiversity to be preserved without being obscured by with its scientific and societal impasses.

Evolutionist perspective of autism as an ADB

According to Oster & Alberch (1982, p. 454) [4], bifurcations in developmental programs "act as a filter, giving order to the random mutations in the genome, so as to present natural selection with a small subset of the possible phenotypes […] upon which natural selection can act as an arbiter of its adaptive design". Bifurcations in developmental programmes, do not oppose order and disorder, but contrast two paths unequally constrained by evolutionary pressure, each with its own programmatic coherence. Relatively small genetic changes can produce large changes in phenotype when acting on developmental bifurcations, each of which has undergone evolutionary constraints [4]. The inclusion of autism in this type of human possibilities profoundly changes its status within human variants. The search for its mechanistic cause loses some of its epistemic importance, in favour of familial predisposition, up to and including the possibility of a random "choice" between two forms of organization. As is the rule in evolution, the crossing of the bifurcation threshold toward an alternative stable state can occur for an almost infinite number of reasons, or even for no reason at all [4, 150].

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AUTHOR CONTRIBUTIONS

LM initiated the concept of the asymmetric developmental bifurcation (ADB), drafted the initial version of the manuscript, contributed to the overall writing, and completed the manuscript. ALC documented the concordance between the ADBs. BB contributed to the neuroimaging aspects and provided feedback on the entire manuscript. GD contributed to the dynamic systems theory aspects and provided feedback on the entire manuscript. SJ provided feedback on the genetic aspects of the model and on the entire manuscript. DG contributed to the development of the model, to the overall writing of the manuscript, and to its revision.

COMPETING INTERESTS

The authors declare no conflict of interest.

ADDITIONAL INFORMATION

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