The '*Pathogenic Exposure*' Paradigm

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Abstract-**The acquired immune system provides inspiration for learning models and algorithms. In conceptualizing such models and algorithms, it is intuitive for patterns of thought to focus on the system itself (such as the shape space and affinity landscape paradigms). An alternative paradigm is to consider the immune system as situated in an environment which may dictate** *what to learn* **and** *when to learn it*. **This work presents a pathogenic-exposure centric paradigm of acquired immunity (clonal selection in particular) and considers how this conceptualization may influence the concerns of designing and investigating acquired immune inspired adaptive models and algorithms.**

Keywords-Antigen, Pathogen, Immune System, Artificial Immune System, Problem Domain, Environment, Antigenic, Pathogenic, Clonal Selection Theory, Paradigm

I. INTRODUCTION

A series of clonal selection inspired algorithms has been defined [2,3,6] and the base clonal selection models have been preliminarily realised as clonal selection algorithms [5]. This work has focused on the clonal selection mechanisms and proceeded with little regard to the causal trigger for the resulting learning processes. Further, a 'colour space' domain [1], and experimental scenarios [4] have been proposed to evaluate the adaptive models without a clear defining model of pathogens or a pathogenic environment.

The clonal selection theory and the models and algorithms inspired by it are meaningless without a discussion of molecules that trigger **anti**body **gen**eration (*antigen*). Pathogens are antigens (agents, typically living organisms) that cause disease in a host, such as viruses and bacteria. This work conceptualises pathogens as external triggers stimulating an internal activation and response of an acquired immune system. This conceptualization is called a '*pathogenic exposure*'. It provides a much-needed perspective on the learning requirements and concerns with regard to realising clonal acquired immunity and selection algorithms.

Section II introduces the 'pathogenic exposure' conceptualization, starting from simple ideas of stimulation-response in a single exposure and raising the complexity to multiple exposures and multiple pathogen types. Section III discusses constraints imposed on the configuration of exposure environments and adaptive model types, and the differences in the concerns of models from the perspective of an exposure environment, from the concerns of the environment from the perspective of the various adaptive model types.

II. CONCEPTUALIZATION

Two previous attempts have been made at elucidating this conceptualisation. In [6] a series of pathogen types were described (static, diverse, evolvable, and transmissible), as well as an environment. The PM1 (pathogenic environment) described pathogen virulence and a 'pathogenic strategy' in terms of the space and time exposure properties of a pathogen on a population of immune systems. In [5], a pathogenic environment design principle was proposed (DP1) describing the general behaviour that an immune system is exposed to the majority of pathogen types early requiring equally early and rapid learning by a immune system. This principle was elaborated to describe pathogen novelty (types), frequency of exposure, and amplitude (magnitude) of exposure. This section further elaborates on this design principle, conceptualising a pathogenic environment from a single exposure, to multiple exposures and multiple pathogen types. It is expected that the various levels of detail for pathogen-immune system interaction provide various interaction-based models that may be useful in designing, realizing, and interpreting clonal selection algorithms in the context of problem domains.

A. *Single Exposure Event*

A system is exposed to pathogen, and this event is referred to as a 'pathogenic exposure'. Pathogen has an origin that is external to the immune system. It arrives to the host after which time it must be identified as a pathogen. If correctly identified, the '*external stimulation*' results in an '*internal activation*' of some lymphocytes in the immune systems repertoire.
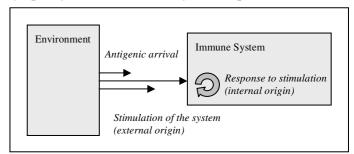

Figure 1 - Depiction of external stimulation resulting in internal activation

The response involves raising a clone of lymphocytes to address the stimulation with regard to the magnitude

and specificity of the response, which is proportional to the pathogenic stimulation. Without the arrival of a pathogen, the acquired immune system cannot respond, thus the exposure event is atomic.

> **Pathogenic Exposure**: An exposure is an event that involves the arrival of pathogen (antigen of external origin) to an immune system. The arriving pathogens are identified by the system stimulating a proportionate immune response. An exposure is an atomic event in that it either occurs or does not occur, without an intermediate.

Figure 2 - Definition of a pathogenic exposure to an immune system

The acquired immune system (via a clonal selection and expansion process) is concerned with raising a good response quickly. The principle of a pathogen is that it may cause harm to the host in the form of tissue damage. The immune system must raise a clone that can address the magnitude of the pathogen exposure, thus the goodness of the response (the specificity) should be proportional to the virulence of the pathogen, and the response size should be proportional to the number of arriving pathogen molecules.

> **Exposure Virulence**: The tissue-damage causing properties of a pathogen are referred to as its virulence. Exposure virulence is a property of the pathogen thus is not likely to change for a given immune system unless the pathogen itself changes. The virulence may define the penalty for not identifying a pathogen, as well as the desired amount of refinement-based learning (resultant clonal specificity) desired or required in a clonal selection and expansion response.

Figure 3 - Definition of pathogen virulence

The former concern (virulence-specificity) is difficult to conceptualise as it defines the amount of refinement-based learning required of the system. The latter concern (number of molecules-responding clone size) may be conceptualised as the amplitude of the pathogen exposure.

> **Exposure Amplitude**: The magnitude of a pathogenic exposure may be referred to as its amplitude. The amplitude of as exposure is an abstraction of the number of pathogenic molecules that arrive to the system from an external origin. The number of simultaneous molecules that arrive to the system defines the number of simultaneous clonal selection responses (amount of work) the system may have to support.

Figure 4 - Definition of the pathogenic amplitude of an exposure event

The number of pathogenic molecules that arrive in an exposure may be more than the number of lymphocytes in the repertoire[1]. Thus, the selection events may be more intense and some may not occur until after the initial cells have proliferated (or additional cells have been recruited). This scenario has two implications. (1) Pathogen may have staying power if it arrives in unexpectedly large quantities. This would result in the pathogen arrival being considered a resources which must be degraded (neutralized over time). (2) The increased selective pressure from the size mismatch may result in the rapid synthesis of a response large enough to address the exposure. This suggests dynamic and variable response size capabilities inherent in the clonal selection and expansion response.

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[1] There exists a natural mismatch between the specificity of the response and the virulence of the pathogen exposure. This mismatch is addressed through the learning (immunity acquisition) achieved via clonal selection, expansion, and affinity maturation via hypermutation.

> **Exposure Amplitude Mismatch**: The amplitude of arriving pathogen to the system may be more than the system is capable of handling at the time of exposure. The system possesses the capability (inherent in the clonal selection theory) of expanding a clone to (and beyond) the size of that required to address the amplitude of a pathogen exposure.

Figure 5 – Definition of the potential mismatch between immune system repertoire size and arriving pathogen amplitude

One may consider the effects of varied exposure virulence and amplitude on an immune system. Both properties affect the amount of work required in an immune response, although in different dimensions. Virulence may determine the desired specificity of a response such that high damage-causing pathogens are neutralised effectively and low damage-causing pathogens are neutralised with less specificity. The amplitude of the exposure defines the number of cells the size of the clonal response. The response strategies to the various virulence and amplitude combinations (in Table 1) may be considered effective (perhaps optimal?) with regard to efficiency and efficacy (space and time complexity).

Exposure		Response	
Virulence	**Amplitude**	**Specificity**	**Quantity**
Low	*Low*	*Low*	*Low*
Low	*High*	*Low*	*High*
High	*Low*	*High*	*Low*
High	*High*	*High*	*High*

Table 1 - Summary of the intuitive effect of exposure on immune response

The exposure amplitude mismatch suggested the continued presence of a pathogen in the event that repertoire was not large enough to address the exposure immediately. An extension to this idea is that a persisting pathogen may also exploit local resources, proliferate itself (attempt to increase in amplitude), and mutate (change in specificity). This concept may be envisaged as a complement to the clonal selection theory (for a single exposure) and is referred to as pathogen expansion. Pathogen persistence may also occur as a result of an expansion or series of expansion events after the arrival of a pathogen to which the immune system was unable to respond to (neutralize sufficiently) in time.

> **Pathogen Expansion**: A pathogen may exploit local resources and replicate after arrival to a system. Thus, a pathogen may persist after arrival and the amplitude of the persisting pathogen population may vary in response to expansion pressures from the pathogen and response pressures from the system. Further, the properties of pathogen may vary during this expansion period such a minor variations in pathogen surface expression (microevolution within the host).

Figure 6 – Definition of pathogen expansion as competition for resources with a repertoire of lymphocytes

B. *Multiple Exposure Events*

A single exposure-response event may be abstracted to multiple pathogen exposure-response events. A principle property of a multiple exposure regime is the concept of exposure frequency. Exposure frequency facilitates conceptualising multiple exposures as a series of atomic and quasi-independent events[2].

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[2] The frequency of exposure events may not be independent given the

Exposure Frequency: The repetitiveness of the arrival of a given pathogen is defined as its frequency. Given a time interval, the frequency of a pathogenic exposure measures how often a system was exposed to the pathogen. An exposure event is atomic (it either occurs or it does not). This binary (exposure, no exposure) distribution function defines the pathogen frequency.

Figure 7 – Definition of pathogen exposure frequency

The exposure frequency may be measured as the pattern of '*exposure*' and '*no-exposure*' events in discrete time over an interval. The pattern may be defined as a probabilistic function, random, uniform, or may be a regular deterministic exposure function.
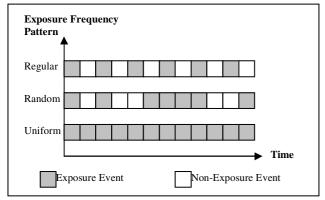

Figure 8 - Example of some different exposure frequency patterns

Given the example patterns of pathogenic exposure-frequency in Figure 8, the concept of a non-stimulation event suggests a downtime when the immune system is not stimulated to respond[3]. The activity of a system may be considered *trigger-based* in which learning and maintenance processes (such as cell aging and removal) only occur when the system is exposed to pathogen. During un-triggered periods, the system may enter a period of stasis awaiting subsequent triggers. An alternative model is that the system persists (*always on*), continuing to execute such maintenance processes in the absence of stimulation. This second system type suggests the potential for the decoupling of the repertoire maintenance and repertoire stimulation internal processes. Such a system would require an effective memory system such that acquired immunity was not lost by the turnover of lymphocytes. The lack of adequate memory for this system type in an extended period of non-stimulation may cause the repertoire to devolve to a quasi-naïve (random) state.

Exposure Downtime: A varied frequency implies that there will be time intervals without pathogenic exposure events. This inactive time is referred to as pathogenic exposure downtime. An immune system may enter a period of stasis (trigger-based system), or may continue internal repertoire maintenance operations (always on-based system). A risk for an always-on system is that without effective memory mechanisms, the repertoires of these systems may devolve to randomness (entropy).

Figure 9 - Definition of pathogenic exposure downtime

Variations in the exposure frequency control *when* the system can and must respond. Variations in the exposure amplitude control the size (scope or *how much*)

potential for an underlying causal structure for the exposure frequency (as will be discussed later)

[3] Such a non-response event may also occur for an exposure event that is not identified by the exposed system.

of the response that a system must synthesize. As has already been suggested in Table 1, variations in exposure virulence and amplitude imply variations in a systems response strategy in terms of response specificity and response quantity. A similar relationship exists with multiple exposures with the addition of exposure frequency and the systems memory of the response (see Table 2).

Exposure		Response	
Frequency	**Amplitude**	**Memory**	**Quantity**
Low	*Low*	*High*	*Low*
Low	*High*	*High*	*High*
High	*Low*	*Low*	*Low*
High	*High*	*Low*	*High*

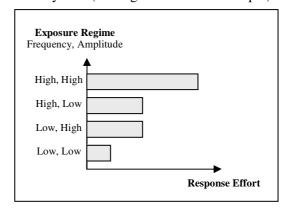Table 2 – Summary of the intuitive effect of exposure frequency on response

There is an inversely proportional relationship between immunological memory and exposure frequency such that when the exposure frequency is low, the memory must be long lived. When the exposure frequency is high, memory is short lived, and in fact may be satisfied with the quantity and specificity effects achieved through 'exposure amplitude' to 'response quantity' densities.

One may consider the effect of combinations of high and low frequency exposures with high and low amplitude pathogen arrival. From a system perspective, the frequency and amplitude of exposures may be compressed (multiplicative relationship) into the amount of work required for the interval of time. This system work is called the *response effort*. This compression of exposure frequency and amplitude may be referred to as the 'exposure regime' of a pathogen to a system through time.

Exposure Regime: The combination of a pathogens variations (or lack there of) in exposure frequency and arrival amplitude for *a given system* may be referred to as its regime. An exposure regime is defined within the context of a given immune system although the characteristics of the regime may be general for the pathogen (not specific). The exposure regime defines the amount of exposure effort a system must exert over the time interval of the defined regime.

Figure 10 - Definition of pathogenic exposure regime

Thus, the simple exposure, amplitude scenarios described in Table 2 may be redefined as exposure regimes, which elicit a measurable response effort from an immune system (see Figure 11 for an example).

The relationship between a pathogen exposure regime and an immune systems response effort is interesting. For a single pathogen exposure 'exposure virulence' defined the amount of tissue damage a pathogen may cause on a host, thus it may provide a fuzzy conception of the amount of specificity refinement (effort) required of an immune system for the exposure. An exposure regime provides a way of crisply defining pathogen virulence as a function of exposures through time. The amount of specificity refinement by the system for the pathogen (response effort) is proportional to the exposure frequency and exposure amplitude (exposure regime).

Pathogen Virulence: Unlike exposure virulence, which describes the virulence of a pathogen for a single exposure, pathogen virulence defines the virulence as a mass distribution function of exposure amplitudes through time. Pathogen virulence is defined by the exposure regime, and defines the amount of clonal selection based refinement to specificity required of an immune system (response effort).

Figure 12 - Definition of pathogen virulence as the combination of an exposure regime and resultant response effort

Pathogen virulence (and exposure regimes) may be expressed as an exposure amplitude graph against time. From this level of abstraction, one may define some exposure regimes as archetypical pathogen virulence strategies with which to subject an immune system (see Figure 13).

In addition to static pathogen virulence, it is possible for virulence to vary through time. The variance in virulence may be intra-causal such that virulence changes in response to the internal actions of the immune system such as an adversarial pathogen. The variance may be extra-causal in that the environment may be responsible for the changes (or there may be some combination of the two). Changes in pathogenic virulence are defined by changes to the exposure regime, which ultimately implies causal changes to a pathogen exposure frequency and exposure amplitude.
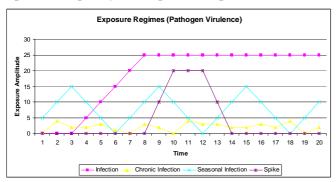

Figure 13 - Example exposure regimes demonstrating some archetypical pathogen virulence behaviours

C. *Multiple Pathogens*

The natural extension of multiple pathogen exposures

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[4] The relationships are proportional to the times scales (frequency) and volume of molecules (amplitude), although the principle of the relationship is unaffected

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is to subject an immune system to multiple concurrent exposure regimes. Each regime is expressed by a distinct pathogen type. Different pathogen types (or species) differ in their surface features such that the immune system has to acquire different immunity characteristics for each. In addition to the varied immunity characteristics, each pathogen type has its own exposure regime, thus in the context of an immune system, the regime elicits a distinct response effort.

Pathogenic Type: In an environment that contains more than one pathogen, each pathogen may be designated a type (classification, species, or variety). Individual examples of a type may vary slightly, although generally have the same characteristics (surface features). Each pathogen type has its own exposure regime.

Figure 14 - Definition of pathogen type such that instances of pathogen may be classified and discriminated

The aggregation of multiple pathogen types is an aggregation of multiple pathogen exposure regimes to an immune system, thus may collectively be referred to as the exposure or pathogenic environment. A given immune system is situated within a pathogenic environment and this is subjected to the exposure regimes of the pathogen types in that environment. In responding to one given pathogen, the repertoire may acquire a level of immunity (specificity) to another different and distinct pathogen type. This effect is called *cross-reactivity* of the immune response and may be conceptualised as reuse of acquired knowledge or generalization of acquired knowledge. This convergent effect may lead to improvements in the efficiency and efficacy of the immune response.

Pathogenic Environment: The aggregation of multiple pathogen types to which an immune system may be exposed is referred to as its environment. A given immune system is situated within its environment, thus must exist, (and thrive) with regard to the pathogen types (and their regimes) to which it is subjected.

Figure 15 - Definition of the pathogenic environment as an aggregation of pathogen types and their exposure regimes

One may consider an immune system to be exposed to the multiple different exposure regimes (pathogen virulence) shown in Figure 13. In this example, the system is exposed to all four different pathogens with varied amplitudes at the discrete time of 11. This is referred to a concurrent pathogenic exposure. Exposure concurrency requires that the repertoire is (1) large enough (with regard to the quantity of lymphocytes), and (2) diverse enough (with regard to lymphocyte specificity) to address multiple pathogen types at the same time. It is expected that the efficiency of the system will be reduced in such a situation, as resources are allocated proportional to the relative virulence of each pathogen type. This effect highlights the requirement of the system to be able to not only respond to multiple pathogen types at the same time, but to integrate the results (expanded clones and shifted specificities) of the concurrent responses.

Concurrent Pathogenic Exposure: In a pathogenic environment, that contains multiple pathogen types (each with their own exposure regime); it is possible for a system to be exposed to two or more different pathogens at the same time. This event is referred to as concurrent pathogenic exposure. The resources of the system may be partitioned relative to the amplitude and virulence of the concurrent exposures.

Figure 16 - Definition of concurrent pathogenic exposures

A graph of exposure regimes as amplitude versus time plots (such as Figure 13) is a useful mechanism for visualising different pathogen types. A spatial (geometric) pathogenic environment, such as a two-dimensional plane provides another way to reconcile the differences in pathogen virulence. Both immune systems (hosts) and pathogens may be allocated coordinates within the spatial environment (a shape space for pathogens and whole immune systems).

> **Spatial Pathogenic Environment**: In reconciling the varied pathogenic types and exposure regimes, a geometric conceptualisation may be adopted. A spatial environment allows pathogens to possess geographic properties resulting in a pathogenic topography in which an immune system may be situated. A point in the topography may have a distinct exposure pattern with regard to the pathogen types and their exposure regimes.

Figure 17 - Definition of a spatial pathogenic environment to reconcile multiple pathogen types and varied exposure regimes

The spatial relationships between pathogens and immune systems (such as distance) may provide a way to realise the differences between pathogen types and their exposure regimes. An environment may be represented (designed or otherwise) as a pathogen-virulence topography in the spatial environment. The virulence (frequency and amplitude) of a pathogen to an immune system may be inversely proportional to the distance the system is in the space to the pathogen origin. This virulence model may be considered conceptually as the static transmissibility of a pathogen within a locality. This may be further extended by introducing dynamic aspects to the transmissibility such that the virulence topography in the space may change in time.
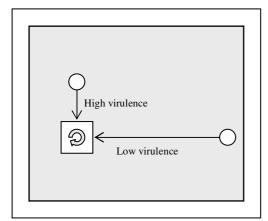

Figure 18 - Depiction of a spatial pathogenic environment with virulence defined by inverse distance

III. SYSTEM AND ENVIRONMENTAL CONSTRAINTS

The *environment* and the *system* (or systems) may be considered two interdependent and required components of which neither is meaningful in isolation. In modelling these two components, one may consider the variable (configurable) aspects of each of which may or may not be within the control of a given simulation.
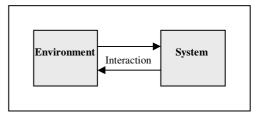

Figure 19 - Depiction of the two main components and their interaction

An intuitive example is to consider the environment (and thus all aspects of pathogen exposure) as outside of the scope of control, and all aspects of the system as inside of the scope of control. In this example the system must do all it can to cope with the pathogen exposures it is subjected to by the environment. The system must operate with finite resource, thus constraints are imposed on the control over aspects the system. This example may be extended further to consider that the evolution of pathogens is influenced by the existence and evolution of the host system and that this relationship is reciprocal (coevolution). Thus, the system has influence (implicit influence via evolution) over aspects of pathogen exposure, and the pathogen has influence (implicit influence via evolution) over aspects of the systems response.

This example may be generalised such that aspects of control are variable across both the environment and the system. Further, in modelling environment and system and their interactions, control may be exhibited over all aspects of both sides of the interaction. It is important to understand the influence for control or lack there of (constraints on control) on a system and its environment. A constraint may be considered the *a priori* fixing (setting) of a configuration parameter of a system or environment. The fixing of a configuration parameter in the environment influences the suitable of other unconstrained (controlled) parameters in the interaction, and the influence is likely to be complementary (such that fixing an aspect of the environment strongly influences the suitability of related parameters of the system and vice versa).
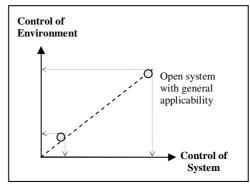

Figure 20 - Depiction of the trade-off between control of the environment and control of the system

This section considers the aspect of constraint from an environmental perspective, highlighting the model behaviours that may be suitable for the varied exposure types. The exposure types are also considered from the perspective of the three model types previously outlined in the series (single and multiple repertoire, and multiple

system).

A. *Exposure Types*

In defining the various different exposure types, a general immune system model was used to provide context. This section elaborates on the various system properties and behaviours that may be expected or required for each exposure type.

Exposure Type	System Concern
Single Exposure	Lymphocyte specificity and quantity
Multiple Exposure	Anticipatory lymphocyte specificity and quantity
Multiple Pathogens	Lymphocyte densities and specificities

Table 3 - Summary of the primary concerns of each exposure types

Single Exposure Model

In a single exposure event, an immune system is only concerned with quelling the pathogen with a response. The scope of the concerns of an immune system for a single exposure is the specificity of the lymphocytes to the pathogens and synthesizing the cells in sufficient numbers. Initial pathogen-identification (to trigger a response) may be assumed. Further, all resources of the repertoire may be allocated to the response for the exposure, as there are no future exposures.
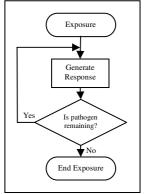

Figure 21 - Flow diagram of a single exposure

This has interesting implications at the limits. (1) The quantity of pathogen may be considered infinite, thus the processes of the response are concerned with improving specificity until improvements cease (specificity convergence). (2) The specificity of the pathogen may be considered infinite, thus the system may be concerned with improving quantity until improves cease (quantity convergence).
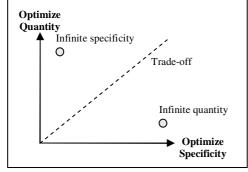

Figure 22 - Depiction of the trade-off in optimizing quantity and specificity

In the first example, the repertoire size is not important (fixed), and each cell in the repertoire represents a point in shape space. The interaction with the unlimited quantity of pathogen results in a response surface (affinity landscape) which the clonal selection process attempts to maximise. In the second example, the specificity is not important (fixed), and the cell repertoire size is varied in response to an unknown exposure size using the clonal expansion process.

Multiple Exposure Model

In a multiple exposure event, the system is primarily concerned with devising a response to each exposure and anticipating the resources needed for future exposures. This exposure model supersedes the single exposure event, and like that event, all resources of the repertoire are allocated to the specific concerns (as there are no other pathogens). The learning that the system may achieve within the context of a single exposure may be limited, as a broader exposure regime may define how often the exposures arrive to the system.
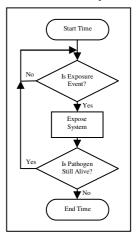

Figure 23 - Flow diagram of multiple exposures

The exposure regime may impose a quantity and specificity capability constraints for a single exposure, meaning that a finite amount of specificity learning and or quantity learning may be achieved for a single exposure event. The system must learn anticipate (1) the specificity of future exposures, and (2) the quantity of future exposures, both in the face of downtime (non-exposure events).

Multiple Pathogen Model

Multiple pathogen exposures supersede the single and multiple exposure models. Unlike the previous two models that were able to allocate all the resources of the repertoire to the exposure, multiple pathogens require a proportional allocation of resources. If the entire repertoire were allocated for each different exposure, then the system would have to re-learn in the event of re-exposures. The proportionality of the response and allocation of repertoire resources is defined by the relative pathogen virulence to other pathogens. That is the relative specificity, quantity, and frequency of other pathogen exposures.

The previous concerns of optimizing specificity, quantity, and the anticipation of these values may be reduced to the systems optimization of lymphocyte densities. The density is representative of the learned

(aggregated from experience) lymphocyte quantity and specificity in the repertoire which facilitates anticipatory responses. Each lymphocyte has an affinity response surface (affinity landscape) for each pathogen it has been (and may be) exposed to. The lymphocyte densities are acquired from the pathogen virulence which is defined as the amplitude and severity of exposures (amount of learning opportunity offered) to the system through time.

B. *Model Types*

There are three principle clonal selection model types as originally outlined in [2], and elaborated in [3,6], and they are the single repertoire, multiple repertoire, and multiple system models. This section discusses each model type in the context of the three exposure types[5].

Model Type	Environmental Concerns
Single Repertoire	Standard, context for introducing the paradigm
Multiple Repertoire	Which repertoires to expose
Multiple System	Which systems to expose

Table 4 - Summary of the environmental concerns for each model type

Single Repertoire Model

The pathogenic exposure paradigm (all exposure types) was presented in the context of a general single repertoire model. Thus, there is little to elaborate on the exposure types from this models perspective. This type of model is expected to be implemented as a stasis-type model (rather than always on). The result is that the frequency of multiple exposures to the repertoire is compressed to a uniform pattern. In the introduction of multiple pathogen types, the density of cells in the repertoire may be directly measurable and comparable to a theoretical optimum (if available). The concurrency of exposures on the repertoire is likely to require a specialised underlying data structure[6].

Multiple Repertoire Model

The multiple repertoire models introduce an additional environment concern: which repertoires of the system to expose to pathogen in an exposure event. For a single exposure event, an intuitive mapping suggests that each repertoire is exposed at the same time (uniform exposure in space and time). The trafficking processes of lymphocytes between repertoires would be concerned with improving the systems response, which would continue in with the lack of stimulation events (always on). The same uniformity of repertoire exposure may be employed for multiple exposure events, although the system is not limited to this configuration. The repertoires exposed to pathogens in an exposure event is defined as the systems repertoire exposure pattern which may be controlled by the system, the environment, or some configuration.

Repertoire Exposure Pattern: A discrete repertoire model may possess (depending on tissue-type configuration) multiple discrete points for interaction with the environment. A given exposure event may occur at all or a subset of repertoires referred to as the system repertoire exposure pattern.

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[5] This section does not consider the extended clonal selection models as they are considered extensions of the base (single repertoire) models

[6] A spatial lymphocyte repertoire structure may efficiently facilitate concurrent exposures and responses. This structure may also facilitate interesting spatial self-organization properties of cell densities if exposures patterns are also spatial and consistent.

The pattern may be defined (controlled) by the system (for example tissue type configuration), or by the environment (for example a spatial pathogenic environment).

Figure 24 - Definition of the repertoire exposure pattern

The repertoire exposure pattern is applicable for both multiple exposures of a single pathogen and multiple exposures of different pathogen types. This additional system configuration concern may be reconciled by conceptualizing a spatial pathogenic environment in which the system is situated and exposures regimes (exposures through time) and repertoire exposure patterns (single exposure through space) may be visualized (for example see Figure 25). Each individual repertoire may be considered to have its own pathogen exposure regime. This is because, although the system as a whole may have a pathogen exposure regime, different individual repertoires may be exposed for a given exposure event given the repertoire exposure pattern.
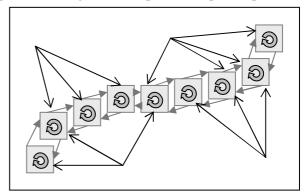

Figure 25 – Multiple repertoire model and the situated spatial properties that may affect antigenic exposure

With regard the anticipation of response, the system may be considered with attaining consistency with regard to lymphocyte quantities and specificities both within an exposed repertoire and across all repertoires. This '*consistency of response*' across the multiple repertories in the presence of (potentially varied) repertoire exposure patterns may also be extended to multiple pathogen types. In this case, consistency would refer to lymphocyte densities (relative quantities and specificities) for exposed repertoires and across all repertoires of the system.

Multiple System Model

The multiple system models supersede both single and multiple repertoire models, thus a single system within this model may have the concerns of either or both of the previously discussed model types. Like the multiple repertoire models, the multiple system models also introduce an additional similar environment concern: which systems of a model to expose to pathogen in an exposure event. In addition, like the multiple repertoire model, this may be reconciled with by conceptualising a spatial pathogenic environment in which the various systems of the model are situated.
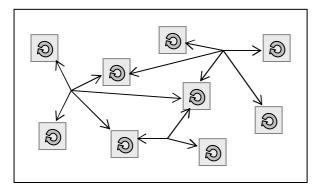
Figure 26 – Multiple system model and the situated spatial properties that affect antigenic exposure

The pathogen exposure regimes (frequency of exposure) vary between systems (system exposure pattern), thus the response specificity quantity and densities between systems vary. The immunity sharing schemes may be concerned with the *consistency of response* across the population of systems, much like the multiple repertoire models consistency of response across repertoires. Further, like the multiple repertoire models, these sharing schemes would continue to operate irrespective of the exposure regimes (always on).

IV. FUTURE WORK

This work presented a paradigm for acquired immune system models and algorithms based upon the concept of a pathogen exposure event triggering an internal learning response. The resultant exposure models provide a framework in which to interpret acquired immunity functions behaviours, and a scenario test bed in which to investigate clonal selection models. Although this work is all conceptual (and highly abstract), it provides a complement and a context for future investigations of the previously outlined series of adaptive models.

Much work remains, such as:

1) The exposures types (environments) may be integrated with the model types such that each model type is realised in the context of each (or all) of the exposure types. This provides (A) a context for model implementation (design decisions), and (B) a context for investigation (problem scenarios for experimental evaluation).

2) The paradigms of shape space and affinity landscape are intuitive and useful for a single pathogen and repertoire (single exposure), although these spatial conceptualizations are less meaningful with the introduction of multiple exposures, multiple pathogens and multiple exposure points. The spatial pathogenic environment provides a conceptualisation for exposures, although additional and more meaningful conceptualizations are required for things such as lymphocyte densities, aggregate affinity landscapes, and exposure amplitudes and regimes through space and time.

3) There may be commonality in the principles behind the concerns involved with the various exposure types for all three adaptive model types. As such, it may be possible to devise a hierarchal and spatial (cell-repertoire-system) structure such that all three of the adaptive models types may be realised and all three of the exposure types facilitated. Some spatial aspects have already been realised in the graph principles that underlie the multiple repertoire models with recirculation, and the multiple system models with immunity sharing. These would be extended to the intra-repertoire (lymphocyte) level and elaborated at all levels. Such work provides an example of (1) where the concerns of the exposure paradigm influence the design of models inspired by acquired immunity properties.

4) It is interesting to consider that general problem domains (such as optimization, classification, and novelty detection) may be interpreted as sets of constraints on environment types and model types. A investigation mapping these domains, and perhaps specific instances onto the exposure types and model types will reveal a lot about the applicability of combinations of these environments and systems.

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