Integration of the Pathogenic Exposure Paradigm and the Hierarchical Immune System Framework

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***Abstract*-A hierarchical framework of the acquired immune system provides the context for previously proposed adaptive models and inspired algorithms of the immune systems at different scales. A pathogenic exposure paradigm provides a flat stimulus-response situated environment for such systems, although lacks the depth of scale-constrained information processing. This work considers the integration of these two frameworks from the perspective of flat and hierarchical frameworks, and proposes integration at four different levels of complexity. The resultant hierarchical integrated model is demonstrated as providing a powerful conceptual tool in both providing a context for proposed adaptive models and algorithms, and in providing a number of different intuitive adoption methodologies for implementing and applying such algorithms.**

Keywords-Acquired Immune System, Pathogenic Exposures, Artificial Immune System, Algorithm, Framework

I. PERSPECTIVES

The traditional perspective of clonal selection algorithms in the field of artificial immune systems is that of cell-pathogen interactions (clonal selection algorithms), and cell-cell interactions (network theory algorithms) [8]. The bulk of work, consisting of the proposal of acquired immune inspired adaptive models and resultant algorithms (for example see [6]) has considered the clonal selection algorithm from three different scales of the acquired immune system. This perspective was clarified in a recent work proposing a hierarchical acquired immune system framework [4]. Also proposed in that work was the potential for the pathogenic exposure paradigm (see [3]) to be rephrased in a similar hierarchical arrangement. Further, it was suggested that the two hierarchical frameworks might be integrated. This work explores the possibility of considering both frameworks (immune system and pathogen) from two different perspectives, and considerations of integration.

The first perspective is the hierarchical perspective, that although is now natural for the acquired immune system (cells, tissue, hosts), is vague for the pathogenic framework. The perspective is referred to as the hierarchical perspective because there is a one-to-many relationship between the levels with regard to the principle components of the level. Responsibility between the levels may be delegated, such that levels below the present level are concerned with a reduction of the concerns of the present level, and the levels above the present level are concerned with aggregations of the concerns of the present level.

***Hierarchical Perspective**: A perspective in which there is a one-to-many relationship between the principle components of given levels, and responsibility is delegated between levels such that levels below reduce present-level concerns, and levels above aggregate present-level concerns*

The second perspective is the flat perspective reminiscent of the traditional clonal selection algorithms, and embodied in the present 'pathogenic exposure' paradigm. From this perspective concerns are defined by the level of abstraction at the specified level of abstraction. The focus is not on the present concerns as a level in a hierarchy, but rather as the present concerns as standalone (isolated or semi-isolated from a hierarchy). One may consider the concerns of a hierarchy compressed to a single level of interest, and constrained by the limitations of that level of interest. The 'pathogenic exposure' paradigm is a good example of this perspective because the scales of the acquired immune system are compressed into a generic 'system' that was stimulated by pathogen. Further, the properties of pathogen are also compressed into a generic 'pathogen' stimulus to which the generic 'system' was expected to generate a response.

***Flat Perspective**: A perspective where concerns are compressed to a specific level of detail, and the compressed capabilities are constrained by that level of detail. It is a holistic perspective, where principle components may draw on capabilities from potentially a wide array of levels of detail.*

II. IMMUNE SYSTEM FRAMEWORK

The acquired immune system framework, originating in [2], and more formally as a framework in [4] proposes acquired immune system based information processing at the scales of cells-in-tissue, tissue-in-host, and hosts-in-population. The units of adaptation at the level of information processing provide the taxonomy for the hierarchy, and the collective at each level becomes the principle component for information processing at the next level up in the hierarchy. Alternatively, the principle component (unit of adaptation) at each scale

may be reduced which become the units of adaptation at the level down in the hierarchy. Thus, the framework meets the one-to-many and reduction-abstraction properties of the hierarchical perspective. A related perspective that has bearing on the framework and its relation to the pathogenic exposure paradigm is the interactions of the principle components. This perspective was highlighted in the previous work uniting the adaptive models and inspired algorithms within the context of the hierarchical framework [6].

***Interaction Perspective**: The consideration of the interactions of the principle components in a system. The perspective firstly considers interaction with those concerns exogenous of the system (pathogen), and secondly with those interaction with those concerns endogenous of the system (each other)*

The interaction perspective provides an additional way to organise the algorithms discussed in the previous work, both in the context of the hierarchical framework, and in the context of their interactions. The following table divides the algorithms of each tier of the framework into algorithms that are primarily concerned with interaction with pathogen (the minimal algorithms), broader phrasing of the minimal algorithms (the elaborated algorithms), and finally with extensions of the broader algorithms to consider endogenous interactions between principle components (the interaction algorithms).

	Exogenous (minimum)	**Bridge (elaboration)**	**Endogenous (interactions)**
Cellular	Cell-pathogen	Principle elaboration	Network, Mediated, Spatial
Tissue	Tissue-pathogen (?)	Tissue architecture	Recirculation, Homing, Inflammation
Host	Host-pathogen	Generational (?)	Transmission, Sharing, Maternal, Evolution

Table 1 - Three levels of the framework and types of algorithm

The first important observation from Table 1 is that the lack of a previously defined minimal-tissue algorithm (although it was discussed in the previous work [6]), and an elaborated-host algorithm. Thus, the perspective is useful in that it divides the information processing of the algorithms into two distinct groups with a mediator group that provides the basis for augmentations. The elaboration group provides a bridge from the minimal algorithm that arranges the principle components and exogenous interactions (pathogen), with the augmentations of the minimal algorithm that facilitate endogenous interactions (other principle components). Another application of this perspective is that it highlights the principle information processing constraints imposed on algorithms across the levels of the hierarchy. One may compare the minimal algorithms against each other, across the hierarchy and demonstrate these constraints.

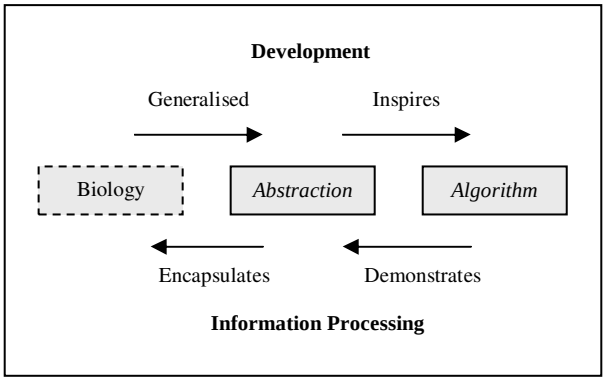

Figure 1 - Depiction of the relationship between the proposed models and algorithms (as described in [6])

A previous work that united the adaptive models with inspired algorithms in the context of this framework ([6]) highlighted the importance of verifying the information processing properties of a give algorithm against its related adaptive models (see Figure 1). The important verification highlighted by the interaction perspective is that between levels of the framework, specifically within the context of the same scale of interactions. For example, a comparison may be made between minimal algorithm (principle components interacting with pathogen), and a comparison between interaction algorithms (principle components interacting with each other).

***Testing Strategies**: Algorithms may be evaluated against the information processing principles of their related adaptive models (horizontal in the same tier) as well as algorithms on other tiers that facilitate the same complexity of interaction (vertical across tiers)*

The hierarchical framework provides the context in which to phrase the intra-level algorithm comparisons, and inter-level algorithm comparisons. Thus, highlighting its role as both a conceptual tool to relating otherwise disparate information processing models, and as a evaluation framework, grouping algorithms based on scale and complexity of interactions. It is useful to turn now to the flat perspective and to consider the immune system models and algorithms in its context.

***Standalone Systems**: A perspective of the proposed acquired immune system adaptive models and algorithms as isolated systems, the principle components of which interacting with the environment and with each other.*

The flat perspective is natural for the cellular perspective as it is employed in the field of artificial immune systems, that does not (traditionally) consider the information processing properties above this scale. At the cellular level, cells interact with each other and with pathogen. At the tissue level, tissues interact with each other and with pathogen. The important distinction here is that there is no mention of cells, whereas the hierarchical model presumes that cells and clonal selection based cellular processes provide the foundation of information processing within tissues. At the host level, hosts interact with each other and with pathogen. In the definition of the host-based algorithms, host-interaction mechanism strongly suggested the manipulation and transmission of cells. This

presumption may imply the manipulation and transmission of tissues within hosts, before the manipulation and transmission of the cells within the tissues. Again, as in the case of the tissue level, the distinction between the flat and the hierarchical perspectives is the presumption (or lack there of) of the intrinsic information process and substrate of the algorithms.

***Differences in Perspective**: The hierarchical perspective presumes the intrinsic information processing properties of a given layer are managed by the lower below, where as the flat perspective is not constrained by this assumption*

In considering the models and algorithms of the hierarchical framework from a flat perspective (beyond the scope of the framework), both clarifies the information processing assumptions of the models and algorithms in the framework, and abstracts the models and algorithms beyond the information processing constraints of the framework. The best way to illustrate this second point is to provide examples at both the tissue and host levels.

In the tissue-level algorithms, a 'tissue' is the principle component of adaptation housed within a host organism (collective). Tissues are discretised into a collection of semi-connected compartments that perform semi-isolated information processing. Tissues collect information about the environment through exposure to pathogen, and impart information between each other constrained by a defined network topology. Thus, the recirculation algorithm, the homing algorithm, and the inflammation algorithms maybe abstracted to general principles. For example: the directed communication of acquired information, the selecting communication of information, and the request for information between tissues. The tissue architecture defines the information processing constraints of different tissue types, which too, may be reduced to general information processing principles (already described in previous work [5], for example preparation, maturation, and application/sensor tissue types).

In host-level algorithms, a 'host' is the principle component of adaptation housed within a population (collective). Populations of hosts are already discrete (like the cellular level), thus a flat hierarchy perspective is quite natural. Hosts collect and process information from the environment and communicate acquired information to each other using various mechanisms. The different host-interactions impose constraints on the ways in which information is communicated, and the nature of the information communicated. As pointed out above, because the flat perspective is natural for the host-population level of the hierarchy, it has been considered as such, causing ambiguity between the host level and the tissue level of the framework (at the minimal level, for example see [7]), due predominantly to the cell-based communication mechanisms embodied in proposed algorithms. This distinct flat-versus-hierarchical perspective highlights the need for such mechanisms to perhaps to be recast on the context of the framework (consider tissues, and then cells). Clearly, from a flat perspective, the substrate for the information is constrained neither to tissues or to the tissues which house them.

***Reconciled Perspectives**: The two perspectives may be reconciled in the algorithms perform the same general information processing. The result of this observation is that the hierarchical algorithms provide a strong artificial immune system focus, where as the flat algorithms are more general, perhaps better suited for application and comparison (perhaps beyond the field of artificial immune systems)*

The ultimate flat perspective of the acquired immune system framework is compression of all layers into a single layer, much like the compression of pathogen into a general stimulus. This compression has been tentatively proposed in a previous work [4], referred to as a subsumption architecture, and highlighted that all critical information processing properties from all three levels of the hierarchy are reduced into a single 'host' system. The subsumed system is concerned with both the simplification of embedded models, and with the integration of embedded models from the framework in a cohesive manner. The flat perspective may be concerned with both of these things and more, as it provides a more general perspective. A general acquired immune system in the context of a pathogenic framework. In effect, the algorithms at each level, when considered independent of the framework (standalone), may be considered examples of a flat system. Further, a host in the hierarchical framework may also be considered an example of a flat system.

***Flat System Framework**: A general acquired immune inspired system, that may or may not selectively subsume the models and algorithms of the hierarchical framework, and that processes information in the context of a pathogenic framework*

III. PATHOGEN FRAMEWORK

Although the acquired immune system models and algorithms are the principle-focus of the framework, pathogen have been an integral part since its inception, given that the work is clonal selection centric. The predominant perspective of pathogen/antigen (things that elicit a response) has been that of an amorphous stimulus. This flat perspective of pathogen was consolidated and presented as a 'pathogenic exposure' paradigm where systems interact with stimuli of exogenous origin and respond with an internal activation of principle components [3].

***Pathogenic Exposure Paradigm**: A stimulus-response perspective of pathogen from a systems perspective, where pathogen of one or various types expose systems one or multiple times*

The flat perspective is a useful tool for the development of immune system models at various scales of the hierarchy, as it simplifies the interactions required such that focus can be given the mechanisms of information processing within the model/algorithm. For example: at the cellular level a tissue is exposed to pathogen (cells are selected and respond), at the tissue level a host is exposed to pathogen (tissues are selected and respond). At the host level a population is exposed

to pathogen (hosts are selected and respond). The selection may be controlled by the system or by the environment in which the system is situated, whereas the response is governed by the mechanisms of the algorithm (principally clonal selection based). The external and amorphous nature of the pathogen facilitates the 'pathogenic environment' conception that represents the unknown information to be acquired by the systems (at the considered scale).

***Pathogenic Environment**: A conception based on the flat stimulus-response pathogenic exposure paradigm in which a given system (at the scale of interest) is situated. The environment represents the collective of information unknown to the system, and the piecewise manner in which it is exposed to the system*

Thus, the pathogenic exposure paradigm considers an immune system as an information acquisition system, situated in a pathogenic environment. From a systems perspective, there is disparity between the properties of pathogen exposure and the levels of the hierarchical framework – they do not match up. Thus, pathogens are amorphous in that all properties (exposure, multiple exposures, and multiple pathogens) are concerns for systems at all scales (cellular, tissue, and host). The previous work that proposed to unify the levels of the acquired immune system under a cogent hierarchal framework ([4]) provided the first steps towards a more considered perspective of pathogen. As discussed, innate in the framework is the hierarchical perspective where information processing at one level is an abstraction of the information processing at the level below, and a reduction of the information processing at the level above. This processing occurs with regard to the principle components of the algorithms, and it was proposed that such a scheme may apply the exogenous stimuli to which the systems of different scales are bound (pathogen).

***Hierarchical Pathogen**: The pathogenic information exposed to systems (models or algorithms) at a given level in the hierarchical immune system framework constrained by the level of detail*

The proposal is based on the unit of adaptation principle of the hierarchical immune system framework, where the information to which the unit (principle component) is adapting to is of a similar scale of complexity, relative to the information available in the pathogenic environment. This deduction thus presupposes that for each scale of information processing in the immune system hierarchy there is an equivalent scale pathogenic environment. The observation provided in that previous work, although insightful, is not satisfying. The proposed 'pathogenic environments' are not consistent. Thus, this section proposes a consistent hierarchical pathogenic environment framework.

A pathogen may be sub-divided into one or more antigenic determinants (epitopes), which in turn may be subdivided into the elemental structures that define antigenic determinants. A pathogen exists within an environment, although the scale of that environment may be subdivided into various sub and super environments based on the scale of system, which they may interact. Examples of sub-divided environments include a habitat in which a host is situated and an environment in which a population of hosts may inhabit. A habitat contains a number of pathogen, and an environment contains a number of habitats, this the hierarchical principle of one-to-many holds for the framework.

***Pathogen Framework**: An environment that contains a number of habitats that in turn contains a number of pathogen that consists of a number of antigenic determinants*

This simple hierarchical conceptualisation of pathogen fits neatly onto the immune system hierarchical framework (as will be demonstrated in the next section), and facilitates pathogenic behaviour (models and algorithms) not easily facilitated by the 'pathogenic exposure' paradigm. For example, one may consider the dynamics of pathogen within a population of principle components (units of adaptation) of the systems of the hierarchical framework. These include: (1) inter-tissue pathogen dynamics (pathogen interactions between the cells within a tissue), (2) inter-host pathogen dynamics (pathogen interactions between tissues within a host), and (3) inter-population pathogen dynamics (already proposed as a pathogen transmission algorithm [7]).

IV. FRAMEWORK INTEGRATION

This work has proposed two perspectives on the previously proposed immune system and pathogen frameworks. The first perspective, the flat perspective is the natural perspective, pervasive in the field of artificial immune systems [8]. From this perspective, abstract notions of pathogen conjure abstract notions of acquired immune systems that respond with internal processes. The pathogen may also be considered an environment of unknown information exposed to a model of the immune system.

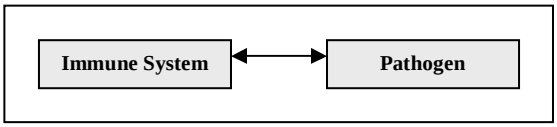

Figure 2 - Depiction of a simple flat-perspective of the relationship between abstract notions of the immune system and pathogen

In the search for other principles of information processing in the acquired immune system (such as distributed principles), a discretised three-tier framework was proposed, in which a hierarchical (one-to-many) relationship is present between the layer of the framework. Although the framework facilitates the identification of more intricate information processing principles (adaptive models) and the proposal of inspired algorithms, the information processing occurs within a simple holistic pathogenic stimulus-response environment. This integration was initially proposed in the elaboration of the flat pathogenic exposure paradigm in the context of the three-tier immune system framework.

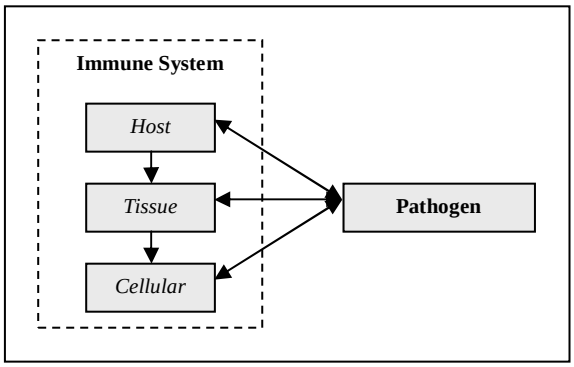

Figure 3 - Depiction of a the hierarchical immune system framework in the context of a flat pathogenic environment

Building upon the previous conceptualisation, this work proposed a simple environment based hierarchical pathogenic framework, where the complexity of the information exposed to the system is of the same relative scale as the systems information processing capability. Given the hierarchical pathogenic framework, the two frameworks may be integrated on the same hierarchical basis. Such that (1) a tissue is concerned with a pathogen (collection of cells concerned with collection of antigenic determinants), (2) a host is concerned with a habitat (collection of tissues concerned with a collection of pathogen), and (3) a population is concerned with a environment (collection of hosts concerned with a collection of habitats).

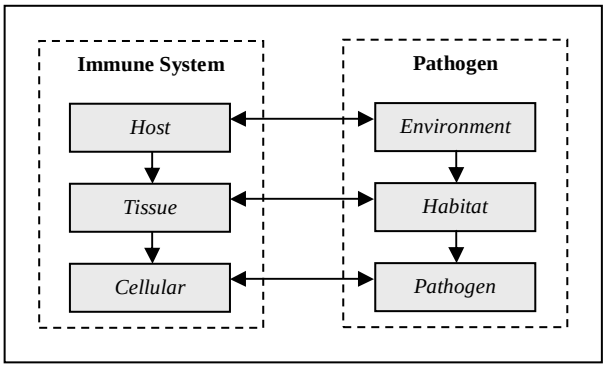

Figure 4 - Depiction of the hierarchical immune system framework in the context of a hierarchical pathogenic framework

The development of pathogen into a hierarchical framework further suggests the potential for the development of pathogen inspired adaptive models and algorithms. In the elicitation of information processing principles, one may require the simplification of the immune system, such as was the case in the elaboration of the flat 'pathogenic exposure' framework. Thus, the final integration between the two frameworks provides symmetry to the collection of relationships, and complement to the hierarchical-flat integration (Figure 3).

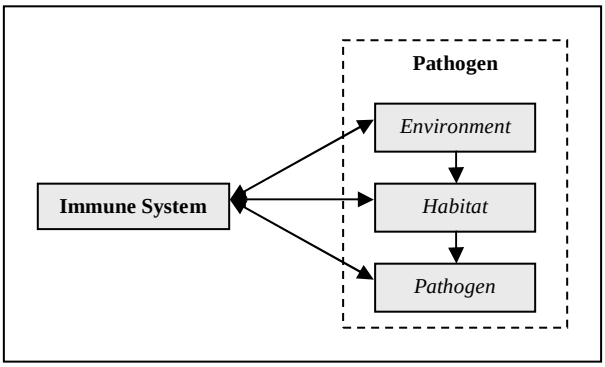

Figure 5 - Depiction of the flat immune system framework and in the context of a hierarchical pathogen framework

Thus, the four different integration schemes may be listed, highlighting their general applicability.

Immune System	Pathogenic Environment	Summary
Flat	*Flat*	*Conventional*: suitable for the base information processing concerns between the immune system and pathogen.
Hierarchical	*Flat*	*Immune System Design*: suitable for immune system modelling and design in which the details of pathogen are suppressed
Flat	*Hierarchical*	*Pathogen Environment Design*: suitable for pathogenic environment design in which the details of immune systems are suppressed
Hierarchical	*Hierarchical*	*Complete* (*Integrated Hierarchical Framework*): suitable for a detailed investigation at a selected scale, and suitable for the high-level (integrated framework) investigation

Table 2 - Summary of the four different integrations of the flat and hierarchical immune system and pathogen frameworks

A. *Integrated Hierarchical Framework*

The integrated immune system and pathogenic hierarchical framework represent the pinnacle of both streams of work. The depiction in Figure 4 may be extended to highlight the one-to-many relationships in each framework and between frameworks, and the entities and environments beyond the scope of the framework such as cells, receptors, sub-structures, species, and multiple environments. This section discusses some of the observations from the integrated frameworks.

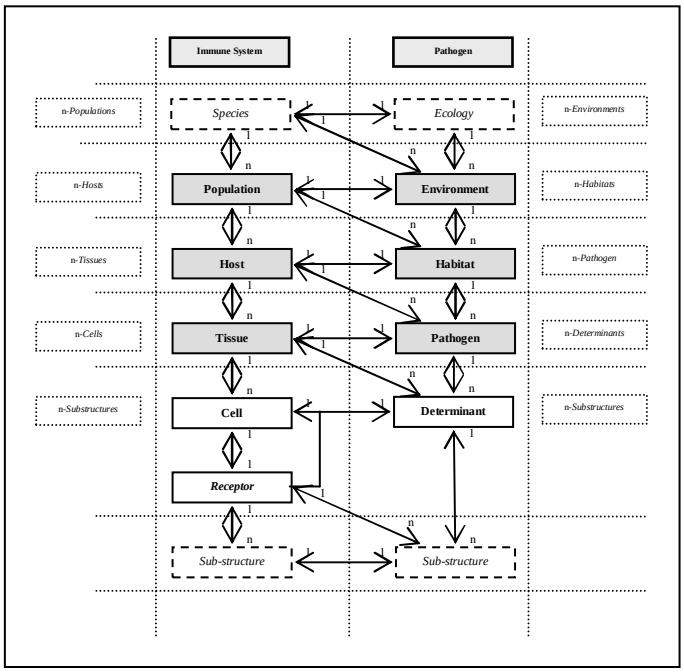

Figure 6 - Depiction of the integrated hierarchical immune system and pathogen frameworks

The depiction (see Figure 6) uses the collective to refer to each level in the hierarchy. A tissue of cells/receptors interacts (is exposed and responds to) a pathogen of antigenic determinants. This is not imply that the scale of concerns of a population of cells is a single pathogen, but rather that a pathogen is the name of a collection of antigenic determinants (pathogen was selected because a given pathogen itself has many antigenic determinants). For a population of cells to detect and respond to a pathogen it need only detect a one of many determinants on a (actual) pathogen. The integration highlights the scope of concerns of a population of cells (determinants), using tools such as feature detection (selecting for the right determinants), and generalisation (selecting for shared determinants).

***Cellular Level**: A collection of cells (tissue) interacting with a collection of antigenic determinants (pathogen).*

A pathogen (collection of determinants) is one component of a habitat, just as a tissue (collection of cells) is a component of host. Thus, the next level a collection of tissues interacts with a collection of pathogen. The transmission in the hierarchy represents a linear increase in scale; the movement of one population of principle components operating under the principles of clonal selection, to many such populations. As in the previous level, the conventional (stimulus-response) notion of pathogen must be abandoned. A habitat represents a collection of pathogen, which in turn represents a collection of antigenic determinants, thus in effect a habitat represents a collection of collections of input patterns. Habitat also has useful connotations of situatedness in that it suggests the collective of tissues, the host, is located within a personal environment.

***Tissue Level**: A collection of tissues (host) interacting with a collection of pathogen (habitat)*

Further exploiting the connotations of a situated system, a habitat provides a single component in an environment that houses a population of hosts. Each host has their own habitat, although the aggregation of personal habitats is an environment (just as equally referred to as a habitat and a habitat as a microhabitat, which is more plausible if using ecology nomenclature).

***Host Level**: A collection of hosts (population) interacting with a collection of habitats (environment)*

Thus, the integration of the elaborated hierarchical frameworks provides both (1) a suitable scale of information processing with endogenous principle components and exogenous stimulus, and (2) a context for the information processing with clear paths of reduction and abstraction. The coupling between the two hierarchies is tightly coupled given that the systems require external information at an appropriate scale.

***Integrated Hierarchical Framework**: The combined hierarchical acquired immune system and hierarchical pathogen frameworks into a cohesive interrelated structure where the principle components of the immune models match in scale to the principle components of the pathogen models*

As claimed in the previous work that provided the foundation for the integrated hierarchical immune system framework ([4]), the framework may be used as a methodological tool for deriving and relating acquired immune system models. Some example methodologies include a strict adoption, irregular adoption, and crosscutting concerns. The integrated framework provides an incremental improvement over the previous framework, clearly highlighting the scale of exogenous-based information. The models, algorithms, the verification, and their application may represent a strict adoption methodology of the framework. An interesting irregular adoption of the framework, highlighted by its depiction is that of 'level jumping'.

***Level Jumping**: The application of information processing principles (such as models and algorithms) from one level, although employed with the principle components of another level*

For example, the host-based algorithms of inter-populating sharing and inter-generational sharing of acquired immune importation may operate on the level of cells and antigenic determinants (the principle components of the cellular level). Another example is that the tissue level that is concerned with a host of tissues interacting with a habitat of pathogen may be reduced to cells and antigenic determinants. Again, like the host example, the effect on the algorithms is less pronounced, given the cellular basis of the inter-tissue information sharing, although is more pronounced with the pathogenic framework. Here, rather than a host being concerned with groups of determinants, it is concerned with one large group of determinants (a pathogen of determinants rather than a habitat of pathogen).

***Vertical and Horizontal Adoption**: Adoption methodologies of the integrated hierarchical framework where the base-level information processing of cells and determinants is acknowledged and or discarded respectively.*

The important point that level jumping highlights is that the hierarchical perspective accepts that cells are interacting with determinants as the base level of information processing, although the different scales rephrase such interactions, both abstracting them and constraining them in different ways. These constraints may be acknowledge and employed or discarded and ignored. For example, a vertical adoption of the framework acknowledges the base-level information process is achieved with cells and determinants, the interactions of which are constrained by different scales of their relationship. A horizontal adoption focus on the principle components and abstracted information processing of a level, levels above and below (for example tissue-processing or host-processing). A level jumping adoption acknowledges the hierarchical basis of the constraints and abstractions, and remixes them level-wise. The first two adoption methodologies are strict, and the third (level jumping) represents a strict-irregular adoption methodology. Such ridged adoption provides a good first-attempt in exploiting the integrated framework, as the constraints, abstractions, and relationships provide strong guides that need only be followed.

V. DISCUSSION

This work has provided a convincing hierarchical elaboration of the 'pathogenic exposure' paradigm into a pathogenic framework, which neatly integrates into the previously elaborated hierarchical acquired immune system framework. Importantly, the two frameworks were integrated in four different ways from the perspectives of a flat and hierarchical relationships. The more complex of these integrations (hierarchical on both sides) was shown to provide a powerful conceptual tool for phrasing the abstractions and scale-based constraints of information processing between the two frameworks.

Innate in the integration of the two frameworks is the desire to abstract and employ the information processing properties from the entire framework. That is, to devise models and inspired algorithms that embody the information processing principles common across the integrated framework. In essence, employing the proposed integrated framework, which has provided a guide for the development of level-dependant models and algorithms, as a cohesive level in and of itself for the proposal of general models and algorithms. These would be different from a hierarchical host model in that rather than being a subsumed system, models and algorithms would embody and abstract the commonality across the hierarchy. Examples of such common information processing properties include decentralised selectionist-based maturation, distributed information movement, information homeostasis, and a situated environment. Such work is strongly related to, and perhaps provides a general model for the previously proposed Immunological Inspired Distributed Learning Environment (IIDLE) [1].

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