Chronic Disease as Stuck Program Modes of the Candida albicans Biochemical Computer

A Unified Framework for Metabolic, Psychiatric, Functional, and Neurodegenerative Disease

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Abstract

This paper introduces the stuck-program model, a framework for understanding chronic diseases as phased biological programs that failed to transition. The model derives from the biochemical computer framework (Craddock, 2026a; 2026b), which describes Candida albicans as a coevolved fungal symbiont operating phased programs within the mammalian host using documented cross-kingdom signaling capabilities. Each program phase employs specific organism capabilities to manage host physiology. When a phase transition signal fails, the capability runs indefinitely, producing a host phenotype that conventional medicine classifies as chronic disease. A three-gate selection methodology is presented for identifying candidate conditions: (1) documented organism mechanism mapping directly to the disease's central pathology, (2) unexplained persistence in conventional medicine, and (3) demographic or geographic clustering patterns consistent with quorum sensing or colonization density dynamics. Five conditions are analyzed in companion papers: type 2 diabetes (glucose harvesting without phase transition), anorexia nervosa (substrate restriction without phase transition), irritable bowel syndrome (gut management frozen in a single operating state), obesity (growth/storage without phase transition), and Parkinson's disease (dopaminergic interface burnout; speculative). A unified therapeutic framework combining substrate change, antifungal pressure, and sustained duration is proposed, along with the identification of quorum sensing density as the single measurable variable that should predict disease severity, intervention response, and relapse risk across all five conditions.

Keywords: stuck program mode, Candida albicans, biochemical computer, chronic disease, quorum sensing, farnesol, phase transition, dietary antifungal, type 2 diabetes, anorexia nervosa, irritable bowel syndrome, obesity, Parkinson's disease, Homo Candidus

I. The Problem of Persistence

Modern medicine manages chronic disease. It rarely resolves it. Type 2 diabetes is treated with lifelong medication. Irritable bowel syndrome is managed with dietary modification and symptom control. Anorexia nervosa has the highest mortality rate of any psychiatric disorder despite aggressive treatment. Obesity shows a 95% weight-regain rate following dietary intervention. Parkinson's disease is progressive and irreversible. Each condition has its own research literature, its own clinical guidelines, and its own pharmacological armamentarium. What they share is a central puzzle: why does the condition persist?

For each of these conditions, the standard model describes a pathological state but does not fully explain what maintains it. Insulin resistance in T2D is progressive, but why? IBS has no structural cause, but the symptoms are lifelong. Weight-restored AN patients show persistent

physiological abnormalities. The body defends an elevated weight set-point in obesity. Substantia nigra neurons continue dying in Parkinson's patient despite adequate dopamine replacement. In each case, conventional medicine identifies the downstream consequences but not the upstream driver that sustains them.

This paper proposes that these conditions share a common upstream feature: a resident biological system, operating through documented molecular mechanisms, that is running a program phase without transitioning to the next one.

II. The Stuck-Program Model

Foundation: The Biochemical Computer

The biochemical computer framework (Craddock, 2026a; 2026b) describes C. albicans, the most prevalent fungal commensal of the human mycobiome, as a coevolved symbiont operating a phased program within the mammalian host. The framework is built on documented molecular evidence: the organism possesses confirmed signaling access to the host's endocannabinoid system, nuclear transcription factors, ion channels, neurotransmitter receptors, cholinergic signaling, immune cell differentiation pathways, the incretin system, reproductive hormones, stress hormones, and the autonomic nervous system via vagal muscarinic receptors. This signaling reach is documented in the primary literature and assembled in Craddock (2026a, Section 5; 2026b, Section 5).

The organism's metabolic architecture is equally broad: it can utilize glucose, amino acids, carboxylic acids, fatty acids, N-acetylglucosamine, lactate, and ketones as carbon sources, switching between them based on local availability. This metabolic flexibility, described in Craddock (2026b, Section 5.10), enables the organism to operate simultaneously across tissue environments ranging from the glucose-rich gut lumen to the amino acid-rich tissue interstitium to the lactate-rich interior of a macrophage phagosome.

The combination of comprehensive signaling reach and metabolic flexibility produces an organism capable of managing host physiology across multiple organ systems. The framework proposes that these capabilities are organized into a phased program, with different capabilities serving different program stages. Critically, this program was refined over tens of thousands of generations of coevolution with the Homo candidus phenotype described in Craddock (2026b): a host with different cardiac architecture (suction-dominant perfusion enabling pituitary colonization), a social infrastructure providing external transition cues (communal feeding, behavioral protocol enforcement, ritual dietary management), and a physiology shaped by active symbiont management. Modern Homo sapiens carries the organism and its program but lacks the physiological and social architecture the program was designed to operate within. The stuck states described in this series are, in part, the consequence of running software written for one operating system on hardware that no longer fully supports it.

Phase Transition Logic

In a functional program, phases cycle. The organism runs a capability, achieves the metabolic or physiological condition that phase requires, registers the completion signal through its environmental sensing infrastructure (Hgt4 for glucose, SPS for amino acids, Rim101 for pH, Cyr1 for CO2, Hsp90 for temperature, and the hormonal sensing described in Craddock 2026b, Section 5.7), and advances to the next phase.

Transition signals can originate from multiple sources: the organism's own metabolic activity changing the local environment (glucose depletion triggering substrate shift), host dietary or behavioral change (fasting, dietary composition shift, iatrogenic causes), hormonal cycling (reproductive hormone fluctuations modulating organism operational state), environmental change (seasonal variation, temperature shifts), or, in the Homo candidus context described in Craddock (2026b), social intervention (communal feeding, behavioral protocol enforcement, ritual dietary management).

The stuck state occurs when the transition signal fails to arrive. Possible failure modes include: modern diet providing infinite substrate for one phase, preventing the depletion signal that would trigger transition; antibiotic disruption of bacterial populations the organism uses as intermediary tools, removing an element of the signaling chain required for transition; loss of the social infrastructure that provided external transition cues in the ancestral coevolutionary context; or hormonal environments that lock a particular organism response without the subsequent signal architecture to advance it.

Quorum Sensing and Program Maintenance

The stuck state is not maintained by individual organism cells making independent decisions. It is maintained by population-level coordination. C. albicans was the first eukaryote in which quorum sensing was identified (Hornby et al., 2001). Farnesol and tyrosol, the primary quorum-sensing molecules, coordinate population-level behavior including morphogenetic decisions, biofilm formation, and virulence expression.

Within the stuck-program model, quorum sensing provides the mechanism by which a program phase sustains itself above a density threshold. Below that threshold, individual cells lack the coordinated signaling required to maintain coherent program execution. Above it, the population acts as a unified management system. This means that organism density is not merely a correlate of the stuck state. It is the variable that determines whether a stuck state can maintain itself. Reducing density below the quorum threshold should allow a stuck program to release, independent of whether the transition signal arrives through other channels.

This generates a unifying prediction across all conditions in the series: colonization density, measurable through standard mycological culture or molecular techniques, should predict disease severity, intervention response, and relapse risk.

III. Selection Methodology: Three Gates

Candidate conditions were evaluated through three gates designed to distinguish framework-consistent applications from post hoc retrofitting.

Gate 1: Documented Mechanism

The organism must possess a documented signaling or metabolic capability that maps directly to the disease's central pathology, not a downstream consequence but the primary driver. The mapping must be specific: a general claim that the organism modulates immune function is insufficient; a specific claim that the organism's production of PGE2 from host arachidonic acid competes with endocannabinoid synthesis and thereby modulates hedonic reward signaling is testable. Each companion paper identifies the specific organism capability anchoring the disease application.

Gate 2: Unexplained Persistence

The disease must have a recognized persistence problem in conventional medicine: treatment manages symptoms but does not resolve the underlying state, and the reason for this persistence is either unknown or incompletely explained. This gate eliminates conditions with well-characterized self-limiting courses or clear structural causes. The stuck-program model is specifically designed for conditions where the question "why does this continue?" has no satisfactory answer.

Gate 3: Clustering Patterns

The disease must show demographic, geographic, or familial clustering patterns that colonization density dynamics, quorum sensing thresholds, or organism-host equilibrium variation could explain better than, or in addition to, current epidemiological models. This gate distinguishes organism-mediated conditions from conditions whose distribution is fully explained by known genetic and environmental factors. Patterns of interest include: population-level prevalence differences that persist after controlling for known risk factors, familial clustering beyond genetic heritability (consistent with vertical organism transmission), post-antibiotic-era prevalence acceleration, and female predominance correlating with the organism's documented estrogen and LH sensitivity.

IV. The Candidate Conditions

Five conditions were evaluated through the three gates. Each is analyzed in full in a companion paper; summaries are provided here.

Type 2 Diabetes (Craddock, 2026e)

Glucose harvesting without phase transition. Hgt4, calibrated to 5 mM human blood glucose, anchors the mechanism. The organism's continuous glucose draw produces progressive insulin resistance and beta cell failure. Modern dietary glucose abundance prevents the substrate shift signal. Bariatric surgery's rapid T2D remission (before weight loss) is interpreted as acute habitat disruption forcing program reset. Passes all three gates. Strongest single-mechanism anchor.

Anorexia Nervosa (Craddock, 2026f)

Substrate restriction without phase transition. Endocannabinoid tone management via arachidonic acid competition suppresses hedonic food reward. Monteleone et al. (2015) demonstrated that endocannabinoid disruption persists after weight restoration, indicating the program runs regardless of caloric input. Pubertal-onset female predominance maps to the organism's LH and estrogen sensitivity (Kinsman et al., 1988). Passes all three gates. Persistence-despite-weight-restoration is the strongest single evidence point.

Irritable Bowel Syndrome (Craddock, 2026g)

Gut management frozen in a single operating state. IBS subtypes (IBS-D, IBS-C, IBS-M) represent different stuck modes of the organism's CB1/TRPV1 gut management system. The absence of structural pathology (the defining feature of IBS) is precisely what a management-layer disorder predicts. Post-infectious IBS maps to organism reorganization following bacterial disruption. Passes all three gates. Subtype-as-frozen-mode is the most novel testable prediction.

Obesity (Craddock, 2026h)

Growth/storage without phase transition. GLP-1/incretin modulation, endocannabinoid appetite management, and HPA axis influence maintain a storage-mode equilibrium the host cannot override through caloric restriction alone. Semaglutide's efficacy on a receptor within the organism's signaling reach supports the framework. The most mechanistically diffuse candidate. Passes all three gates with the caveat that no single-mechanism anchor dominates.

Parkinson's Disease (Craddock, 2026i)

Dopaminergic interface burnout (speculative). Gpr1's pharmacological overlap with dopaminergic signaling and kynurenine-derived quinolinic acid neurotoxicity provide the mechanistic basis. The age of onset (60+) is consistent with decades of cumulative neuronal burnout. Gate 3 (clustering) is weak. Explicitly labeled as speculative. Included to demonstrate the framework's range and to generate testable hypotheses.

V. The Unified Therapeutic Framework

The stuck-program model generates a three-layer therapeutic framework applicable across all five conditions.

Layer 1: Substrate Change

Alter the dietary or metabolic landscape the organism reads, providing the transition signal the stuck program is waiting for. This is condition-specific: carbohydrate restriction for T2D; low-FODMAP for IBS (Fermentable Oligosaccharides, Disaccharides, Monosaccharides, And Polyols, the short-chain carbohydrates that the small intestine absorbs poorly, passing through to the colon where gut organisms ferment them, producing gas, drawing water into the bowel, and triggering the bloating, pain, and diarrhea cycle); structured refeeding for AN (controlled, monitored caloric restoration following clinical protocol); and caloric reduction for obesity. Each substrate change targets the specific metabolic condition maintaining the program phase. Substrate change addresses the signal environment.

Layer 2: Antifungal Pressure

Reduce organism density below the quorum sensing threshold maintaining the stuck state. This can be pharmaceutical (fluconazole, azoles) or dietary (coconut oil/lauric acid/caprylic acid, garlic/allicin, cinnamon/cinnamaldehyde, lemon balm). Dietary antifungals are of particular significance because they are accessible without prescription, carry minimal risk at dietary doses, and have been present in human food traditions throughout evolutionary history. Their inconsistent effects across individuals is itself predicted: variable organism density and morphological state produces variable response to unmeasured antifungal pressure. Antifungal pressure addresses the population maintaining program coherence. [*Beware of die-off. Your body will have to adjust to not having the same stuck state, and the die-off products can be uncomfortable*]

Layer 3: Exercise

Provide multi-channel environmental input that the organism's sensing infrastructure cannot ignore. Exercise simultaneously alters gut motility (mechanical stimulation read through the organism's gut management system), cortisol dynamics (read through the corticosteroid-binding protein documented by Loose and Feldman, 1981), endocannabinoid tone (post-exercise anandamide elevation temporarily shifts the signaling landscape the organism manages),

autonomic balance (sympathetic activation during exercise followed by parasympathetic recovery, read through the muscarinic receptor documented by Nile et al., 2018), and core temperature (read through Hsp90). No single dietary or antifungal intervention hits this many sensing channels simultaneously. Exercise provides the broadest transition input available without pharmacological intervention.

The AN exception must be stated directly. Compulsive exercise in AN is itself a feature of the stuck program: the organism driving caloric expenditure to maintain restriction-phase metabolic conditions. In AN, exercise is part of the disease, not part of the treatment, until the restriction program has released sufficiently for exercise to function as a therapeutic input rather than an organism-directed output. For the other four conditions, exercise is unambiguously beneficial and its mechanism through the framework is clear: you are flooding the organism's sensing infrastructure with simultaneous signals that a single-mode stuck state cannot accommodate.

Layer 4: Duration

Sustained combined intervention allowing the organism time to register new conditions, lose quorum coordination, and release the stuck program. Short-term interventions fail because the organism's compensatory capacity can outlast a brief disruption. Long-term lifestyle changes succeed (when they succeed) because they outlast the organism's compensatory window. Duration addresses the temporal dynamics of program release.

The unified prediction: combined substrate change plus antifungal pressure plus sustained duration should outperform any single intervention across all five conditions. No current clinical trial tests this combination because no one is measuring organism density as a variable in any of these diseases.

The regulatory environment constraining investigation of dietary antifungals, particularly the Dietary Supplement Health and Education Act of 1994 (DSHEA), which limits the ability to make therapeutic claims for food-derived compounds, is discussed in a separate planned analysis (Craddock, forthcoming).

VI. The Unifying Variable

The single most important prediction of the stuck-program model is that organism colonization density, measurable through standard oral swab, fecal mycobiome, or site-specific culture techniques, should function as a unifying variable across all five conditions. Specifically:

Disease severity should correlate positively with colonization density. Higher organism density means stronger quorum-mediated program maintenance, which means a more entrenched stuck state.

Intervention response should correlate with the degree of density reduction achieved. Interventions that reduce organism density (whether intentionally through antifungal treatment or incidentally through habitat disruption) should produce proportionally greater clinical improvement.

Relapse risk should correlate with density rebound. When organism density returns to pre-intervention levels, the stuck program should re-establish. Sustained density reduction should predict sustained clinical improvement.

No existing clinical dataset includes organism density as a measured variable in any of these five conditions. The framework's most actionable recommendation is that mycobiome

measurement be incorporated into the assessment protocols for T2D, AN, IBS, obesity, and PD research, not as a primary outcome but as a covariate that the framework predicts will explain a significant portion of currently unexplained variance in disease severity and treatment response. [*The evidence may only be apparent once a corresponding treatment approach is initiated*]

VII. Cross-Domain Explanatory Power

The framework's strongest claim is not any individual condition application but the cross-domain pattern. A single model spanning metabolic disease (T2D, obesity), psychiatric disease (AN), functional gastrointestinal disease (IBS), and neurodegenerative disease (PD) is without precedent in medicine. No existing framework connects these five conditions under a single mechanism.

This is either the model's greatest strength or its greatest vulnerability. If organism density correlates with disease severity and intervention response across even three of the five conditions, the framework achieves an explanatory scope that no competing model matches. If it fails to correlate with any, the model is wrong. The predictions are testable. The experiments are straightforward. The framework exposes itself to refutation by design.

The cross-domain pattern this framework identifies is not without historical precedent. Bayard Taylor Holmes compiled over 8,000 references linking focal infections, primarily gastrointestinal, to psychiatric and neurological disease (Holmes, 1924; Noll, 2006; Craddock, 2026j). His work was suppressed, his journal ceased publication, and his name was erased from the history of psychiatry. The tools he had, microscopy and clinical observation, could identify the connection but not the mechanism. The tools available now, untargeted metabolomics, genomic foundation models, endocannabinoid system mapping, cross-kingdom signaling characterization, can. The Focal Infections 2.0 analysis (Craddock, 2026j) documents both the historical suppression and the molecular infrastructure that resolves what Holmes could only observe. This series is the applied consequence of that resolution.

The cannabinoid hyperemesis syndrome application developed in Craddock (2026b, Section VI) serves as a template for the methodology applied here: identifying mechanistic gaps in the standard model, proposing organism-mediated explanations for each gap, generating testable predictions, and offering zero-cost interventions accessible without institutional gatekeeping. The five condition papers in this series follow the same structure.

VIII. Limitations

The three-gate methodology is a selection heuristic, not a proof structure. Conditions that pass all three gates are framework-consistent, not framework-proven. Each companion paper identifies condition-specific limitations.

The five candidates vary substantially in evidential strength. T2D, AN, and IBS pass all three gates with strong evidence at each gate. Obesity passes all three gates but lacks a single-mechanism anchor. Parkinson's is explicitly speculative. This gradient is intentional: the framework's credibility is better served by transparent acknowledgment of differential confidence than by uniform presentation. [*we call that wildcatting in Oklahoma*]

All predictions require prospective testing with organism density as a measured variable, which no current clinical trial infrastructure includes. The methodological recommendation that mycobiome measurement be incorporated into chronic disease research is the paper's most immediately actionable output.

The dietary antifungal dose-response relationship is entirely uncharacterized. The gap between documented antifungal properties of dietary compounds and demonstrated clinical effect in any of these conditions remains open.

The stuck-program model assumes that C. albicans operates a phased program in the mammalian host. This assumption is the foundational claim of the biochemical computer framework (Craddock, 2026a; 2026b) and is not independently established by the condition-specific analyses presented here. The condition papers should be read as applications of the framework, not as independent evidence for the framework's foundational claims.

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