Review Article

# The Bio-Psycho-Social Holobiont Model of Health: Integrating the Biopsychosocial Paradigm, Microbiota Science, and Psychoneuroendocrinoimmunology

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**This article proposes the Bio-Psycho-Social Holobiont Model as a contemporary theoretical framework that integrates the complexity of the traditional biopsychosocial model with recent advances in microbiota science. While the biopsychosocial model has long represented one of the most comprehensive approaches to understanding health and disease, emerging evidence regarding the human microbiota and the holobiont concept suggests the need for a broader conceptual framework capable of incorporating the ecological and functional interdependence between human and microbial components.**

**Within the Bio-Psycho-Social Holobiont Model, health is conceptualized as an emergent property arising from the functional coherence of reciprocal interactions among biological, psychological, social, and microbiotic processes occurring within and between human and non-human cellular systems.**

**In this context, by the term "coherence" of mutual interactions between biological, psychological, social and microbiotic processes, we mean the informational convergence of the different bio-psycho-social teleonomies[1][2].**

**The model proposes that health and disease cannot be fully understood by focusing exclusively on human biological processes, but rather require consideration of the dynamic interactions among the host, its microbiota, psychological functioning, and sociocultural environment.**

**The article discusses the theoretical foundations of the model, its implications for the conceptualization of health and disease, its relationship with Psychoneuroendocrinoimmunology**

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**(PNEI), and its potential relevance for future interdisciplinary research and clinical practice. The Bio-Psycho-Social Holobiont Model is proposed as a theoretical extension and integration of the traditional biopsychosocial paradigm that is more consistent with contemporary developments in systems biology, complexity science, and microbiota research.**

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## Introduction

Human beings have long been conceptualized as complex adaptive systems characterized by continuous interactions among biological, psychological, and sociocultural teleonomies[1][3] (Engel, 1977), each possessing partially independent goals and "memory spaces" that contribute to the regulation of behavior and adaptation[4].

The biopsychosocial model was originally proposed by George Engel (1977) to overcome the epistemological and clinical limitations of the classical biomedical model, which focused almost exclusively on biological determinants of health and disease. Engel argued that a comprehensive understanding of human illness requires the simultaneous consideration of biological, psychological, and social factors, thereby providing a more complete framework for understanding health-related phenomena.

Although the biopsychosocial model has been widely recognized as one of the most scientifically grounded and conceptually sophisticated approaches to health and disease, its practical application in clinical settings has often proven challenging. This limitation may partly derive from insufficient communication among the professional disciplines that constitute the biopsychosocial triad, including medicine, psychology, and the social sciences, as well as from the inherent difficulty of translating systemic complexity into operational clinical models.

The three human teleonomies—biological, psychological, and sociocultural—can be represented as partially overlapping systems. Some areas of overlap reflect shared goals among all three teleonomies, whereas others involve only two systems or remain specific to a single domain[1]. Human behavior emerges from the continuous interaction among these partially autonomous yet interdependent systems. At a global level, this dynamic interaction can be described in terms of fitness, health, and psychophysical well-being[1].

From a conceptual perspective, each teleonomic system may be understood as an evolving informational system that changes over time according to principles characteristic of complex adaptive and evolutionary systems[1][5][6][7][8][9][10]. In other words, biological, psychological, and sociocultural dimensions all satisfy the criteria of informational systems capable of evolving, adapting, and partially operating independently from one another.

During recent decades, two scientific concepts have significantly enriched and expanded the complexity of the biopsychosocial framework: the concepts of the microbiota and the holobiont. These developments suggest that a more comprehensive understanding of human health may require extending the traditional biopsychosocial paradigm beyond exclusively human biological processes and toward a broader conception of the individual as an integrated bio-psycho-social-microbiota system.

## Microbiota and the Holobiont Concept

In recent decades, two scientific concepts have substantially enriched the complexity of the biopsychosocial model: the concepts of the **microbiota** and the **holobiont**.

The microbiota can be defined as the collection of microbial communities that stably or transiently colonize a given organism, interacting both with one another and with the host through complex ecological, metabolic, immunological, and neuroendocrine processes[11][12][13][14][15][16][17][18][19][20].

In humans, the microbiota primarily consists of bacteria, archaea, viruses, fungi, and protozoa distributed—albeit in different concentrations—across multiple body sites, including the gastrointestinal tract, skin, oral cavity, respiratory system, and genitourinary tract. These microbial communities contribute to the maintenance of physiological homeostasis and play a significant role in both health and disease.

The second concept that has further expanded the complexity of the biopsychosocial model is that of the **holobiont**.

The term *holobiont* refers to a biological unit composed of a host organism and its associated microbiota, including the sum of their genomes (the *hologenome*) and the integrated phenotypic outcomes generated through their interactions. Contemporary definitions converge on two principal components: (i) the host organism together with its associated microbial communities, and (ii) the ecological and evolutionary interdependence linking host and microbiota, which may include vertically transmitted, horizontally

acquired, or environmentally derived microorganisms[21][22][23][24][25][26][27][28][29][30][31][32][33][34][35][36][37][38][39].

The emergence of holobiont theory has challenged traditional views of biological individuality by suggesting that organisms should not necessarily be considered isolated entities. Rather, they may be more accurately conceptualized as ecological and functional assemblages whose physiological and adaptive capacities emerge from continuous interactions between host and microbial partners.

This perspective has profound implications for understanding health, disease, adaptation, and evolution. Increasing evidence indicates that microbial communities participate in regulating immune responses, metabolism, neuroendocrine signaling, and even behavioral and cognitive processes. Consequently, the boundaries of the individual organism become less clearly defined, giving rise to a more systemic and relational conception of biological identity.

## The Bio-Psycho-Social Holobiont Model

Having examined both the biopsychosocial model and the holobiont concept—including the role of the microbiota—it becomes possible to integrate these perspectives within a single theoretical framework: the **Bio-Psycho-Social Holobiont Model**.

The **Bio-Psycho-Social Holobiont** may be defined as an integrated functional unit composed of the human organism, its biological, psychological, and sociocultural context, and the symbiotic microbial communities that inhabit it. This unit is characterized by continuous co-regulation among biological, mental, and sociocultural processes, mediated through neuroendocrine, immune, metabolic, epigenetic, and bioinformational networks.

Although the convergence of these concepts may appear intuitive, it is important to note that, at the time of writing, searches combining the terms *holobiont* and *bio-psycho-social* or *biopsychosocial* yield virtually no results on the PubMed search engine. Consequently, the present model may represent one of the first attempts to formally integrate these theoretical traditions into a unified conceptual framework.

The Bio-Psycho-Social Holobiont Model proposes that human beings should not be understood solely through the interaction of biological, psychological, and social processes occurring within human cells and tissues. Rather, these processes must also be interpreted within the broader context of the dynamic relationships linking human and microbial systems.

From this perspective, biological processes, psychological experiences, social interactions, and microbial ecosystems are not independent domains but interconnected dimensions of a single adaptive system. Changes occurring within any one of these dimensions may propagate throughout the entire system, generating effects that extend beyond their original level of organization.

Accordingly, the human organism may be viewed as a multi-level informational network in which human and microbial components participate in continuous processes of mutual regulation. The resulting state of health or disease emerges not from the functioning of any isolated subsystem but from the overall degree of coherence, integration, and adaptive coordination characterizing the holobiont as a whole.

The Bio-Psycho-Social Holobiont Model therefore represents an extension of the traditional biopsychosocial paradigm that incorporates contemporary developments in microbiota science, systems biology, and complexity theory. By doing so, it offers a broader and potentially more accurate framework for understanding human health, disease, adaptation, and well-being.

## Theoretical and Clinical Implications of the Bio-Psycho-Social Holobiont Model

The Bio-Psycho-Social Holobiont Model has several important conceptual, epistemological, clinical, and research implications. These implications arise directly from reconceptualizing the human being as an integrated functional system composed not only of human biological, psychological, and sociocultural processes but also of the microbial communities that participate in the regulation of health and disease.

### *1. Overcoming Biological Anthropocentrism*

One of the most significant implications of the proposed model is the need to move beyond a biologically anthropocentric conception of the individual.

Traditionally, human beings have been understood as entities whose biological functioning is exclusively determined by their own cells and genetic material. The Bio-Psycho-Social Holobiont Model challenges this assumption by proposing that humans should instead be regarded as complex biological communities composed of both human and non-human cellular systems that continuously co-evolve and co-regulate physiological and behavioral processes.

This perspective substantially expands the traditional biopsychosocial framework by recognizing the microbiota not merely as an external influence on health but as a constitutive component of the human organism itself. Consequently, biological individuality becomes a relational rather than exclusively organism-centered phenomenon.

## *2. Redefining the Concept of Health*

According to the definition established by the World Health Organization[40], health is not simply the absence of disease or infirmity but a state of complete physical, mental, and social well-being.

The Bio-Psycho-Social Holobiont Model extends this multidimensional conception of health by incorporating microbial dimensions into the understanding of human functioning.

Within this framework, health is not defined merely as equilibrium among biological, psychological, and social variables. Rather, it is conceptualized as an emergent property arising from the functional coherence of interactions among the multiple components that constitute the holobiont.

The greater the degree of integration, cooperation, and adaptive coordination among biological, psychological, social, and microbiotic processes, the greater the likelihood of observing resilience, effective adaptation, and optimal well-being.

Accordingly, health should be viewed as a dynamic process rather than a static condition. It emerges from the capacity of the holobiont to maintain coherent and adaptive patterns of organization despite ongoing internal and external challenges.

## *3. A New Interpretation of Pathological Processes*

The model also offers a novel interpretation of disease and pathological processes.

From this perspective, pathological conditions may be understood as manifestations of incoherence, maladaptation, or disalignment among the multiple teleonomies that constitute the holobiont.

Conditions such as dysbiosis, chronic low-grade inflammation, persistent psychological stress, social isolation, and maladaptive lifestyles should not be regarded as isolated phenomena. Instead, they may be interpreted as different expressions of a broader systemic disruption affecting the functioning of the holobiont as a whole.

Disease therefore becomes less a localized dysfunction of a specific organ or system and more a manifestation of reduced informational coherence across multiple levels of biological, psychological,

social, and microbial organization.

This interpretation is consistent with contemporary systems approaches to medicine and with growing evidence regarding the interconnected nature of physiological and psychological regulation.

## *4. Epistemological Reinforcement of Psychoneuroendocrinoimmunology (PNEI)*

The Bio-Psycho-Social Holobiont Model may also provide a unifying conceptual framework for Psychoneuroendocrinoimmunology (PNEI).

PNEI has demonstrated that nervous, endocrine, immune, and psychological processes are deeply interconnected and mutually influential. However, many formulations of PNEI have historically focused primarily on interactions occurring within human biological systems.

The proposed model extends this perspective by explicitly incorporating microbiota processes into the same explanatory framework.

Within the Bio-Psycho-Social Holobiont Model, neuroendocrine, immune, metabolic, epigenetic, psychological, and microbiotic processes are understood as causally interconnected regulatory dimensions of a single adaptive system. The microbiota may therefore be considered one of the principal biological mediators through which psychological and social experiences influence physiological functioning.

This perspective strengthens the theoretical foundations of PNEI while simultaneously expanding its explanatory scope.

## *5. Clinical Implications for Integrated Healthcare*

From a clinical perspective, the model suggests the necessity of more integrated approaches to assessment and intervention.

Many chronic and complex disorders may require simultaneous consideration of biological, psychological, relational, social, and microbiotic variables.

Consequently, effective healthcare may increasingly depend upon interdisciplinary collaboration among physicians, psychologists, psychiatrists, gastroenterologists, nutritionists, immunologists, and other health professionals.

The model encourages clinicians to move beyond reductionistic diagnostic frameworks and toward a broader understanding of the patient as a multidimensional adaptive system.

Such an approach may be particularly relevant in conditions characterized by complex interactions among psychological distress, immune dysregulation, inflammation, gastrointestinal dysfunction, and microbiota alterations.

### *6. Implications for Future Scientific Research*

The Bio-Psycho-Social Holobiont Model encourages the development of truly multidisciplinary research programs capable of simultaneously investigating biological, psychological, social, and microbiotic dimensions of human functioning.

Future studies should increasingly integrate biomarkers, microbiota analyses, psychometric measures, behavioral assessments, and social variables within unified research designs.

Such an approach may contribute to a more realistic understanding of the mechanisms underlying health and disease while reducing the risk of reductionistic interpretations that isolate single causal factors from the broader systems in which they operate.

Furthermore, the model encourages researchers to investigate the principles governing coherence, adaptation, and information exchange across multiple levels of biological organization, potentially opening new directions for both theoretical and applied research.

## The Microbiota–Gut–Brain–Mind Axis

Within the perspective of the Bio-Psycho-Social Holobiont Model, the terminology commonly used in the international literature—such as *gut–brain axis* or *microbiota–gut–brain axis*—[41] may be considered conceptually and epistemologically incomplete.

The present model proposes replacing these expressions with the term **Microbiota–Gut–Brain–Mind Axis**, which more accurately reflects the complexity of the regulatory processes involved[42].

This revised terminology allows the integration of both top-down and bottom-up mechanisms within a single coherent conceptual framework.

Top-down processes refer to the influence of psychological states, emotions, cognition, beliefs, and social experiences on physiological and microbiota functioning.

For example, recent findings by Chang and colleagues[43] identified a mechanism through which psychological stress can induce both intestinal dysbiosis and systemic inflammation through vagal

modulation of Brunner's glands, providing further evidence for the causal influence of psychological processes on gut physiology and microbiota regulation.

Conversely, bottom-up processes refer to the influence of microbiota communities and gastrointestinal physiology on immune, endocrine, cognitive, emotional, and motivational processes. An expanding body of evidence indicates that the microbiota contributes to the regulation of neurobiological and psychological functioning through multiple interacting pathways.

The concept of the Microbiota–Gut–Brain–Mind Axis therefore appears more consistent with the Bio-Psycho-Social Holobiont Model because it explicitly recognizes the central role of psychological processes as both causes and consequences of holobiont regulation.

## Conclusions

The present article has proposed the **Bio-Psycho-Social Holobiont Model** as a theoretical extension of Engel's biopsychosocial framework in light of recent developments in microbiota science, systems biology, and complexity theory.

The integration of the concepts of microbiota and holobiont within the biopsychosocial perspective allows human beings to be conceptualized as complex functional systems emerging from the continuous interaction among human cells, microbial communities, psychological processes, and sociocultural dynamics. Within this framework, health can no longer be adequately understood as the simple absence of disease or as the isolated functioning of biological systems. Rather, it emerges from the degree of coherence, integration, and adaptive coordination among the multiple informational processes that constitute the human holobiont.

Accordingly, the Bio-Psycho-Social Holobiont Model proposes a broader conception of health as an emergent property arising from the dynamic interplay among biological, psychological, social, and microbiotic dimensions. Conversely, disease may be understood as the manifestation of systemic incoherence, maladaptation, or disruption in the informational integration that characterizes the functioning of the holobiont.

The model also provides a conceptual framework capable of integrating contemporary evidence derived from Psychoneuroendocrinoimmunology (PNEI), microbiota research, systems medicine, and complexity science. In doing so, it contributes to overcoming residual forms of reductionism that continue to characterize certain biomedical and psychological approaches to health and disease.

Particularly noteworthy is the model's capacity to incorporate both top-down and bottom-up mechanisms within a single explanatory system. Psychological processes may influence microbiota, immune, endocrine, and metabolic regulation, while microbiota ecosystem may simultaneously shape cognitive, emotional, motivational, and behavioral functioning. This bidirectional perspective appears consistent with current evidence regarding the **Microbiota–Gut–Brain–Mind Axis** and supports a more comprehensive understanding of human adaptation and health regulation.

Beyond its theoretical implications, the Bio-Psycho-Social Holobiont Model may also offer practical value for clinical assessment, healthcare organization, and interdisciplinary research. By encouraging the simultaneous consideration of biological, psychological, social, and microbiotic variables, the model supports the development of more integrated approaches to prevention, diagnosis, treatment, and health promotion.

Naturally, the present proposal should be regarded as a preliminary theoretical framework requiring further conceptual refinement and empirical validation. Future research will be necessary to clarify the mechanisms through which coherence emerges within the holobiont and to identify reliable indicators capable of operationalizing the construct in both clinical and research settings.

Nevertheless, the Bio-Psycho-Social Holobiont Model offers a promising perspective for understanding the human condition in a manner that is more consistent with contemporary developments in biology, psychology, microbiota science, and complexity theory.

By recognizing the individual as an integrated network of human and microbiota processes embedded within social and cultural contexts, the model may contribute to the emergence of a more systemic, relational, and scientifically grounded conception of health in the twenty-first century.

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