Autism Spectrum Disorder as Developmental Stuck-State

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1. Abstract

Autism spectrum disorder is conventionally described as a heterogeneous neurodevelopmental condition with strong genetic contribution, frequent gastrointestinal comorbidity, variable regression history, immune and microbiome associations, and circuit-level differences across multiple brain regions. Under the Redacted Science framework, those observations are not discarded. They are reorganized. This paper proposes that a subset of autism spectrum disorder represents developmental stuck-state program execution by the organism-host governance system within critical developmental windows, with clinical phenotype determined less by a single autism mechanism than by timing of stuck-state onset relative to neurodevelopmental stage.

The core contribution is a two-trajectory model. Trajectory A is perturbation-triggered regression: typical development proceeds for months or years, then an immune, microbial, dietary, antibiotic, inflammatory, or other ecological event pushes a susceptible system into a locked program mode. Trajectory B is early-locked development: the stuck state is established prenatally or in the first months of life, so gut-brain signaling, immune calibration, sensory integration, sleep architecture, synaptic pruning, and myelination develop around the altered signal set. The same governance error therefore produces different observed outcomes depending on when it captures the developmental process.

This model extends the biochemical computer framework of *C. albicans*, the Saline Oscillation coevolution model, the Pan-Mammalian transmission frame, and the Stuck-State Umbrella into neurodevelopmental disease. Sandler et al. documented vancomycin-responsive regressive-onset autism in 2000 with relapse after discontinuation and an ecological signature centered on absent Peptostreptococcus species and anaerobic cocci. Qiao et al. later demonstrated a host-susceptibility-plus-activation-event architecture in Shank3 haploinsufficient mice, where LPS challenge produced behavioral regression through inflammatory microglial and synaptic mechanisms. The framework reads these as clinical and preclinical support for Trajectory A. The claim is not that autism has one cause, that vaccines cause autism, or that antifungal therapy is a universal treatment. The claim is narrower and testable: autism heterogeneity should stratify by developmental timing, regression history, mycobiome burden, gastrointestinal severity, and response distribution. Measure the organism layer, or keep calling architecture mystery.

2. Keywords

Autism Spectrum Disorder; Developmental Stuck-State; *Candida albicans*; Biochemical Computer; Neurodevelopment; Regression; Gut-Brain Axis; Mycobiome; Microbiome; SHANK3; Microglia; TLR4; Synaptic Pruning; Gastrointestinal Comorbidity; Endocannabinoid System;

Pituitary-Hypothalamus Interface; Mammalia candidus; Homo candidus; Redacted Science Research Initiative; #TheArchitect

3. Introduction

The Redacted Science framework proposes that *Candida albicans* functions as a coevolved biochemical computer in mammalian hosts, not as a mere opportunistic passenger waiting for weakness. It senses the host, reads substrate availability, modulates immune tone, communicates through vesicles and soluble effectors, interacts with the endocannabinoid system, and operates across the gastrointestinal, endocrine, autonomic, and neurological interfaces that modern medicine often studies separately (Craddock, Biochemical Computer). The organism is not magic. It is biology doing what old biology does: survive, remember, and calculate without asking permission.

The Saline Oscillation Hypothesis places that architecture in evolutionary context. The organism-host relationship is proposed to have been shaped by environmental pressure, especially electrolyte and perfusion stress, such that the symbiont developed governance capability over mammalian physiology under conditions where host survival required rapid internal recalibration (Craddock, Saline Oscillation). The Pan-Mammalian extension then widens the frame: the relevant interface systems are not uniquely human. The hypothalamic-pituitary axis, the endocannabinoid system, renal concentrating mechanisms, phagocytic immune pathways, sodium-potassium pump dynamics, and developmental stress-response architecture are conserved mammalian infrastructure (Craddock, Pan-Mammalian).

The Stuck-State Umbrella translates that framework into chronic disease logic. A stuck state is a biological program phase that should have transitioned but did not. In adults, that produces persistent disease phenotypes recognizable as type 2 diabetes, obesity, IBS, anorexia nervosa, or other chronic conditions depending on which program is frozen and which tissue compartment is involved (Craddock, Stuck-State Umbrella). In neurodevelopment, the same logic becomes more consequential. A child is not an adult system with smaller parts. A child is an active build process. A stuck program during construction does not merely change output. It changes the architecture being built.

This paper applies that model to autism spectrum disorder. The conventional autism literature already contains the clues: strong heritability, incomplete penetrance, heterogeneous phenotype, gastrointestinal comorbidity, regression in a subset, immune activation, microbiome signatures, maternal immune activation models, SHANK3 susceptibility, circuit-specific defects, and mixed intervention results. Under the framework, those clues are not competing explanations. They are different windows into a developmental governance problem.

The proposed reading is direct: autism spectrum disorder includes a subset of developmental stuck-state outcomes produced when the organism-host governance system locks during critical windows of neurodevelopment. The phenotype depends on when the lock occurs. If typical development begins and then a perturbation pushes the system into a stuck state, the child presents through Trajectory A, perturbation-triggered regression. If the stuck state is established before developmental baselines form, the child presents through Trajectory B, early-locked development. The difference is not merely severity. It is timing. [Architecture does not look broken when it was built around the wrong blueprint from the beginning.]

4. Framework Basis

Paper A supplies the hardware. *Candida albicans* is treated in the Redacted Science framework as a distributed biochemical computer with cross-kingdom signaling access to host immune, metabolic, endocrine, gastrointestinal, autonomic, and neurological systems (Craddock, Biochemical Computer). Autism, under this paper's reading, does not require the organism to invent a new autism program. It requires only that the organism's existing interface tools operate during a developmental window where immune tone, synaptic pruning, gut-brain signaling, sleep, sensory calibration, vagal signaling, and endocrine rhythms are actively being built.

Paper B supplies the evolutionary frame. Developmental windows are substrate-surface events: times when the host is unusually plastic, unusually sensitive to signaling, and unusually dependent on correctly timed transitions (Craddock, Saline Oscillation). In the ancestral model, those windows would have been managed by an organism-host-social architecture built around stable ecological cues. Modern life changes the cues: antibiotics, processed diet, maternal immune activation, altered microbial inheritance, C-section delivery patterns, environmental chemicals, and repeated immune perturbations. The old program sees inputs. It does not necessarily know modernity changed the operating system.

The Stuck-State Umbrella supplies the logic. Chronic pathology persists because a phase fails to transition (Craddock, Stuck-State Umbrella). In autism, the relevant failure is developmental. A stuck state during early synaptogenesis, immune calibration, microbiome assembly, or sensory integration can become a persistent neurodevelopmental phenotype because later systems develop around the locked state rather than replacing it.

The IBS paper supplies the bowel-comorbidity template. Autism has a substantial gastrointestinal signal, and GI severity correlates with autism severity in existing literature (Adams, Gastrointestinal Symptoms in Autism). Under the framework, bowel symptoms are not merely a co-occurring nuisance. They are evidence that the organism-host interface is active in the same compartment from which gut-brain signaling, microbial metabolites, vagal traffic, immune tone, and endocannabinoid modulation emerge (Craddock, IBS Stuck State).

The Pan-Mammalian paper supplies the inheritance reframe. Autism's strong heritability is real, but heritability does not require a single genetic cause. A vertically transmitted symbiont, inherited microbial ecology, maternal immune state, and host genetic susceptibility can produce familial clustering without reducing the phenotype to a DNA-only model (Craddock, Pan-Mammalian). Genetics loads the circuit board. Ecology decides which subroutine boots.

5. Mechanism

The mechanism proposed here begins with susceptibility. Susceptibility may include host genetics such as SHANK3 haploinsufficiency or other synaptic-risk architecture; inherited or maternal microbiome state; early-life antibiotic exposure; inflammatory timing; fungal burden; bacterial co-governance disruption; maternal immune activation; gut-barrier instability; or some combination of these. None of these must be universal. The framework expects heterogeneity because the organism-host state at the time of the perturbation is not uniform across children.

Trajectory A begins with typical or apparently typical development. Speech, social engagement, motor patterning, sleep, feeding, or adaptive function proceeds until an activation event

changes the operating state. Sandler et al. treated regressive-onset autistic children with oral vancomycin and documented significant improvements in behavior and communication, followed by deterioration after treatment discontinuation and return toward baseline over follow-up (Sandler, Oral Vancomycin). The fecal finding is the buried fuse: absent Peptostreptococcus species and anaerobic cocci in the sampled children against high presence in adult controls. The authors proposed a gut-brain connection and neurotoxin-producing opportunistic organisms. The Redacted Science reading adds the missing fungal extension: bacterial disruption creates ecological space, Candida persistence survives antibacterial pressure, and the organism layer remains unmeasured.

Qiao et al. provide the preclinical counterpart. In Shank3 haploinsufficient mice, baseline phenotype is absent or limited. After LPS challenge, behavioral impairment appears: motor changes, anxiety-like behavior, excessive grooming, microglial activation through TLR4, synapse engulfment, and inflammatory gene shifts (Qiao, Inflammation and Shank3 Regression). Anti-inflammatory treatment partially rescues. This is the exact shape of Trajectory A: susceptibility plus activation event produces a locked behavioral phenotype that was not visible before the event. The bacterial LPS trigger is demonstrated. The framework predicts organism-mediated inflammatory triggering through Candida-accessible TLR4, microglia, vagal, endocrine, and gut-brain channels.

Trajectory B begins earlier. The stuck state forms prenatally, perinatally, or within the first months of life, before typical developmental baselines are visible. In this pathway, the altered signal set becomes the environment in which neurodevelopment occurs. The gut-brain axis, immune calibration, sensory gating, sleep architecture, myelination, feeding, pain response, interoception, social salience, and synaptic pruning all develop under the wrong governance tone. Imaging may show fewer discrete abnormalities, not because the phenotype is less biologically real, but because there was no before-and-after event for the scanner to capture. The baseline was already shifted.

This explains the Rochat paradox. Rochat et al. found more imaging abnormalities in higher-functioning children than developmentally delayed children under age five (Rochat, MRI in ASD Under Five). Conventional intuition expects the opposite. Under the two-trajectory model, the finding is predicted. Higher-functioning cases are enriched for Trajectory A: more retained cognitive infrastructure, more visible event signature. Developmentally delayed cases are enriched for Trajectory B: the system built itself around an atypical signal environment, so imaging reads less like injury and more like alternate construction.

SHANK3 sharpens the model because it does not produce one brain-wide autism module. Gao et al. document hippocampal synaptic impairment in an R1117X model (Gao, R1117X Shank3). Wu S. et al. localize autistic-like behavior to hypothalamic AgRP neurons and p38 alpha inflammatory mediation at the pituitary-hypothalamus interface (Wu S., Shank3 AgRP). Wang et al. localize repetitive behavior to striatopallidal indirect-pathway medium spiny neurons with DREADD-based rescue (Wang, Striatopallidal Shank3). Together, these papers support distributed-circuit vulnerability. Different symptoms map to different vulnerable circuits. That matters because the Redacted Science framework is also distributed. It predicts that the organism does not need one autism switch. It needs access to developmental circuits through inflammatory, endocrine, vagal, metabolic, and microbial routing.

NCT00936182 is the institutional artifact. A three-site, double-blind, randomized, placebo-controlled trial of fluconazole in children with ASD was registered in 2009, with enrollment contingent on pyrosequencing-positive yeast and a pre-specified behavioral outcome hypothesis. It was the

obvious fungal-extension test after Sandler's 2000 bacterial-ecology signal. Seventeen years later, no results are available. [When a registered trial asks the right question and then disappears into the fog, that fog becomes part of the data.] This paper does not claim the missing results prove the framework. It claims the silence marks exactly where the framework says the measurement should have occurred.

6. Predictions

1. **ASD cohorts should show differential *C. albicans* mycobiome burden compared with controls, and the ASD distribution should be bimodal rather than normally distributed.** Existing support is partial through Adams et al., Kantarcioglu et al., and Strati et al. (Nirmalkar, Bimodal Candida in ASD; Kantarcioglu, Yeast Species in ASD; Strati, Gut Mycobiome in ASD). [Evidence class: cohort mycobiome sequencing with distribution analysis.]
2. **Regression history should distinguish an antifungal-responsive subgroup from non-regressive cases.** The strongest response signal should occur in Trajectory A subjects with documented regression, GI symptoms, Candida enrichment, or post-antibiotic onset. [Evidence class: adaptive-enrichment clinical trial.]
3. **Gastrointestinal comorbidity severity should correlate with intervention response magnitude, especially when paired with Candida burden or bacterial anaerobe disruption.** Adams et al. reported a strong GI-autism severity correlation (Adams, Gastrointestinal Symptoms in Autism). [Evidence class: prospective cohort with paired GI severity, behavioral measures, and mycobiome testing.]
4. **Antifungal response should be bimodal rather than normally distributed. A uniform small effect would argue against the framework.** A responder/non-responder split enriched by regression history and mycobiome burden would support it. [Evidence class: randomized trial with pre-specified responder distribution analysis.]
5. **Maternal antibiotic exposure should correlate more strongly with Trajectory B presentations than Trajectory A presentations**, especially when exposure timing intersects fetal or early infant immune and microbiome calibration windows. [Evidence class: retrospective birth cohort with timing-specific antibiotic exposure and operational Trajectory A/B coding.]
6. **NCT00936182 results**, if recovered, should show bimodal response in the pyrosequencing-positive-yeast subset rather than a flat population average. (Evidence class: recovered trial dataset or registry-linked results analysis) [*Where are those results, folks? 3 centers involved*]
7. **The fluconazole rescue reported in SHANK3-related mouse work should correlate with baseline gut Candida burden if banked samples exist**. If authors did not measure mycobiome state, the omission itself identifies the decisive covariate for replication. [Evidence class: secondary analysis or replication study with mycobiome covariates.]
8. **In Shank3 haploinsufficient mice, gut mycobiome burden at inflammatory challenge should predict severity of regression phenotype**; antifungal pretreatment should attenuate Qiao-like LPS-triggered behavioral regression; and organism bloom or dysbiosis should produce regression-like phenotype in the susceptible genotype even without LPS. [Evidence class: preclinical replication with mycobiome covariates.]
9. **Sandler's ecological disruption signature, especially absent Peptostreptococcus species and anaerobic cocci, should replicate in modern regressive-ASD cohorts using paired 16S and**

ITS sequencing. The absent-commensal state should correlate with Candida burden and antifungal-intervention response. [Evidence class: replication study with paired bacterial and fungal sequencing in regressive-ASD cohorts.]

7. Discussion

The two-trajectory model resolves several autism puzzles at once. It accepts heritability without reducing autism to genetics alone. It accepts regression without making regression universal. It accepts early developmental delay without forcing a discrete injury model onto children whose altered signaling environment may have been present before observable milestones. It accepts gastrointestinal comorbidity as central rather than incidental. It accepts immune activation as a trigger class rather than a single cause. Most importantly, it explains why one autism spectrum can contain children with sharply different onset histories, cognitive profiles, sensory presentations, bowel involvement, and intervention response patterns.

The model also clarifies why average-effect trials fail. If the population contains Trajectory A responders, Trajectory B early-locked cases, non-framework autism, different microbial ecologies, different host genotypes, and different developmental timing, then a single intervention averaged across the full spectrum should dilute signal. That is not failure of biology. That is failure of stratification. [Averaging a circuit board and a smoke alarm gives you a number. It does not tell you which one is beeping.]

Sandler et al. matters because the paper did not merely report behavior change. It reported relapse after discontinuation, brief hyperactivity early in treatment in several children, and a specific ecological abnormality in the sampled fecal flora (Sandler, Oral Vancomycin). That pattern is not easily dismissed as placebo. It looks like a system perturbed, briefly improved, and then restored itself after pressure was removed. In stuck-state language, the intervention disrupted the state but did not reset the architecture.

Qiao et al. matters because it demonstrates a clean susceptibility-plus-activation-event model in SHANK3 haploinsufficiency (Qiao, Inflammation and Shank3 Regression). The mouse does not require every autism feature to be present at baseline. The event reveals the vulnerability. That is the same logic parents describe when a child develops typically and then changes. The framework does not need to adjudicate every claimed trigger. It asks whether a susceptible organism-host system can be pushed into a locked developmental state by inflammatory activation. The preclinical answer is now yes.

The SHANK3 circuit literature further prevents simplistic mechanism. Hippocampus, hypothalamic AgRP neurons, striatopallidal circuits, prefrontal remodeling, microglia, lipid rafts, IGF1R, and inflammatory mediators all appear in the surrounding evidence. The organism layer could access those circuits through multiple routes: gut-derived immune activation, vagal signaling, endocannabinoid modulation, pituitary-hypothalamic governance, microbial metabolites, Candida cell wall ligands, prostaglandin and arachidonic acid competition, and substrate-state shifts. The framework's point is not that one molecule explains autism. The point is that a distributed biological computer acting during development would produce distributed phenotype.

NCT00936182 sits at the center of the institutional question. A trial of fluconazole in pyrosequencing-positive-yeast ASD children was registered with the right design shape: three sites, randomized, double-blind, placebo-controlled, yeast-positive enrollment, behavioral outcomes. It

followed Sandler by nine years. It then produced no visible answer. A framework-neutral Clear Evidence paper can stand on that silence alone. The full Architect Report uses the silence differently: as a pointer to the unmeasured layer that autism research repeatedly approaches and then fails to resolve.

8. Counter-Arguments Addressed

1. Vaccines cause autism. This paper does not make that claim. The framework treats immune activation events as a broad trigger class in susceptible hosts. Infection, antibiotics, inflammatory challenge, dietary shifts, microbial disruption, environmental exposures, maternal immune activation, and other perturbations could all serve as transition events. That is categorically different from a single proximate-cause claim.

2. Autism is approximately 90 percent heritable, so it is genetic. High heritability does not identify mechanism. It identifies familial clustering of liability. Vertical symbiont transmission, inherited microbial ecology, maternal immune tone, shared environment, host genetic susceptibility, and true genetic variants can all contribute to heritable phenotype. SHANK3 illustrates the point: genetic susceptibility may be silent until an activation event reveals it.

3. Regression reports are unreliable. Regression history is imperfect, but it is not disposable. Under this framework, regression is Trajectory A's primary observable. Finegold et al. already identified regression-specific microbiome signatures (Finegold, Regressive Autism Microflora). Sandler's entire cohort was regressive-onset, and response to vancomycin was documented prospectively (Sandler, Oral Vancomycin). The right response is not to discard regression. It is to operationalize it.

4. Spectrum heterogeneity defeats unitary-mechanism models. Correct. It defeats crude unitary-mechanism models. The two-trajectory model is not a crude unitary mechanism. It predicts heterogeneity as the consequence of stuck-state onset timing interacting with developmental stage, host genotype, microbial ecology, immune activation, and circuit vulnerability. Different phenotypes are expected because different build stages were captured.

5. Shaw 2000 was never replicated. That is not reassuring. Shaw et al. reported open-label nystatin-associated improvement in a pediatric ASD cohort (Shaw, Nystatin in Autism). Kantarcioglu later confirmed yeast species and antifungal susceptibility in ASD stool samples (Kantarcioglu, Yeast Species in ASD). NCT00936182 then registered the proper fluconazole trial and disappeared from the visible record. The framework does not treat non-replication as proof. It treats measurement avoidance, missing results, and absent stratification as the problem to be solved.

6. This could stigmatize autistic people. It should not, and the paper must be read carefully on that point. The framework does not reduce autistic people to pathology, infection, or deficit. It proposes that some developmental trajectories may be organism-host stuck states with testable biological signatures. A mechanism paper should not erase personhood. It should make intervention, stratification, and understanding more precise. [The point is not to flatten people. The point is to stop flattening the biology.]

9. Conclusion

Autism spectrum disorder is not solved by naming heterogeneity. Heterogeneity is the observation. A mechanism must explain why different children arrive at different phenotypes under the

same diagnostic umbrella. The Redacted Science two-trajectory model offers one answer: timing. A stuck state during a developmental window produces different outcomes depending on whether it interrupts typical development or becomes the baseline around which development forms.

The evidence now justifies a first full-spectrum Architect Report. Sandler et al. supplied clinical Trajectory A evidence in 2000: regressive-onset autism, gut-ecology intervention response, relapse after discontinuation, and a striking anaerobe absence signal. Qiao et al. supplied preclinical Trajectory A validation: genetic susceptibility, inflammatory trigger, behavioral regression, microglial TLR4 activation, synapse engulfment, and partial rescue. SHANK3 circuit studies show distributed vulnerability rather than a single autism module. Existing ASD mycobiome and GI studies supply partial ecological support. NCT00936182 supplies the missing-trial artifact.

The next steps are straightforward. Stratify autism cohorts by regression history, GI severity, maternal antibiotic timing, SHANK3 or other susceptibility markers, and developmental timing. Measure both bacterial and fungal ecology. Include Candida burden and absent-commensal status as pre-specified covariates. Analyze response distribution for bimodality, not just average effect. In SHANK3 models, measure gut mycobiome burden before inflammatory challenge and antifungal rescue. The framework can be wrong, but it is wrong in a useful way if it fails these tests.

Autism research has spent decades describing circuits, genes, immune signatures, bowel problems, microbial differences, and regression as if they are separate rooms in the same building. This paper proposes they are connected by the management layer. Open the door between them. Measure the organism where the signal begins.

10. Closing Declaration

This Architect Report AS#017 V1 was generated through the Redacted Science Seed Analysis Process, from Seed 017 of the Paper Seed Master, under the Redacted Science Research Initiative. Issued 20260424 by Jim Craddock, #TheArchitect. Authenticity verifiable at jimcraddock.com/architect-reports. Papers claiming any A-series designation not listed in the registry are not authentic Architect Reports. V1 advances the full-spectrum autism deployment path and integrates Sandler 2000, Qiao 2026, NCT00936182, and SHANK3 distributed-circuit literature into the developmental stuck-state model.

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12. Suggested Additional Citations

None inserted. Seed 017 already specifies the citation set used in this first draft. Additional systematic MRI-stratification, maternal antibiotic timing, pediatric mycobiome normative data, and operational Trajectory A/B definition citations should be reviewed during the editorial pass before V2.