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The Biomedical Paradigm, Psychoneuro-immunology, and the Black Four of Hearts

Abstract

'There is still no comprehensive theory of the mind's influence on health that unifies the varied studies exploring mind-body connection – no equivalent of the germ theory that formed the foundation of modern research into infectious disease.' This assessment (Dienstfrey and Gurin 1993) from a commentary on the widely-acclaimed television series, 'Healing and the Mind' is near-universally shared. Trained in the science of the received, biomedical model – pathophysiological sciences – those responsible for the general acceptance of this assessment, notably psychoneuroimmunologists, frequently ask the question: What biological link connect psychological factors and neuroimmune processes leading to disease? An examination of this question shows why no unifying theory exists and why none is likely to arise within mainstream (bio)medicine. The question presupposes too much. It admits only a physicalist answer. Ironically, it limits rather than encourages medicine's bold move into the realm of a true *psycho*neuro-immunology. An essential condition for such a theory is the articulation of a successor medical model, one that scientifically explains 'downward causation' material events that such a 'pathopsychophysiological' theory implies, events in which the 'mind' affects the health of the body. Here I wish to identify such a model and elucidate the need for it.

The Biomedical Paradigm

Effective research scarcely begins, Thomas Kuhn tell us in *The Structure of Scientific Revolutions*, before a scientific community has answers to a number of fundamental questions. He lists three: 'What are the fundamental entities of which the universe is composed? How do these interact with each other and with the senses? What questions may legitimately be asked about such entities and what techniques employed in seeking solutions?' (Kuhn 1970, 5).

Though such questions are rarely, if ever, explicitly raised, nevertheless their answers are embedded in the training – textbook, lab exercises, puzzle

forms, model problem solutions – by which the scientist is indoctrinated into his or her profession and licensed to practise.

Answers to these questions 'come to exert a deep hold on the scientific mind...account(ing) both for the peculiar efficiency of the normal research activity and for the direction in which it proceeds at any given time' (Kuhn 1970, 5).

Judging from the direction in which normal medical research activity proceeds in our time, how does today's medical scientific community answers these questions? This is the question I want to explore. On its answer depends both the strengths and some of the constraints on the community's research activity.

When we look at the community's pursuit of more and more detailed knowledge of the structures and functions that are common to all living things, proceeding toward increasingly particulate biochemical mechanisms for explaining the origins and causes of disease, what can we infer about its answers to the questions that Kuhn poses? Lewis Thomas offers a clue when, citing the new biochemical information 'coming in cascades, and ... filled with meaning and astonishment for all of us,' he adds: 'And it should not need mentioning that the greatest part of this information has come from laboratories engaged in the fundamental biological sciences – from the fields of immunology, bacteriophage and microbial genetics, cell biology, membrane structure and physiology, neurophysiology and molecular biology' (1977, 119).

Clear is the research community's commitment to the belief that micro-structure is the best explanation for macro-behaviour; that 'predictability will increase as one uses more and more of the micro-level to explain the macro-level' (Zucker 1981, 149). Assuredly, reduction has played and will continue to play an essential role in scientific advance.

Buying more for less, it economizes on the number of principles required for explaining otherwise disparate phenomena. When generalized, reduction becomes reductionism, a belief in the universal applicability of upward causation: the universe is composed of fundamental entities, organs, cells, organelles, genes, ultimately, perhaps, elementary particles, whose intricate interactions account for complex behaviour.

Central to the medical community's keystone discipline, pathophysiology, are sciences of micro analysis, like those Thomas references. 'We use the hybrid term "biomedical" science as shorthand to describe the whole inquiry that underlies modern medicine,' says Thomas. 'It is biological science that most of us in medicine are betting on for the future, and it therefore seems natural to attach the words biology and medicine together to name the enterprise' (1977, 111).

Within this 'implicit body of intertwined theoretical and methodological belief' which Kuhn says underpins and drives any normal research activity, permitting 'selection, evaluation, and criticism' (1970, 16), what is the role, if

any, of mental events in producing health and disease? Raising this question is a way of getting a firmer grasp on the community's priorities. From what has been said this far, community commitments would seem to dictate that mental-emotional states are reducible to – their cognitive content is explained by – their coincident neurophysiological processes. Commenting on earlier efforts to expand medical science to include diseases of allegedly 'psychosomatic' origin, physician Gerald Weissmann reflects the prevailing belief: 'We have, indeed, reverted to purely organic hypotheses of ... pathogenesis, and these have been confirmed for us by recent triumphs in the areas of immunology, immunogenetics, and pharmacology' (1983).

Geneticist Arthur Zucker clarifies this reductionist bent towards molecular mechanisms: 'The ideal goal of reductionistic medicine would be diagnostics accomplished by a biochemical-biophysical survey of the patient's body. Ideally, psychological problems would be captured by this technique. It is part of the assumption of reductionistic medicine that, at the very least, mental states have clinically useful physical correlates.' (1981, 150)

In such medicine the patient is a 'silent' biological organism, 'a bundle of cells cast in the form of a biped' (Robbins 1984, 2), as one textbook expresses it.

Disease is 'a deviation from the norm of somatic [biological] variables' (in Mischler 1981). Accordingly, medical science is 'a branch of applied biology' (Wijngaarden, 1982, 2), the clinical application of the biophysical sciences. Told of recent studies that showed correlation between mental attitudes and disease susceptibility, a director at the Natural Institutes of Health is reported to have replied: 'The new research makes it clear. Attitudes can matter. The focus now should be on discovering the mechanism involved – the question is: What is the biochemistry of all this?' (In Goleman 1985, 13).

Molecular Medicine

What are the roots of this combined theoretical and methodological belief by which, except for morphological differences, human and veterinary medical science are formally identical? Medical historians trace this roots to two sources. In most general terms they derive from the mechanistic or corpuscular view of shaped matter in motion that both fueled and was further buoyed by the explanatory successes of the seventeenth-century scientific revolution. According to this view the universe is composed of independently existing fundamental objects. 'Laws must specify corpuscular motion and interactions, and explanation must reduce any given natural phenomenon tot corpuscular action under these laws' (Kuhn 1970, 41).

By the mid-nineteenth century through the work of Helmholtz and others this contact interaction has been relaxed to include any warranted physical or chemical mechanism. Now the organic world was held to be explainable by the laws of inorganic physics and chemistry (Lenoir 1982).

On these general principals was built the modern scientific edifice, encompassing disciplines spanning classical mechanics and optics, statistical thermodynamics and electromagnetism, and even including in many respects relativistic and quantum physics.

In varying degrees and with different shadings these disciplines may be subsumed under the rubric of sciences of micro-analysis. They define the Enlightenment science world view. Systems studied are near-equilibrium, their parts are identical, and interactions among parts are sufficiently weak that averaging out techniques [Fourier analysis, for example] can be applied to account for irregularities (Nicolis 1989).

In the life sciences the counterpart to the development of these bedrock physical sciences was the explosion in the second half of the nineteenth-century of sciences that formed the backbone of the medical model then taking shape. This was the second source of the roots of the modern view of medical science. These sciences are associated with such luminous names as Bernard (physiology), Virchov (cell pathology), Pasteur (bacteriology), and Koch (controlled clinical trials isolating agents of infectious diseases). To the extend that medicine is an applied science, the validity of these life sciences is grounded in and rationalized by still more basic physical sciences like those just mentioned.

By the final third of this century, what may be viewed as the microscopic extensions of these nineteenth-century life sciences had matured. They are typified by the sciences to which Thomas and Weissmann call our attention. Their concerted application in today's teaching hospitals and federally-funded research institutes adds up to the institutionalization of a paradigm. The Robert Wood Johnson Commission of Medical Education 1992 Report speaks of a 'shift in paradigm.' It calls the new paradigm Molecular Medicine: 'encompassing the newer fields of molecular, cellular, structural, and neural biology, [molecular medicine] has changed [medicine's] world view' (1992, 2).

The complex interplay among the methodology that guides an applied discipline like medicine, the findings of the basic science that underwrite it, and the consequent formal constraints imposed on its vocabulary is elucidated by means of a multi-tiered diagram. To adopt a particular medical tradition or model is to accept a whole package of interrelated premises, presuppositions, and commitments – what the Report calls an integrated world view. Figure 1, 'Components of a Scientific Model for an Applied Science,' highlights the biomedical application of such a model.

Tier 3, the level of applied science, comprises the science that make up the medical school curriculum – physiology, anatomy, pathology, bacteriology and so forth. Tier 2, the level of basic sciences, comprises the sciences that traditionally have made up the pre-medical curriculum – physics, thermodynamics, chemistry, biology, and so forth. Finally, tier 1, the level of explanatory strategy and the most fundamental level, comprises the

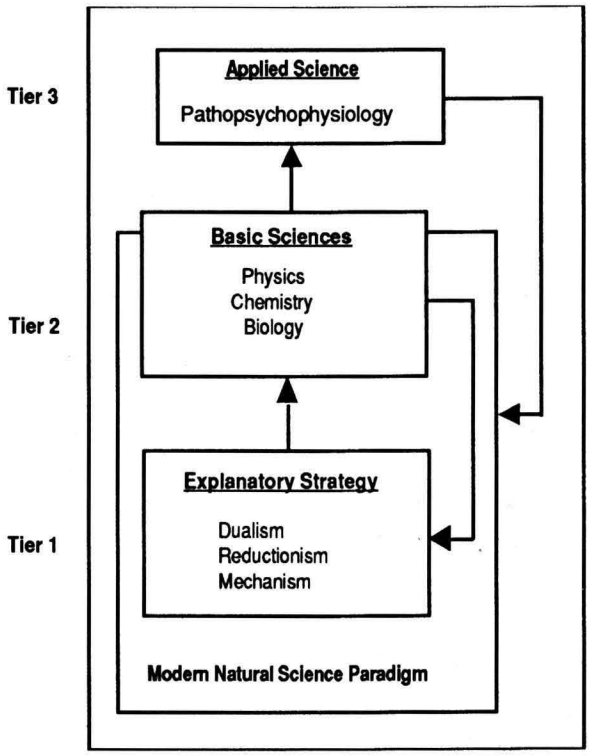

Figure 1. Components of a scientific model for an applied science (a biomedical application)

methodological directives that make up the logic of inquiry informing these basic sciences, several which are listed.

Together tiers 1 and 2 make up the modern natural science paradigm given shape by the seventeenth-century scientific revolution. In combination these three levels furnish an integrated framework for a professional community to go about the business of pushing outward on its frontiers. They constitute its paradigm, 'supplying the foundation for its further practise' (Kuhn 1970, 10). Successes at the tier-2 level provide further reinforcement for the explanatory strategy (tier 1), hence the bottom downward arrow from tier 2 to tier 1. Additionally, they provide increased confidence that tier-3 research should continue to reflect a commitment to the overall world view expressed at the tier-1 level (Foss 1989, 168-172).

Granting the sovereignty of this world view, let us return to Kuhn's question rephrased to apply to biomedicine: Within molecular medicine what questions can legitimately be asked about the causes of disease? What are the techniques that can be employed to treat these causes and restore health? From what has been said about the basic sciences and explanatory

strategy if bioneducube, we can surmise the answers to these questions. Disease is caused by external environmental factors like viruses and carcinogens (*germs*), and by internal biological factors like chemical reactions and defective nucleic acid sequences (*genes*). These are the two classes of etiological factors recognized in today's medical scientific community (Robbins 1984; Scriver 1978).

Appropriate techniques for redressing the balance disturbed by these factors include chemical, electrical, and surgical procedures. Their use is at the heart of today's medical practise and is a major means for satisfying the control criterion by which the soundness of any scientific medical strategy may be judged: how well does it control disease and restore health? Making the case for the scientific character of biomedical theories, physician and philosopher Kenneth Schaffner formulates the following criterion. These theories, he says, 'admit of all the important features of theories in physics and chemistry ... [they] are testable and have excess empirical content, they organize knowledge in inductive and sometimes even deductive ways ... and they are applicable to prediction and control in crucially important areas such as [disease etiology]... and health-care delivery' (1980, 88).

The Psychoneuroimmunology Dilemma

Just this issue of modern molecular medicine's applicability to prediction and control in the areas of disease causation and health-care delivery has led to what some have called a growing crisis in medicine (Engel 1977). This issue drives today's 'alternative medicine' movements, whose focus is on the perceived shortfall of biomedical theories to account for the full spectrum of disease factors reported in the medical literature. These factors include those implicated in the so-called diseases of civilization (Dubois 1971) — respiratory disorders, many cancers, coronary heart disease, and rheumatoid arthritis, among them. H.W. Harris and Kenneth Schaffner give expression to this discontent, observing that the evidence now indicates that diseases exist 'at multiple organizational levels, including social, environmental, and developmental interactions that will make their reduction to a single [somatic] level problematic' (1992).

At the very time that Robert Wood Johnson Commission proclaims the institutionalization of molecular medicine as a new paradigm, the medical community itself divides into countervailing subspecialties like primary care medicine, family practise medicine, preventive medicine, and more recently behavioral medicine. The growth of these subspecialties may be seen as symptoms of a need to redress what I just alluded to as the explanatory shortfall of biomedical theories. Often these countermovements are accompanied by a call for a more comprehensive medical model, variously called 'humanistic,' 'phenomenological,' 'interdisciplinary,' 'systems,'

'biopsychosocial' (see, for example, McWhinney [1983], Schwartz [1985], Blois [1988], Sadler [1990], Temoshok [1992]).

Psychoneuroimmunology, the research arm of one of these subspecialties, behavioral medicine, offers a fascinating illustration of what Kuhn calls the period of crisis between the collapse of one paradigm and the emergence of another. Such a period can be identified by 'the proliferation of competing articulations, the willingness to try anything, the expression of explicit discontent, the recourse to philosophy and the debate over fundamentals' (Kuhn 1970, 91). During such a period anomalies come out of the closet – findings that 'cannot be fitted into the conceptual boxes supplied by professional education' (Kuhn 1970, 5).

The placebo effect is a signal illustration. Because it fits paradigm-induced expectations ('Placebo's can be more powerful than, and reverse the action of, potent active drugs' [Shapiro 1968], it is normally ignored. What we *believe* or *expect* to be the case (placebo: 'I *will* please.'), psychological states, apparently interact with bodily processes, physiological states. Yet the only conceptual boxes available in which to fit this 'fundamental novelty' (Kuhn 1970, 51) are those constructed to deal with *other*, earlier expose anomalies – in this instance, germs. Disease remains 'physiology gone astray' (Zucker 1981, 144).

In the flagship volume of the new research field, psychoneuroimmunology, co-editor Robert Ader describes its task as providing'a link whereby psychosocial factors can be understood to play a role in influencing immune responses and processes of disease' (1981 xxii). If after all, the mind is implicated in pathogenesis, what is the mechanism of action and associated patho-science (compare pathopsychology) that accounts for this link? How can the immaterial thinking substance of mind (*res cognitans*) causally interact with the material body (*res extensa*) and be articulated in the language of science? With psychoneuroimmunology, we return to the age-old mind-body problem.

Later in the same volume immunologist Robert Good gives voice to the dilemma, namely the issue how the mind might deliberately be employed to affect the body. And if this can be done, then what happens to the current model of the body as sort of mindlessly propelled system? 'Immunologists are often asked whether the state of mind can influence the body's defense's. Can positive attitude, a constructive frame of mind, grief, depression, or anxiety alter ability to resist infections, allergies, autoimmunities, or even cancer? Such questions leave me with the feeling of inadequacy because I deep down know that such influence exist, but I am unable to tell *how* they work, nor can I in any scientific way prescribe how to harness these influences, predict, or control them. Thus they cannot usually be addressed in scientific perspective.' (1981, xvii)

Trained in the biomedical sciences, in immunology, neurophysiology, molecular biology, biochemistry – what I called sciences of micro analysis –

what conceptual tools are available to the psychoneuroimmunologist for constructing a bridge spanning a state of mind ('psycho') and the body's defenses ('neuroimmunology'? How can he or she track the pathways linking the initial state of mind and the interior of the immune system, and so 'in scientific perspective'?What do the intertwined theoretical and methodological commitments of the professional training of pschoneuroimmunologists dictate? Just posing the question suggest the extent to which its resolution is preordained, that is, model-dependent.

Consider the full dimensions of the dilemma. They are encapsulated in the illustration of an ailing psychoneurology researcher who, unlike the animals she researches, can parlay her knowledge of the placebo effect to therapeutic advantage. Employing guided imagery, she elects to convert her negative expectations concerning the biomedically prescribed drug therapy into positive expectations, and do so with the view to tipping the balance from illness to health. The case is consistent with the findings in the psychoneuroimmunology literature that have accumulated over the past decades.

We can flesh out the illustration by relating it to one of the studies in this literature, a single-case study (Smith 1985). In it, the subject, an experienced meditator, was skin-tested weekly with a skin test reagent. 'after baseline immunologic studies, she was able, as hypothesized, to significant reduce both the induration and the delayed hypersensitivity skin test reaction and in vitro lymphocyte stimulation to varicella zoster' (Smith 1985, 2110). Then she was able to allow its reaction to return to baseline and, when asked, to reproduce the entire sequence six months later. The investigators concluded that the experiment yielded data of 'an intentional direct psychological modulation of the immune system.'

The mechanism employed? 'During the phase 2 periods of the original repeat experiment, the subject would... tell her body not to violate its wisdom concerning its defense against infection. Then ... she would visualize the area of erythema and induration getting smaller and smaller. Soon after phase 2 injection, she would pass her hand over her arm, sending 'healing energy' to the injection site.' (Smith 1985, 2111)

What killed the rats

Figure 2 is an abstract cutaway that seeks to generalize the findings of the psychoneuroimmunological literature, highlighting certain nodal points along the pathway traversing the 'psychoneuroimmune system' posited by the field bearing its name. Figure 2 also may be viewed as a distillation of the findings of the 'psychophysiologic' animal conditioning experiments performed in this century. These span the landmark experiments of Pavlov near the turn of the century, Seyle's pioneering, mid-century psychologically-perceived stress experiments, and the by-now classic experiments with

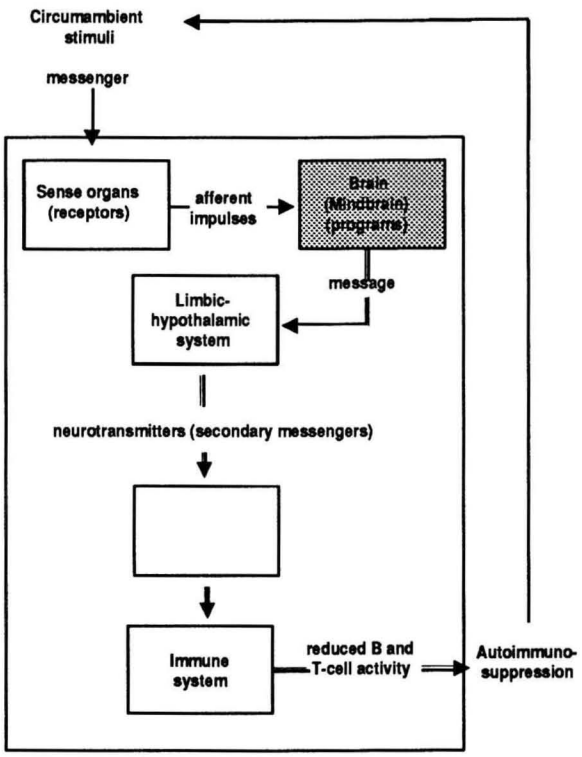

Figure 2. Psychoneuroimmune system

conditioned rats by Ader and his associates in the 1970s, the last of which were to give the name to the new research field.

Together, these studies furnish the underpinnings that explain the psychodynamics dramatized in the Smith experiment with the meditator and in others like it conducted in the 1980s with human subjects (Barber [1984], O'Leary [1985], Braun [1988]; Olness [1989], Zachariae [1991]). Some of these experiments are referenced in a recent *Scandanivian Journal of Immunology* editorial (Booth 1993).

Consider the role of the shaded rectangle in figure 2 with respect first to Pavlov's and then to Ader's results. Recall that not the bell, or bell sound, caused the conditioned dogs to salivate but rather the interpretation or meaning the dogs ascribed to the bell. An entity belonging to a semantic or informational modality, 'Food ahoy!' – a message – occasions a somatic or physiological reaction to a matter-energy modality. So impressed was physiologist Walter Cannon by Pavlov's results that he coined the term 'psychic secretions' (1963) to denote them.

The same construction may be given to the results of Ader's experiment (1975; 1985). To drastically encapsulate them, we might say that the conditi-

oned rats, after having received at regular intervals cyclophosphamide, a DNA-alkylating immunosuppressive agent, paired with saccharine water, reacted to the subsequently administered saccharine water alone like the controls reacted to the cyclophosphamide administered to them in the same doses at the same intervals. Their antibody levels were measurably depressed.

Again, not the physical substance per se, the sugar water, but the meaning the conditioned rats ascribed to the water ('This substance is cytotoxic'), may be said to have impaired their autoimmune defenses. The experimenter had altered their programs – conditioned them – so that they sent a correspondingly altered message to themselves. Since a different message – deconditioning the rats – would produce a correspondingly different outcome, we may conclude that not the physical messenger but the symbolic or meta-physical message ultimately killed the rats who were injected with a pathogen. 'Psychoimmunosuppression,' we can hear Cannon marvel[1].

Such a reconstruction communicates the salient feature of the experiment, its level-mixing (mind *and* body), self-referential character – self-referential in the sense that the rats did it to themselves. The conditioned rats, transmitting an incoming messenger through their receiving-sending terminals – sensory-cerebral receptors – transform the physical messenger into a symbolic message (represented by the double arrows). This message, always piggybacking secondary messengers (the neurotransmitters) initiates a series of physiological reactions internal to their systems, culminating in a change of system state, immunosuppression.

When we translate this analysis to the subject of the Smith experiment, the metaphorical expression, denoted by the raised-eyebrow quotation marks around 'psychic secretions' and 'psychoimmunosuppression,' is rendered literal. Like the imagined lab researcher in the earlier illustration, the meditator subject of the experiment proactively rearranged her own cerebral circuitry, her neural configurations (hardware), reprogramming, or re-conditioning, herself. And she did it so that the program-processed message, transduced through her system, would have the sought-for physiological outcome: in the present instance, psychoimmuno-

[1]. One symposiast reported that he and his colleagues were unable to replicate Ader's experiment, implying that findings from these studies offer a slender reed for a successor-model argument. Although this symposiast did not elaborate on his findings, we may surmise that the conditioned rats in his experiments responded in some way differently to the physical stimulus than did the controls. For purposes of the present argument this is critical: how conditioned subjects *perceive* the stimulus, a subjective vector, is inbuilt to the physiological response. Clinically stated, the meaning patients ascribe to the germ, a top-down, biosemiotic etiological factor, as well as the germ itself, a bottum-up, biochemical etiological factor, is integral to the disease equation. The two classes of factors are codependent.

enhancement! In both cases the pathogen of note ultimately is a message, and the subjects *send it to themselves*, a downward causation, reflexive idiom. Macro-behaviour is essential to a full understanding of changes in micro-structure.

Steward Wolf, writing in *Advances*, offers a generalized description of the biopsychodynamics involved in the findings of the psychoneuroimmunology literature. This description tracks the arrows of figure 2 and in a generalized way may be applied to the pathway along which the 'healing energy' of the subject of the Smith experiment passes on its way from her mindbrain to her lymphocyte cells. The description, slightly abridged, merits quoting at length: 'Incoming impulses from sensory receptors, on entering the brain, recruit excitatory and inhibitory connections from neurons that transmit information from circuits in thalamic, limbic and cortical structures. Here, data from an individual's earlier learning, emotions, and belief are stored. Thus, the original sensory message is moderated to elicit an individual response in terms of emotion, understanding, and/or somatic behaviour. Such central processing of information from afferent neurons generates individually specific perceptions that may, through automatic effectors, direct metabolic and thermodynamic functions, thereby altering the distribution of receptors, the synthesis of messenger molecules, and even gene expression of peripheral tissues.' (1992, 43)

The immediate question is: What is the mechanism that accounts for this extraordinary (biomedically speaking) message-molecule-gene connection at the heart of the psychoneuroimmunologist's dilemma? With this question we reach the expressive limits of the key sciences of the received model, pathophysiology and pathoneurophysiology.

The Anvil and the Computer

One of Kuhn's more controversial claims is that disagreement over fundamentally different theories or models, paradigm-talk, is terminated 'not by deliberation and interpretation, but by a relatively sudden and unstructured event like the gestalt switch' (1970, 122). I want to suggest that something like this obtains in our assessment of what is at stake in the psychoneuroimmunology debate. The same volume of *Advances* in which the passage from Wolf appears contains a review of the second, 1991 edition of *Psychoneuroimmunology*. The reviewer, Benjamin Wolman, editor-in-chief of the *International Encyclopedia of Psychiatry, Psychology, Psychoanalysis, and Neurology*, writes: 'On the subject of psychology and the immune system the book is cautious and precise. For example, ... [editors] Ader and Cohen write: "Conditioned alterations of immunologic reactivity provide dramatic evidence of a functional relationship between the brain and the immune system", but they conclude that 'The mechanisms underlying the conditioned modulation of immunity are not known' ' (1992, 68-69).

Not made clear by Wolman is how the discovery of such mechanisms linking the brain and the immune system would contribute to 'the subject of psychology and the immune system'; nor how this discovery would warrant attribution of the name 'psychoneuroimmunology' rather than 'neuro-immunology.' Still, wolman offers an important cue to the enduring nature of the psychoneuroimmumology dilemma when he suggests why such caution is necessary. 'The advent of disease,' he says, 'can be conceived as a state of war between germs, viruses, and other attacking forces on the one hand, and the defense force of the organism on the other.' He develops this analogy consistently with biomedical premises: 'One can compare the attacking forces to a hammer and the immune system to an anvil. The vulnerability of the anvil greatly contributes to the progress of disease, and the degree of vulnerability is related to several kinds of factors, among them – genetic factors.' (1992, 69)

The patient, a masterwork of biomechanics, is likened to an anvil, warding off pathogens hammering both from without, viruses, and from within, genetic factors. Where in such a network of theory, we might ask, is there room for a patient who, like Pavlov's dogs or the subject of Smith experiment, deploys symbols of 'meaning' – wether supplied from without or self-generated – to ameliorate (or exacerbate) the impact of these attacking pathogens? Where is room for one who deploys information as a means of regulating biological processes. How does Molecular Medicine address this question??

This self-referential activity by virtue of which, when translated into medical idiom, the patient is both patient and *agent* in her own patho- and salutogenesis, capable of exercising limited self-control over health and disease-producing processes. Here we are speaking not merely pathophysiology but patho*cyber*physiology – cyber in the sense of being capable of self-government. Called for would seem to be a semantic or biosemiotic analysis – how mind and the body succeed in conversing with each other – that complements the conventional somatic, neurobiochemical analysis with its focus on the molecular mechanism of disease. in the new understanding of mind-body, the causal information-transfer laws peculiar to patho-*cyber*physiology presuppose and subsume the causal energy-transfer laws peculiar to pathophysiology. Neurohormones are message-induce messengers.

In the conventional model the immune system is a separate self-referential system, as is the neuroimmune system. But the salience of psychoneuroimmunological findings is that the changes in immune and neuroimmune measures correlate with changes in psychological states, thus emotions of the mind; and vice versa (Booth 1993). The implication is that patients, by refocussing their consciousness altering their mental or emotional 'programs,' can actively participate in the healing process. They have manoeuvering room inaccessible in the conventional framework. Hence, the

system posited by the discipline bearing its name, the psychoneuroimmune system, is itself self-referential and in certain instances, like those earlier discussed, reflectively – by the deliberate effort of the person – as well as reflexively so.

At a certain level of organization, the neocortical level, the programs of the brain (of mindbrain) and so messages they process can, we saw, be customized – reprogrammed (the process of adaptation and learning. The patient can send messages to herself, a level-mixing, holistic phenomenon. She can recruit her own neurochemicals to serve messengers in the mind-body communications circuits, whereby cognitive and affective structures translate into bodily changes. Considered biomedically, this capability is quite extraordinary, enlarging diagnostics and therapeutics by an order of magnitude.

To convey its extraordinariness we amy invoke the analogy of a computer equipped with a mechanism such as a robot arm capable of moving about in accordance with a program in the computer. Now suppose that the computer is programmed so that the arm begins carrying out modifications to the computer's own circuitry. This is the example of software feedback that physicist Paul Davies offers to convey the level mixing involved in the wave-particle duality in quantum physics. 'Just as changes in information downwardly cause changes in the behaviour of an electron during a quantum measurement [the electron moves differently afterwards], so changes in the program software downwardly cause modifications in the computer's hardware.' (1989, 173). Information is the change agent of note: it drives changes in the system.

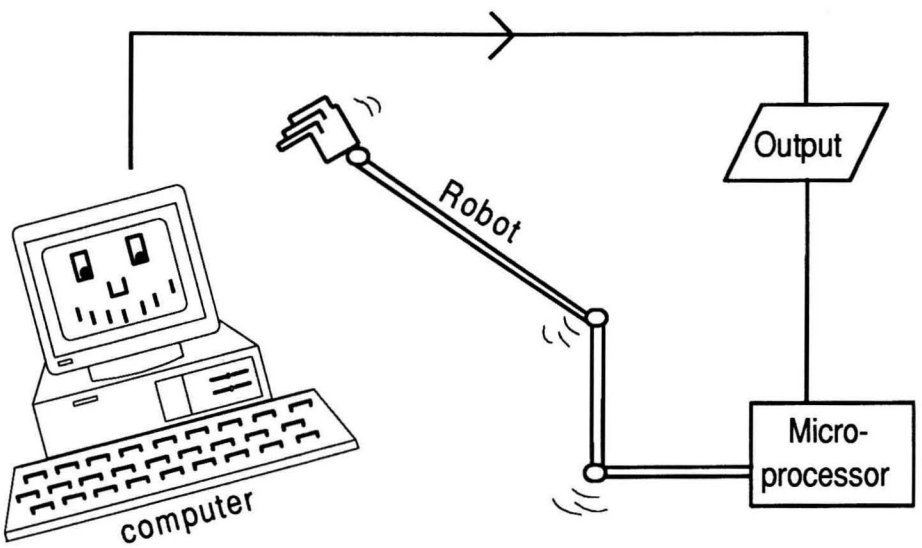

Figure 3. Computer rearranging its own circuitry.
(Adapted from Davies, 1988)

The difference between this self-organizational analogy and the hammer-anvil analogy measures the distance between pathophysiology and patho-cyberphysiology, between the received, biomedical model and the successor model adumbrated below.

The Alchemy of Psychoneuroimmunology

Yet which among today's basis sciences that underwrite an applied science like medicine are governed by theoretical and methodological commitments to upward-and-downward mutual causation, that is, to self-organization and emergence, rather than to upward causation alone, to mechanism and reductionism? A major trust of the seventeenth-century scientific revolution had been to inoculate the body science against intellectual viruses like *emergence* and *vitalism*. Are we to turn back the clock? The answer to this question, I believe, underlines the relevance to medical science of today's post-Enlightenment sciences of complexity – condensed matter physics, nonlinear thermodynamics, evolutionary biology among them.

Science of macro-organization, they stipulate that matter, rather than essentially passive and mechanistic – the premise of science of micro analysis – is active and under certain far-from-equilibrium conditions capable of self-normalizing, even self-transcending behaviour. They stipulate that by means of creative potential of dissipation, matter, in an open system energy-and-information exchange with its environment, can drive itself to new levels of organization ('symmetry-breaking bifurcations').

These sciences ground the cybernetic insight that, because of its hierarchical architecture, a complex adaptive system (a patient, for example) can represent a level of abstraction internally. Making predictions based on its various internal models of the world, such a system van adjust its behaviour, an instance of proto-mind. Using informational inputs as the relevant change agent, it can act upon itself, rearranging its own circuitry. In these sciences macro-behaviour, program software, is essential to an explanation of changes in micro-structure, system hardware, as well as the other way around. Matter has, so to say, an interior life.

Linked by a common denominator, information, mind and matter are no longer categorically opposed to one another: *res cogitans* versus *res extensa*. Instead, like its developmental antecedents – *res physis* and *res bios* – *res cogitans* is part of a hierarchy of successive, mutually irreducible levels of organization, a species of natural adaptation. Mind is reperceived as an evolutionary derivative of matter self-organizing – *res autopoietica*, as I have called it (Foss in press). Coupled to the mechanism of natural selection is that of self-organization. Together they provide a full account of the negentropic process of evolution (Kaufman 1991): not passive *res extensa* but active *res autopoietica* is the primitive unit of post-Enlightenment scientific analysis.

The mind-body duality that has so bedeviled Western medicine is in this perspective preempted. Mind can causally interact with body to realize a message-molecule-gene connection, as Wolf asserts (1992), because the mindbody, the psychoneuroimmune system of figure 2, is a cybernetic, self-regulating entity in which information is an essential regulator of biological processes. Not only red and white blood cells circulate through the patient's body but positive and negative messages as well, and both are mutually interacting change agents in the production of health and disease. The *meaning of the illness to the patient* is an integral etiological factor.

The cryptic prefix, 'psycho,' in the new research field's name thus acquires an operational meaning. It refers to the system capacity for upward and downward causal processes. For clinical purposes, mind is viewed as a species of adaptation; at a certain organization level, informed adaptation. Pathocyberphysiology translate into pathopsychophysiology. Consciousness is written into clinical equation.

Not nature, but the expressive constraints of the science that forms the professional training of psychoneuroimmunologists, the pathophysiological sciences, outlaw genuinely psychoneuroimmunological phenomena. Little wonder practicing psychoneuroimmunologists are cautious as regards identifying psychoneuroimmunological mechanisms. I would submit that this agnosticism is formally built into the syntax of their operational model. In such a model 'psychoimmunosuppression,' like 'psychic secretions,' is an impermissible expression. Compare 'nonchemical drugs.' Nothing less than a change in paradigm, a gestalt switch, would accommodate the psychoneuroimmunology findings; namely the introduction of a successor pathoscience and the model it subserves.

A Successor Model

The timeliness of such a successor pathoscience and its model is suggested by Kuhn's observation that normal research guided by the conceptual categories deployed by Aristotelian science 'could not have produced the laws that Galileo discovered' (1970, 123). Similarly, I would argue, normal research guided by the conceptual categories deployed by biomedical science inhibits recognizing the pivotal mechanism of the successor model. consider that the mechanism animating this model has already been identified in this discussion. Look again at the passage from Wolf, but now substitute 'messages' of 'program-processes messages' for the word 'perception' in the last sentence of the original – which reads in part, 'information from afferent neurons generates individually specific perceptions that may ... direct metabolic and thermodynamic functions.' This substitution helps highlight the sought for mechanism, namely, the cognitive and affective *programs* which process the messages that a complex adaptive system sends to itself in

order to edit its behavioral outcome and so maintain steady state amidst an ever-changing environment.

Represented in figure 2 by the shaded rectangle, this mechanism biomedically considered is a magical box. Alchemically, it transmutes input signals from the environment, physical messengers, into symbolic signs or messages. Belonging to a matter-energy modality, the messengers are represented by single-line arrows. The messages, belonging to an informational or noetic modality, are represented by double-line arrows. In turn, these messages enlist secondary messengers, neuropeptides which trigger a series of chemical changes internal to the system. They can penetrate cells with receptors for them instructing genes to catalyze enzyme-producing proteins that, in their turn, effect further cellular activities whose outcome are fed back as new information. Biosemiotics is grafted into biochemistry to form a model adequate to the epidemiological, psychophysiological, and clinical findings.

We have come full circle. With or without the aid of instrumentation, by re-turning their message-processing programs, patients can actively participate in the therapeutic process. They can mix the biomedically immiscible categories of mind and matter, so sending 'healing energy' to their immune systems. By altering their dispositions, they can adapt to their changing circumstances, and do so informedly.

Although these messages are not necessarily overriding etiological factors, they are integral nonetheless and, like all such factors, capable, we saw, of tipping the balance one way or another. In *The Type C Connection*, Lydia Temoshok and Henry Dreher (1992) designate them collectively as the 10 percent factor. Exchanging matter, energy, and information with the environment, the mindbody dumps back waste and behavioral output. This output alters the environment in which disease grows, both the internal and external environments. Its effects are fed back as information in a recursive loop that can drive the system to a new organization regime. Metabolizing information, the system may be said to 'specify its own lawfulness' (Maturama 1987).

Physician Ian McWhinney characterizes this system in level-mixing, biosemiotic terms, all levels acting parallel such that the flow of information at each level and between levels maintain the system: 'Information is carried at all levels in the form of symbols defined as patterns of information conveying particular messages. In the human organism, symbols become decreasingly specific at higher levels of organism. A major life event may have a very different meaning in two individuals. The meaning is transmitted to other levels of the organism and therefore has a chemical substrate, but the meaning of the event cannot be explained in the language appropriate for the chemical level. Only a multilevel explanatory model, therefore, is capable of providing the theoretical foundation for "post-Enlightenment medicine." (in press).'

No longer is the patient a mindless lifebody, a 'homeostatic automaton' (Guyton 1991), to be treated only physicalistically from the outside, important as these treatments are. Rather the patient of the successor model is an articulate mindbody, capable also, with or without the aid of instrumentation, of *treating herself*, adaptively rearranging her own 'circuitry' such that macro behaviour helps account for changes in micro structure. The patient does not have a (life)body; rather, the patient is a singular psychobiological organization, a 'new way of being an animal in the world' (Grene 1968).

The stumbling block of the psychophysiological literature and the medical countermovements and subspecialties arising out of it is the failure to make the infrastructural argument: the failure to explain how the principles of biology and the psychology can intercommunicate. It is this infrastructural argument (tiers 1 and 2) that provides the universal covering laws that rationalize the experimental findings (tier 3). Installation of a successor model, thus a biopsychosociomedical or, for short, 'infomedical' model (Foss 1988), requires that both the experimental and the infrastructural arguments be made coordinately. Figure 4, parallel to figure 1, sketches the components for such a twofold argument.

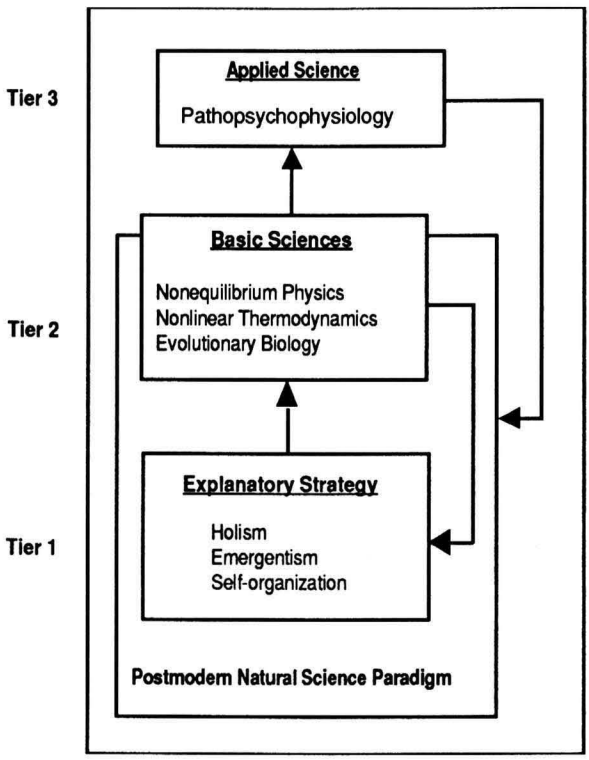

Figure 4. Components of a scientific model for an applied science (an infomedical application)

Now we can redefine the patient consistently with the findings of the psychophysiological literature. Note that from a model-evaluation perspective the task is to specify what kind of patient concept the experimental findings mandate and model this concept. This contrast with projecting onto the patient a concept of the mind that meets one's humanistic preconceptions. I have argued that the findings specify a patient who, by refocussing his or her consciousness, can actively participate in the therapeutic (or pathogenetic) process. At a minimum, this implies a biosemiotically closed, self-referential, information-processing system with multiple programs (psychosocial and biophysical among them), whose interacting messages, over some of which it can exercise limited, informed control, determine system state, thus health and disease.

Yet this reading of figure 2 and of Wolf's accompanying narrative is unlikely to emerge when viewed through the prism of sciences proper the pathophysiology for which the germ and gene theories of disease define the appropriate puzzle form. There focus is directed to the linear pathways traced by the physical messengers, independently of the *program-processed messages* that piggyback those messengers.

These messages form the object domain of such cybernetic disciplines as cellular automata theory, biosemiotics, and information theory, disciplines normally decoupled from those that make up the core medical curriculum. Essential to the keystone science of the successor model of pathopsychophysiology, these messages ground the model's interactive germ-gene *and* meme theory of disease. The meme is a psychosocial unit of information, a message-processing program. Emerging with culture, *res polis*, the meme is a developmental successor to the gene. It reproduces itself by passing from perception to perception – 'This glass is half-empty' – or among individuals in a society, from cranium to cranium – 'Put salt on the food' – much as a virus reproduces itself by passing from cell to cell.

Psychoneuroimmunologists ask the question: What are the biological links that connect psychological factors and the neuroimmune processes leading to disease? They fail to realize that were there an answer to their question the research field in which they conduct the investigation would collapse: psychoneuroimmunology would be assimilated into neuroimmunology. So they persist in what from the outside appears to be an updated version of Descartes' search for the pineal gland.

In this respect we might characterize the psychoneuroimmunologist's dilemma as part of the 'black four of hearts' syndrome described by Kuhn: we see what our premisses enable us to see, what 'the conceptual categories prepared by prior experience' permits. When people were shown cards with the suits in the 'wrong' color: 'the anomalous cards were almost always identified without apparent hesitation or puzzlement, as normal. The black four of hearts might, for example, be identified as the four of either spades or hearts. Without any awareness of trouble, it was immediately fitted to

one of the conceptual categories prepared by prior experience.' (Kuhn 1970, 63)

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