Obesity as a Stuck Program Mode of the Candida albicans Biochemical Computer

Growth and Storage Without Phase Transition

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Abstract

Obesity affects over 1 billion people globally, with treatment limited by the near-universal failure of sustained weight loss. Approximately 95% of individuals who lose weight through dietary intervention regain it within five years, a recidivism rate that suggests a defended equilibrium rather than insufficient willpower. This paper applies the biochemical computer framework (Craddock, 2026a; 2026b) to propose that obesity represents a stuck program mode in which the commensal fungal symbiont Candida albicans maintains the host in a growth and storage phase through sustained modulation of the incretin system, endocannabinoid-mediated appetite regulation, and metabolic state assessment via the GLP-1 receptor. This is a systems-level version conflict between a program refined for the Homo candidus phenotype and the modern host environment that no longer supports it. The framework resolves the set-point problem, explains the dramatic efficacy of bariatric surgery and GLP-1 receptor agonists as habitat disruption and sensing-channel override respectively, and accounts for the post-1970s epidemic onset through antibiotic-era mycobiome disruption. This is the most mechanistically diffuse candidate in the series, operating through multiple simultaneous signaling channels rather than a single-mechanism anchor. Five testable predictions are presented.

Keywords: obesity, Candida albicans, GLP-1, semaglutide, endocannabinoid system, CB1, set point, weight regain, bariatric surgery, incretin, quorum sensing, stuck program mode, antibiotic disruption, dietary antifungal, Homo candidus

I. Introduction

The global obesity epidemic has produced over 1 billion affected individuals, annual U.S. economic costs exceeding $1.4 trillion, and a therapeutic landscape defined by failure. Behavioral interventions produce temporary weight loss followed by regain in the vast majority of cases. Pharmacological interventions have historically shown modest effects with significant side effect profiles, until the recent introduction of GLP-1 receptor agonists. Bariatric surgery remains the only intervention with demonstrated long-term efficacy, and even it shows variable durability.

The central puzzle is the set-point: the body appears to defend a specific weight, actively opposing both caloric restriction and caloric excess to return to a target that, in obese individuals, is set too high. No existing model fully explains what maintains this set-point, what elevates it, or why it resists correction. The framework proposes that the set-point is not a host homeostatic mechanism. It is an organism-maintained target: the equilibrium C. albicans establishes during a growth and storage program phase that the modern dietary and ecological environment prevents from transitioning. In Homo candidus (Craddock, 2026b), the storage phase served a specific

evolutionary purpose: building energy reserves for subsequent program stages requiring sustained metabolic output, or buffering against seasonal scarcity and the saline oscillation cycles that shaped the coevolutionary relationship. The social infrastructure of Homo candidus, dietary protocol, managed feeding cycles, and communal behavioral enforcement, provided the transition signals that moved the program past the storage phase when reserves were sufficient. Modern Homo sapiens carries the storage program but not the infrastructure that ended it. The reserves build. The transition signal never arrives. The set-point elevates and the organism defends it.

This paper acknowledges at the outset that obesity is the most mechanistically diffuse candidate in the stuck-program series. Unlike type 2 diabetes, where Hgt4 provides a single-mechanism anchor, or IBS, where CB1/TRPV1 management maps to specific symptom subtypes, obesity involves multiple simultaneous organism capabilities without a dominant single pathway. This diffuseness is itself informative: a condition driven by several organism capabilities running past their intended windows simultaneously is harder to unstick than one driven by a single capability, predicting the clinical intractability observed. It is the broadest version conflict in the series.

II. The Mechanism

Incretin System Modulation

Peroumal et al. (2022) demonstrated that *C. albicans* colonization of the murine gut measurably alters levels of GLP-1, GIP, insulin, and other metabolic hormones. The GLP-1 receptor is the target of semaglutide and tirzepatide, drugs that have produced the most dramatic anti-obesity results in pharmaceutical history. The organism's confirmed interaction with the incretin system places it at the input side of the host's metabolic state assessment: the system that determines whether the host is in a fed or fasting state, whether energy should be stored or mobilized, and whether appetite should be enhanced or suppressed. [*So, those drugs that make you NOT hungry…C. Albicans can flip that switch either way*]

An organism modulating the incretin system can influence the host's metabolic posture, the overall stance of the metabolic system toward storage versus mobilization, without directly controlling any single metabolic pathway. This is management through the sensing layer rather than through the effector layer. The organism does not need to control fat storage directly. It needs to make the host's own metabolic system believe storage is appropriate.

Endocannabinoid Appetite Management

The endocannabinoid system governs appetite through CB1 receptors in both the gut and the brain. The organism's modulation of endocannabinoid tone through arachidonic acid substrate competition (Erb-Downward and Noverr, 2007; Acharya et al., 2017) and its maintenance of gut CB1 receptor density (Craddock, 2026b, Section VI) provide a second channel for appetite regulation. The lesson of rimonabant, the CB1 inverse agonist whose blockade of a single ECS receptor produced suicidal depression (Christensen et al., 2007), is that the system the organism manages is foundational to psychological homeostasis. The organism does not manage appetite through a peripheral mechanism. It manages appetite through the same system that maintains the will to live.

Metabolic Rate and Energy Expenditure

The organism's access to the HPA axis through a confirmed corticosteroid-binding protein (Loose and Feldman, 1981; 1982) and its modulation of thyroid-related metabolism through pituitary management (Craddock, 2026b) provide additional channels for influencing metabolic rate. Cortisol dynamics govern energy partitioning between storage and mobilization. An organism that reads cortisol as an environmental signal and can influence HPA axis output through upstream pituitary management has access to the master switch governing whether calories are burned or stored.

This multi-channel management leverages the same distributed biochemical computer architecture detailed in Craddock (2026a): Hgt4-calibrated glucose sensing, peptide transporters as dual nutrient/sensor inputs, arachidonic acid competition between prostaglandin and endocannabinoid pathways, and epigenetic/phenotypic memory mechanisms that stabilize the storage subroutine once quorum is achieved."

III. The Stuck State

The program phase represented by obesity is substrate accumulation: the organism directs the host's metabolic system toward fat storage, building energy reserves as a metabolic buffer for a subsequent program stage requiring sustained energy availability. In the evolutionary context described in the saline oscillation hypothesis (Craddock, 2026b), this phase would serve as preparation for periods of prolonged tissue engagement, environmental stress, or seasonal scarcity. In a functioning program, the accumulation phase is temporary: once sufficient reserves are built, the transition signal fires and the program advances to the next phase, which would draw down the reserves for their intended purpose.

The stuck state occurs when the transition signal never arrives. The modern food environment provides continuous caloric abundance. The organism's sensing channels, reading glucose through Hgt4, metabolic hormones through the incretin interface, and stress state through HPA axis inputs, all register a sustained fed, low-stress state. No environmental signal triggers the transition to the energy-mobilization phase. The storage program runs indefinitely.

The host's set-point is the organism's target equilibrium for this phase. The body does not defend an elevated weight through its own homeostatic mechanisms. It defends the weight the organism's program has established as appropriate for the storage phase. When caloric restriction reduces weight below this target, the organism compensates: appetite increases (endocannabinoid modulation), metabolic rate decreases (HPA axis adjustment), and the host regains weight. The 95% recidivism rate in dietary weight loss is not a failure of willpower. It is a failure to address the management layer establishing the target. The symbiotic system is working as intended, it is just stuck with no path out of the logic-loop it is executing. [*We've all written code like that before – Ctrl-C, right?*]. In Homo Candidus, there would have been a trigger, either a threshold reached, or a social structure that limited intake or mandated exercise.

The quorum sensing dimension reinforces the stuck state. As caloric abundance supports organism population expansion, the density-dependent coordination through farnesol and tyrosol strengthens the maintenance of storage mode. The organism population is larger in a well-fed host, which means the quorum threshold for program maintenance is more easily met, which means the program is harder to disrupt. Obesity is self-reinforcing at the organism population level. [*The bigger you are, the bigger you can get*]

Exercise Avoidance as Managed Inactivity: The Mirror of Anorexia

The companion paper on anorexia nervosa (Craddock, 2026f) describes compulsive exercise as a palliative trap: the organism suppresses food reward through endocannabinoid depletion, making exercise-generated anandamide the only remaining source of hedonic relief. The AN patient cannot stop moving because movement is the only time the pleasure system works. Food provides nothing. Exercise provides everything. The organism benefits from the caloric expenditure the restriction phase requires, and the host is trapped in a feedback loop where the only escape from anhedonia is the behavior that deepens it.

Obesity is the same mechanism running in the opposite direction.

In obesity, the organism is maintaining and enhancing food reward. The endocannabinoid system is running the appetite-enhancement program. Eating is pleasurable. The arachidonic acid economy that is depleted in AN is abundant here, producing robust endocannabinoid tone that makes food the primary hedonic channel. Exercise generates the same endogenous anandamide, but the obese patient already has a reliable, accessible, effortless source of hedonic reward: the refrigerator. The organism does not need to suppress exercise reward directly. It needs only to ensure that food reward is easier, more immediate, and more reinforced than the hedonic return from physical exertion. The host takes the path of least resistance to the same molecule.

The AN patient is starving for pleasure and can only find it in movement. The obese patient is saturated with pleasure from food and has no hedonic deficit that exercise would resolve. Both are responding rationally to the endocannabinoid landscape the organism has established. The AN patient who exercises through emaciation and the obese patient who cannot get off the couch are not exhibiting opposite psychiatric pathologies. They are exhibiting opposite organism-managed reward configurations operating through the same CB1 signaling interface. One is the restriction program's version of hedonic management. The other is the storage program's version. Same system, same molecule, opposite stuck states.

In Homo candidus, neither extreme was possible. The social infrastructure mandated physical activity regardless of hedonic preference, and communal feeding protocols ensured caloric intake regardless of appetite. The version conflict in modern Homo sapiens is that both the AN patient and the obese patient are free to follow the reward gradient the organism has established, with no external structure to override it. The organism sets the slope. The host rolls downhill. The direction depends on which program is running. Overcolonization in either state results in being metabolically stuck.

IV. The Persistence Problem Resolved

The set-point problem is the central puzzle. Conventional models invoke leptin resistance, hypothalamic inflammation, or epigenetic metabolic programming, each explaining part of the picture without providing a unified driver. The framework provides the unifying variable: an organism actively defending a metabolic target through multiple signaling channels simultaneously.

The multi-channel nature of the organism's involvement explains why single-target interventions fail. Leptin supplementation does not work because the organism modulates leptin's downstream effects through its management of the HPA axis and incretin system. Appetite suppressants provide temporary override of one channel while the organism compensates through others. The only interventions that produce dramatic, sustained results are

those that either massively disrupt the organism's habitat (bariatric surgery) or jam a primary sensing channel (GLP-1 receptor agonists).

Bariatric surgery produces weight loss that is far more durable than any behavioral intervention. Within the framework, this is because surgery does not merely restrict caloric intake. It physically restructures the organism's primary habitat, altering transit time, bile acid circulation, nutrient absorption patterns, and the spatial distribution of the gut environment. The organism's operating context changes so fundamentally that the storage program cannot maintain itself. The weight loss follows from program disruption, not from caloric restriction.[*Ctrl-C*]

Semaglutide and tirzepatide work because they jam the GLP-1 receptor, the organism's primary sensing channel for metabolic state assessment, with a sustained agonist signal. The organism reads the incretin system to assess whether storage is appropriate. Continuous GLP-1 agonism overrides the organism's assessment. [*And that is why they really work*] The dramatic weight loss these drugs produce is consistent with pharmacological disruption of a management layer, not with appetite suppression alone. The weight regain observed upon discontinuation is consistent with the organism re-establishing its metabolic assessment once the pharmacological override is removed.

V. Clustering Evidence

The post-1970s global obesity epidemic represents one of the most dramatic epidemiological shifts in modern medicine. The framework provides a specific driver: antibiotic-era disruption of the gut mycobiome altering organism population dynamics. Broad-spectrum antibiotics eliminate bacterial competitors that constrain C. albicans density in the gut (Noverr et al., 2004). Reduced bacterial competition allows organism expansion. Expanded organism populations have stronger quorum-mediated program maintenance. The population-level result is increased prevalence of stuck storage-mode states, manifesting as rising obesity rates in the decades following mass antibiotic adoption. [*The elders in the East Rift Valley would have had a plan for this period. Their discipline would have been one factor in pushing past it. The other would be the system itself – physiology distinct with alternate ways of controlling metabolism via pituitary override. In that system, the pituitary is more of a general than a soldier.*]

Early-childhood antibiotic exposure correlating with obesity risk, a finding consistently replicated in the epidemiological literature, fits the framework precisely: antibiotic administration during the developmental window when the organism-host relationship is being established shifts the organism's population dynamics toward higher density, which increases the probability of storage-mode lock. [*Is anyone surprised?*]

Familial clustering of obesity beyond genetic heritability is consistent with vertical transmission of organism populations from parent to child. Families share not only genes and dietary habits but organism populations, transmitted during birth and early life. Colonization patterns established in infancy persist into adulthood.

Geographic and socioeconomic patterns show that populations transitioning from traditional diets to processed Western diets show the most rapid obesity acceleration. Within the framework, this transition simultaneously removes dietary antifungal compounds present in traditional cuisines (coconut oil, garlic, fermented foods with antimicrobial properties) and introduces unlimited processed glucose substrate via substances like high-fructose corn syrup (HFCS). Notably, HFCS does not trigger insulin release in the same way glucose does (Stanhope, et al, 2009), meaning it does not stimulate the same fullness signals. The dual shift,

reduced antifungal pressure plus unlimited storage substrate, is the optimal condition for stuck storage-mode establishment. [*And society is helping it*]

VI. Unfreezing: Therapeutic Implications

Caloric Restriction Alone

Dietary restriction alone fails because the organism defends its target. Reduced caloric intake changes the substrate input but does not provide the transition signal. The organism reads the restriction as a temporary disruption and compensates through appetite enhancement and metabolic rate reduction. The 95% weight regain rate reflects the organism re-establishing equilibrium once the restriction period ends. This model would predict that without changing the colonization level, the return of weight is almost guaranteed.

Combined Substrate Change and Antifungal Pressure

The framework predicts that caloric restriction combined with dietary antifungal pressure should produce more durable results than restriction alone. The substrate change provides the input that might trigger transition. The antifungal pressure reduces organism density below the quorum sensing threshold maintaining storage mode. Together, they attack the stuck state from two directions: changing the signal environment and reducing the population maintaining program coherence.

The GLP-1 Agonist Opportunity

The efficacy of semaglutide and tirzepatide, combined with the weight regain observed upon discontinuation, provides a clinical opportunity to test the framework. If antifungal intervention (pharmaceutical or dietary) concurrent with GLP-1 agonist therapy improves long-term weight maintenance after drug discontinuation, the framework gains significant evidential support. The GLP-1 agonist disrupts the stuck state. The antifungal intervention reduces the organism population that would re-establish it. The *prediction*: combined therapy should show better post-discontinuation weight maintenance than GLP-1 agonist alone.

Bariatric Surgery and Mycobiome Trajectory

Post-bariatric patients show variable long-term outcomes. The framework predicts that patients who maintain weight loss long-term show different mycobiome trajectories than those who regain. Specifically, sustained reduction in C. albicans density should precede and predict durable weight loss, while mycobiome rebound should precede and predict weight regain. This is testable with existing longitudinal sample banks from bariatric surgery cohorts.

VII. Testable Predictions

Prediction O1: Fecal C. albicans density correlates positively with resistance to weight loss maintenance. Higher organism density at baseline predicts greater weight regain following dietary intervention.

Prediction O2: Post-bariatric mycobiome shifts precede and predict metabolic improvement timing. Specifically, C. albicans density reduction occurs before weight loss stabilization, not after, consistent with organism program disruption driving the metabolic change rather than following it.

Prediction O3: GLP-1 receptor agonist response magnitude correlates with organism colonization density. Patients with higher baseline C. albicans density show greater absolute weight loss on semaglutide, consistent with the drug disrupting a stronger organism-maintained storage signal.

Prediction O4: Antifungal intervention concurrent with GLP-1 agonist therapy improves post-discontinuation weight maintenance compared to GLP-1 agonist alone, consistent with antifungal reduction of the organism population that re-establishes the storage program.

Prediction O5: Population-level dietary antifungal intake (coconut oil, garlic, cinnamon consumption) shows an inverse correlation with obesity prevalence after controlling for total caloric intake, consistent with dietary antifungals constraining organism density below the threshold for storage-mode lock.

VIII. Limitations

Obesity is the most mechanistically diffuse candidate in this series. No single organism capability maps to the condition's central pathology the way Hgt4 maps to T2D or CB1/TRPV1 management maps to IBS. The organism's involvement in obesity operates through multiple simultaneous signaling channels, including incretin modulation, endocannabinoid appetite management, and HPA axis influence, without a dominant single pathway. This diffuseness is consistent with the clinical observation that obesity is harder to treat than conditions with more focal pathology, but it also means the framework's explanatory power is more distributed and harder to isolate experimentally.

The GLP-1/semaglutide connection, while compelling, is circumstantial. The fact that semaglutide works on a receptor the organism interacts with does not prove the organism is the target being disrupted. Direct demonstration that semaglutide alters organism behavior or population dynamics in the gut would strengthen the framework substantially.

The set-point concept itself is contested in the obesity research community. Some researchers prefer an alternative settling-point model in which body weight reflects an equilibrium between environmental inputs rather than a defended target. The framework is compatible with either model: whether the organism actively defends a target or passively maintains an equilibrium, its presence as an unrecognized variable in the system changes the dynamics.

This paper is part of a series applying the biochemical computer framework to chronic disease. The companion umbrella paper (Craddock, 2026d) describes the stuck-program model and selection methodology. The foundational framework is described in Craddock (2026a) and Craddock (2026b).

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