Realizing Elementary Discrete Repertoire Clonal Selection Algorithms

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***Abstract*-The natural progression from a clonal selection algorithm, is to employ that algorithm in a loose architectural model of the acquired immune system. A series of multiple discrete repertoire models were previously proposed to do just that. These models are briefly reviewed in this work, and elaborated to a multiple repertoire system. This system is defined in the context of a series of principle effects, design principles and behavioural expectations. It is demonstrated that the path to realizing this broader system is to employ a bottom-up approach using a number of low-level algorithms. This work completes with a summary of a number of experimental investigations and studies that provide a framework for further extensions of this work.**

Keywords- Adaptive Models, Migration, Discrete Repertoire Models, , Lymphocyte Recirculation, Homing, Trafficking, Recruitment, Algorithms

I. INTRODUCTION

A series of discrete repertoire models was originally proposed in [1] and later elaborated [4] based on an understanding of lymphocyte recirculation and physiology presented in [3]. A specialised problem domain called 'colour space' was contrived for investigating adaptive systems and presented in [2], and specific immune-inspired scenarios where proposed in [5]. Along with the specific scenarios, a summary of the expected behaviour of the discrete repertoire models was provided, preliminarily suggesting some information dissemination concerns. To complement the series of clonal selection inspired adaptive models, a pathogen exposure paradigm was presented in [6] that proposed three different exposure scenarios. Also included in that work was an a general expectation as to how the discrete repertoire models may generally behave in each scenario.

With these previous works in mind, and in particular, the two cited examples of system expectations, this work unites the series of discrete repertoire models with the pathogen exposure paradigm and realizes the models as a discrete repertoire clonal selection algorithms. This work is inspired by the approach taken in [7] in realizing single-repertoire clonal selection system of algorithms. Given that that previously was completed before the exposure paradigm was proposed, this work will also seek to highlight concerns of the multiple repertoire models in the face of the exposure paradigm that may also be concerns for single repertoire models.

Section II summarises the series of discrete repertoire clonal selection models and related architectural concerns. Section III summarises the general concerns of the models in the face of the pathogen exposure paradigm, and focuses on the spatial and temporal aspects of clonal memory. Section IV summarises the principles effects of a multiple repertoire model, highlighting spatial self-organization and consistency of response as perhaps the guiding principles of such a model. Section V highlights algorithm design principles, and system behavioural expectations that may provide a starting point in the implementation, configuration, and ultimate investigation of the realized algorithm. Section VI proposes a series of algorithms to assist in the realizing of a discrete repertoire system. Section VII proposes a series of general experimental concerns for investigating the behaviours and interrelationships between algorithms and broader system behaviours. Finally, section VIII summarises some interesting work going forward with the realized algorithms.

II. REVIEW OF DISCRETE REPERTOIRE MODELS

Two discrete repertoire models were originally proposed in [1], and later elaborated [4] into a series of architectural components, cellular components, movement types, and models. This section briefly summarises the core principles of the components and models in this series.

Architectural Components (Tissue Types)

The architectural components provide the infrastructure of the model. The focus of these components is the graph-structure of lymphocyte repertoires (nodes) and the circulatory system (edges), defining connectivity between the nodes. This section also describes tissues types, which may house repertoires and germinal centres, which facilitate the clonal expansion process.

AC1 – Discretised Repertoire: A network model of interconnected discrete lymphocyte repertoires, where each repertoire acts like a single clonal selection system. Movement of cells between repertoires is facilitated by the connectivity of an artificial circulatory system between tissues.

AC2 – Tissue Nodes: Generic tissues, which may house a repertoire of lymphocytes and antigen-lymphocyte interactions.

AC3 – Primary Lymphoid Tissue: A node type inspired by primary

lymphoid tissues that are responsible for the preparation and release of naïve (antigen independent) lymphocytes. This node types does not facilitate the interaction of cells with antigen, and the traffic from this node is predominantly outbound.

AC4 – Secondary Lymphoid Tissue: A node type inspired by secondary lymphoid tissue that supports the presentation of antigens to lymphocytes and the resultant interaction. The traffic is both in-bound and out-bound lymphocytes as well as inbound antigens.

AC5 – Tertiary Lymphoid Tissue: A node type inspired by non-lymphoid tissue that that supports the penetration of antigens into the system from an external source which are filtered to secondary lymphoid tissues. The tissue supports small amounts of lymphocytes, sentinel cells, and potentially inflammation effects.

AC6 – Germinal Centre: An effect that occurs within secondary lymphoid tissues where antigen and cells interact and go through a process of expansion, mutation, and selection (clonal selection theory).

AC7 – Circulatory System: The connectivity between nodes in the tissue model that provides transport for cells and potentially for antigen. Connectivity between tissues may have regeneration properties in the event of damage.

Figure 1 - Summary of architectural components

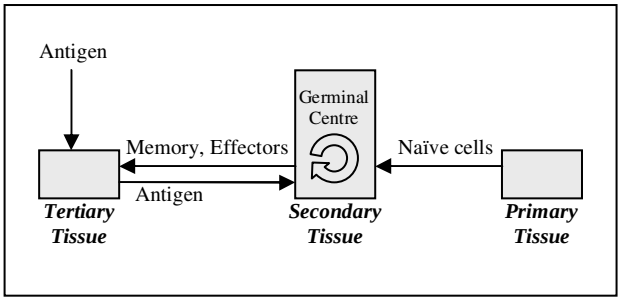

Figure 2 - Depiction of the various tissue types in the network (graph) based discrete repertoire model

Cell Components

Lymphocytes cells are the selection, learning, and knowledge substrate of the model. Pathogens also provide information packets of external origin that trigger a response in the substrate. This section describes the generic cellular components of the model.

CC1 – Antigen: Trigger a response from the cells of the system, likely entering in the tertiary tissues, and presented to lymphocytes for interaction in the secondary tissues. Their exposure to the system is a necessary aspect of the systems immunity acquisition role.

CC2 – Lymphocyte Cell: A lymphocyte cell represents a generic information packet in the system that abstracts the various specific cell types. The information in the cell is immutable (cannot change after its creation), and lymphocytes may interact with antigen in a clonal-selection fashion. The specific cell types define the general functional behaviours of the lymphocyte.

CC3 – Naïve Cell: Create in an antigen-independent environment and posses the capability for interacting with antigen. The cells are likely created in the primary lymphoid tissue and recirculate in an effort to maximise the likelihood of interacting with antigen.

CC4 – Effector Cell: Effector cells are an abstraction of both plasma cells and the antibodies they produce. They are intended to represent a defensive response within the system at the site of antigen-cell interaction. Effector cells cannot directly interact with antigen. Effector may migrate to mitigate an antigen that may have infiltrated the entire system.

CC5 – Memory Cell: Memory cells are like naïve cells in that they may interact with antigen and produce an immune response, although like effector cells, their specificity may be adjusted (for better or worse) relative to the cells progenitor. Further, memory cells are highly mobile, and have a longer lifespan than all other cell types.

Figure 3 - Summary of cellular components

Movement Operators

Cellular mobility is a critical feature of the multiple repertoire model. Without the movement of lymphocytes between nodes in the network model, the repertoires may be treated as islands. The factors that influence movement include the tissue type, the cell type, and the spatial and temporal exposures of the site to antigen. Thus, the concerns of cell mobility are multi-level, multi-factored, and fine-grained (bottom-up). Further, movement is a controlling factor in the trade-off between localizing a response, and disseminating a response.

MO1 – Migrating: A general operator that abstracts the notion of cell and antigen mobility. The various cellular types define the mobility of which they are capable.

MO2 – Stationary: The lack of cell mobility that arrests movement and maintains cellular components at a location. Examples include the presentation of antigen to cells in secondary lymphoid tissues.

MO3 – Recirculation: The movement of cells between tissue types. The recirculating pool primarily consists of memory and naïve lymphocytes as well as effectors shortly after an immune response. Cell recirculation occurs between the tissues of the system, with the majority of the time spent in secondary tissues. Recirculation does not reach primary tissues.

MO4 – Recruitment: During and after an exposure to pathogens, a tissue may become inflamed and recruit recirculating cells to address the pathogen. Thus, recirculating cells are sequestered by inflamed tissues.

MO5 – Homing: Memory cells have a tendency to return to and potentially linger at the tissues of their creation. This homing effect facilitates the spatial anticipation of pathogen.

Figure 4 - Summary of movement behaviour types

Migration is a general behaviour, lymphocytes and antigens are general cellular components. Thus, Table 1 provides a match-up of specific cell types and specific movement behaviours.

	Naive	Effector	Memory
Stationary	-	Yes	-
Recirculating	Yes	Some	Yes
Recruitment	Yes	Some	Yes
Homing	-	-	Yes

Table 1 - Summary of the behaviours expectations of each cellular component with each movement type

Discrete Repertoire Models

The discrete repertoire models make use of the architectural and cellular components and their respective behaviours and functionalities. The four models proposed in [4] are a an elaboration of the models presented in [1].

DRM1 – Base Recirculation: A networked discrete repertoire model that makes use of generic lymphocytes and generic tissue types to house the cell repertoires. All tissue types perform all generic functions, and all lymphocytes are open to all cellular component movement behaviours.

DRM2 – Differentiated Tissue: A discrete repertoire model that makes use of generic lymphocyte types, although differentiates the tissue types into the full range of primary, secondary, and tertiary tissue types. Each tissue type provides functional differences such as the creation of lymphocytes, the acceptance of antigens and the presentation of antigens to lymphocytes.

DRM3 – Differentiated Cells: A discrete repertoire model in which generic tissues are employed, although the cell types are differentiated permitting differentiated cellular component movement behaviour. All tissue types create

naïve cells, accept antigen, and present antigen to lymphocytes.

DRM4 – Differentiated Recirculation: A combined model that makes use of both differentiated tissue types, as well as differentiated cell types. Thus the full range of tissue functionality and cell movement behaviours are available to the model.

Figure 5 - Summary of discrete repertoire models

III. EXPOSURES

The pathogenic exposure paradigm [6] provides a context in which to consider the functions and behaviours of the discrete repertoire models. The paradigm may be broken down into three exposure types, which increase in complexity: (1) single exposure, (2) multiple exposure, and (3) multiple pathogens. The primary different between this model type and a single repertoire model, is that the system has multiple points of exposure. The resultant effect is that movement is required to share information between the points of exposure. A concern raised with regard to reconciling the exposure model with multiple points of exposure was the *repertoire exposure pattern*. This pattern is the selection of repertoires, which are exposed to pathogen when an exposure event occurs on the system[1].

For example, the natural inclination may be to use a uniform repertoire exposure pattern for a single exposure (see Figure 6).

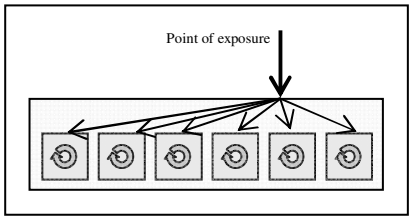

Figure 6 - Depiction of a single point of exposure distributed to all repertoires

In the case of multiple (sequential) exposures, a uniform exposure pattern may not be desirable. Pathogens may be considered to penetrate the system in different locations thus; the pathogen-to-repertoire patterns may be irregular. In the final case of multiple pathogens (with multiple exposures), not only may the exposure patterns be irregular, but also the timing of pathogen-type exposures. Further, exposure may occur concurrently to the system across different repertoires. Thus, the relationship of exposures-to-repertoires may be generalized from one-to-all, to one-to-many (and subsets), to many-to-many (and subsets).

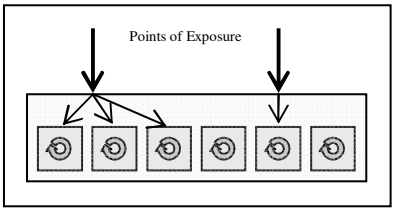

Figure 7 - Depiction of multiple points of exposure showing one-to-one and one-to-many relationships with exposures and repertoires

Given these examples and the resultant generalized possibility space of exposure-to-repertoire patterns, one may begin to phrase questions of lymphocyte movement types in the context of desirable system behaviours. Table 2 provides a summary of desirable behaviours for each exposure type and related movement types that may assist in realizing the behaviour.

	Desirable Behaviour	**Movement Types**
Single Exposure	Sharing best lymphocytes	Recirculation
Multiple Exposure	Consistency of repertoire	Homing
Multiple Pathogen	Right lymphocyte in the right repertoire at the right time	Recruitment

Table 2 – Summary of exposure types and desirable system behaviours

The match-up of desirable behaviours and movement types provided in Table 2 initially seems reasonable, although on further inspection may appear dubious. All three behaviours are desirable for all three exposure types.

Irrespective of the exposure properties, the concern of the system is *what repertoires are exposed at what times*. Thus, the concerns may be generalized to that of spatial and temporal consistency of exposure of repertoires. Temporal consistency means the system may anticipate the amount of memory required. Spatial consistency means that the system may anticipate the positioning of lymphocytes in a repertoire. A lack of consistency in either dimension removes the ability of a system to anticipate specifically, requiring general (all-repertoire, all-time) anticipation. This relationship of consistency with specific anticipation is summarized in Table 3.

	Consistency	**Behaviour**	**Mechanism**
Temporal	*High*	Specific	Memory (decay or sustain)
	Low	General	
Spatial	*High*	Specific	Location (move or remain)
	Low	General	

Table 3 - Summary of the relationship of spatial and temporal consistency with specific and general anticipation of response

It is important to highlight that the temporal memory applies system wide without spatial memory (in the face of spatial inconsistency), and spatial memory applies for all time without temporal memory (in the face of temporal inconsistency). Thus, the default case is *remember everything everywhere for all time* in the face of spatial and temporal inconsistency. The role of movement is to exploit patterns in the combination of spatial and temporal consistency of system exposures such that the response memory may be generated and shifted (adapted) in response to changes in the spatial or temporal properties of the exposure. This property may be referred to as the *spatial self-organization of lymphocytes*.

IV. PRINCIPLE SYSTEM EFFECTS

The single repertoire models [1] and algorithms [7] were primarily concerned with convergence of the repertoire and densities of cellular memory, perhaps more suited to the single exposure type than the multiple exposure and multiple pathogen exposure types. The multiple repertoire models [1,4] may be more concerned with general plasticity, and getting the best response possible for a given set of circumstances. This section discusses some principle system behaviours and how

[1] Henceforth, the system refers to all repertoires in the model.

these behaviours may relate to one another.

Temporal Memory Effect

A discussion of the systems memory of exposures was neglected for the single repertoire models, although its importance is pronounced in the context of multiple repertoires (as was made clear in the previous section). Temporal memory refers to the systems capability to retain an impression of an exposure event and recall that impression to provide an improved (compared to random) response under similar circumstances in the future.

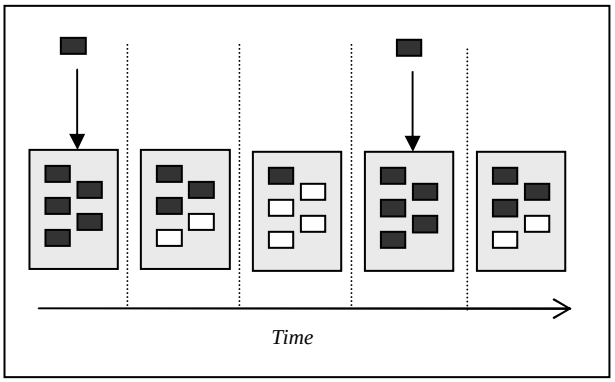

Figure 8 - Depiction of the temporal memory effect

The effect is relatively obvious for a single repertoire model where it may be facilitated by memory cells. The exploitation of the cells becomes a probabilistic function of the antigen encountering a memory in the repertoire. The multiple repertoire models further requires the dissemination of that memory across multiple repertoires. The memory represents a system-wide spatial anticipation of future exposures to the same or similar pathogen.

Short Term: A response results in a large short-term memory in the form of effector cells (short lifespan), which are useful initially at the point of exposure, and disseminated throughout the system
Long Term: A response results in a small long-term memory in the form of memory cells (long lifespan), which also disseminate throughout the system
Memory Size: The larger the pathogen dose, the larger the short-term and long-term memories
Memory Stability: With the increases in the frequency of exposures (over the systems lifetime), the larger and more stable the long-term memory. The memory size is expected to reach a point of stability where pathogen-to-memory cell match is practically assured

Figure 9 - Summary of principles of the temporal memory effect

Spatial Self-Organization Effect

The spatial organization effect is an emergent property of point-wise exposure of repertoires in the face of lymphocyte recirculation. The exposure and stimulation of a repertoire results in an response to the pathogen. The exposure is spatial, thus the response is spatial. Additional effects facilitate the self-organized emergent effect.

Clonal Response (response maturation): The clonal selection principle raises a maturated response to the pathogen that results in effectors and memory cells. Some of the raised clone disseminates early, although the majority remains during the stimulation of the repertoire. This is the formation of a germinal centre and constraints are imposed on outbound lymphocytes.
Recruitment (response amplification): The repertoire tissue becomes inflamed resulting in the increased intake of recirculating lymphocytes, a response amplification effect via lymphocyte sequestration. The inbound cells may be naïve cells, effector cells, or memory cells and may or may not have improved specificity for the pathogen than the cells already in the repertoire.
Homing (preferential recirculation): Memory cells created in a specific repertoire, preferentially recirculate back to that repertoire, in an effort of spatial anticipation of the same pathogen in the same place.

Figure 10 - Summary of the principles of spatial self-organization

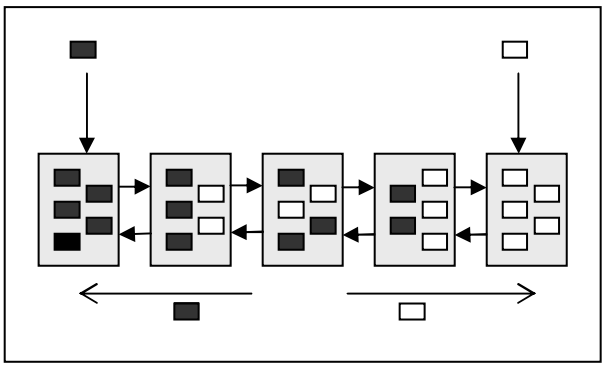

Figure 11 - Depiction of the spatial self-organization effect

The result of the general behaviours of the tissues and the cells is a specific spatial response strategy that attempts to (bottom-up) get the best from the system at the point of exposure. The spatial organization may extend through time, such that in addition to the patrolling effectors and memory cells that disseminate throughout the system, effectors may remain behind and provide a short-term memory and spatial anticipation of response.

Localization: Specific response at the time and the location of the exposure. Natural spatial-temporal response.
Surveillance: Long-term and short-term memory in recirculation anticipating the exposure system wide. The premise that the system may be exposed to the same pathogen again the future.
Sentinels: Short-term memory, stationary at the point of exposure, anticipating exposure at the same location. The premise that a location that has been exposed may be exposed again.

Figure 12 - Summary of the principles following spatial self-organization

Spatial Consistency of Response

Spatial anticipation is facilitated in the short-term by sentinel effectors and in the long-term by memory cell homing patterns. In addition to the spatial organization effect, the system mixes (perhaps disorganization) the acquired immunity across the repertoires of the system. The principles of spatially mixing response effectors and memory provide a system-wide uniform (or consistent) response to a previously encountered pathogen. This ensures that immunity learned at one exposure point of the system, may be exploited elsewhere (anywhere) in the system.

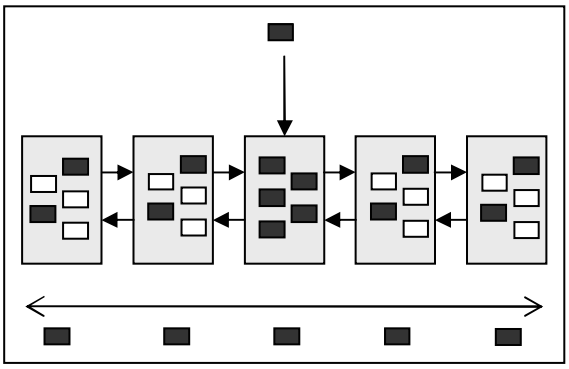

Figure 13 - Depiction of a consistent effect

This effect is achieved through the information dispersal properties of lymphocyte recirculation that ensure that a fraction of the larger lymphocyte pool is motion between the repertoires (immuno-surveillance). The effect promotes system-anticipation rather than spatial-anticipation, and provides a distributed knowledge or memory that may rapidly self-organize to varied repertoire exposure patterns.

The consistency provided is not strictly uniform, rather it is quasi-uniform, driven by the fundamentally stochastic properties of lymphocyte recirculation. From a lymphocyte perspective, movement in the face of unknown exposure patterns provides the personal goal of antigen-selection maximisation. That is, lymphocytes exist to be selected by antigen, thus the behaviours of movement between, and residence within repertories (tissues) seeks to maximise the change of this event occurring. As already described, this is already facilitated by the homing behaviour of memory lymphocytes, and the patrolling recirculation behaviour of effectors and naïve lymphocytes.

Some concerns of this behaviour are (1) the quantity of the immunity acquisition, and (2) the rate of dispersal of the memory (see Figure 14).

Acquisition Quantity: The system response may be proportional to the exposure, although the memory (both short-term and long-term) must be sufficient to provide coverage to all repertoires of the system. This memory is additive, and is expected to expand in proportion to addition exposures by the same pathogen.
Acquisition Dispersal: The memory of an exposure originates at the point of exposure, and the delay of dispersal is a function of the (1) quantity of the memory, (2) the size (number of repertoires) and connectivity of the system, and (3) the rate of recirculation. Dispersal of acquired immunity must be such that coverage (probabilistic) of all repertoires is obtained within a reasonable amount of time.

Figure 14 - Summary of the concerns with achieving consistency of response

Sharing Effect

The dispersal or mixing effect in the consistency of response facilitates the blind (recirculation) and specific (recruitment) sharing of acquired immunity between repertoires. Sharing may refer to the exploitation of specific immunity at a exposure location different from that at which it was acquired. Further, sharing may also refer to the cross-reactive effects achieved through less specific acquired immunity. This effect includes the ability of the system to generalize from varied exposure types such that new variations and combinations may also be exploited.

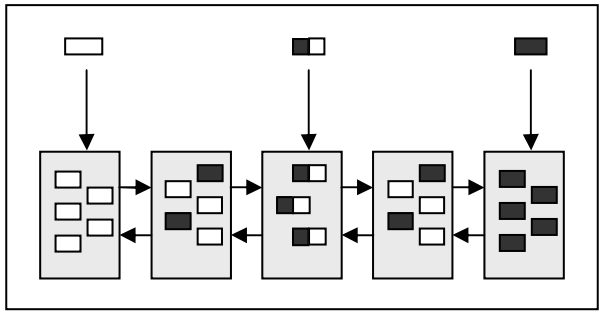

Figure 15 - Depiction of information sharing and a cross-reactive response

Integration

The integration of these features is a system that is plastic in its response capability, although is capable of generating, maintain, and self-organizing a specific response to external stimulation. This behaviour may represent a trade-off in efficiency and efficacy of response between (1) system-wide consistency of response, and (2) segregation of response into specialised spatial compartments. The system may be configured to achieve one or the other of these effects, although achieving both effectively and concurrently may represent a challenge.

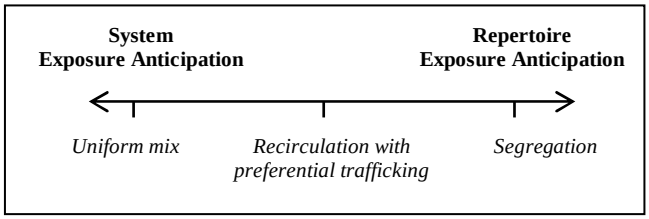

Figure 16 - Depiction of the trade-off between anticipation of exposure and spatial exposure anticipation

V. DESIGN PRINCIPLES AND EXPECTATIONS

This section summarises some algorithm design principles and algorithm behaviour expectations. The design principles may be imbued into algorithms as configuration parameterization, and the behavioural expectations may be employed as testable hypotheses during experimentation.

Design Principles (Configuration)

This section summarizes some general multiple repertoire algorithm design goals, expected to assist in the implementation and configuration of algorithms.

Design Principle	Summary
DP1 – Recirculating Pool Size	The size of the recirculating pool is a small percentage of all lymphocytes (sum of all repertoires) in the system
DP2 – Repertoire Size	Stimulated repertoires have more lymphocytes (for a time) than unstimulated repertoires. Thus a fixed system capacity is shifted based on the repertoire exposure patterns. A repertoire exposed to pathogen is stimulated into a response and inflames resulting in a rapid increase in the total number of lymphocytes.
DP3 - Memory	Memory cells have a long lifespan and a high affinity, effector cells have a short lifespan and moderate to high affinity.
DP4 – Naive Cell Ubiquity	One naive cell is as good as another (random equals random). Naive cells do not need to be migrated, they may be generated at the time they are needed.

DP5 – Synchronized Repertoires	Different tissue types may have different recirculation rates (inbound or outbound), although repertoire processes still occur on the same time scales.
DP6 – Optimized Repertoire Organization	The cells and cell types may be structurally organized for pathogen exposure within a single repertoire. A pathogen may first be exposed to effectors, then memory cells, then naïve cells. The age of the cell is also expected to play a role in the structuring – younger cells are likely to be more adapted than older cells.

Table 4 - Summary of discrete repertoire algorithm design principles

Behavioural Expectations

This section summarise a number of multiple repertoire behavioural expectations. These expectations may be later used as hypotheses that may be investigated and tested. The behaviours described in this section extend the previously discussed principle system effects (section IV).

Behavioural Expectation	**Summary**
H1 – Satisficing Strategy	The lymphocytes that are exposed to pathogen are expected to be an average of the systems capability. The response is better than random, although not likely to be the best that the system may offer.
H2 – Scalability	The generality of the strategy, and bottom-up self-organization facilitate the addition and removal of repertoires and lymphocytes.
H4 – Redundancy	Individual repertoires and individual lymphocytes are redundant, the system is not dependant on any single repertoire or lymphocyte, or even groups of each.
H5 – Fault Tolerance	The competitive and memory (forgetting) properties of the system make the responses tolerant to faults (learning faults) such as sub-optimality (antigenic sin).
H6 – Adaptive	The system is adaptive at multiple scales, such as: spatially adaptive, temporally adaptive, and genetically adaptive.
H7 – Irrespective Dispersal	The dispersal properties occur irrespective of the utility of the objects being dispersed. Dispersal good or bad.

Table 5 - Summary of multiple repertoire behavioural expectations

VI. MULTIPLE REPERTOIRE ALGORITHMS

Given the many principle components offered for this class of model, the combinatorial properties alone allow for may different algorithm types. What has been made clear, is that a general system strategy underlies the models proposed. Namely: a system that facilitates the trade-off between spatial self-organization, and consistency of response. The architecture and properties discussed thus specify bottom-up requirements for a discrete repertoire algorithm. This section enumerates the various sub-algorithms that make up the broader system. All algorithms operates at the repertoire scale, although their combined effects result in the intended emergent behaviours.

A1 – Recirculation Algorithm

This algorithm operates independent of pathogen exposures and is responsible for removing a small proportion of lymphocytes from the current repertoire and sending them to a neighbouring repertoire. Recirculation is directional (vascular inspired).

Step1: Select a proportion of lymphocytes
Step2: Remove selected lymphocytes from repertoire
Step3: Send to neighbouring repertoire (directional)
Step4: The receiving repertoire discriminate the inbound lymphocytes

Figure 17 - Summary of the lymphocyte recirculation algorithm

The lymphocyte selection mechanism is the selection process that facilitates sentinel cells, inflammation, and consistency of response. A generic selection strategy is indiscriminate, randomly selecting a sample for migration (percentage of total repertoire size). A random sample is naturally biased by the densities of cell types (effector and memory), and by the densities of clonal types (results from differing pathogenic exposures).

The receiving repertoire discriminates the inbound lymphocytes, probabilistically selecting those cells that may enter the repertoire. The mechanism has a particular meaning during the inflammation of a repertoire (an exposure event) when the repertoire is less discerning.

A2 – Germinal Centre Algorithm

A germinal centre forms when a repertoire is exposed to pathogen. A few moderate-to-high affinity cells are selected to initiate the centre. These cells clone and maturate the response producing effectors and memory cells.

Step1: Repertoire is exposed to a dose of pathogen
Step2: A small sample of cells are selected to respond
Step3: A germinal centre forms and bouts of expansion and mutation occur
Step4: A large number of effector cells are released into the repertoire
Step5: A small number of memory cells are released into the repertoire

Figure 18 - Summary of the germinal centre (clonal selection) algorithm

This algorithm is a manifestation of the clonal selection algorithm described in [7] (A5 in that work), although both effector and memory cells are released into the repertoire.

A3 – Inflammation Algorithm

When a repertoire is exposed to pathogen, it becomes inflamed. This has the effect of (1) increasing the holding capacity of the repertoire, (2) slowing the outbound lymphocyte traffic, (3) and increasing the inbound lymphocyte traffic. These three properties occur proportional to the amount of inflammation, which is controlled by the size of the does of pathogen.

Step1: Repertoire is exposed to a dose of pathogen
Step2: The germinal centre algorithm takes effect (A2)
Step3: The holding capacity for the repertoire increases
Step4: The outbound lymphocyte traffic decreases
Step5: The inbound lymphocyte traffic increases
Step6: Steps 2-5 decrease with dose neutralisation (time)

Figure 19 - Summary of the inflammation algorithm

A4 – Homing Algorithm

The homing algorithm is the preferential recirculation of a memory cell into (residence) the tissue from which it originated. The homing intentions of a cell influence a

tissues reception of the cell during recirculation, and the reduced selective pressure of the cell for outbound recirculation.

Step1: Memory cell recirculates with tagged knowledge of its birth
Step2: If arriving at birth tissue, increased change of acceptance
Step3: If at birth tissue, decreased chance for recirculation

Figure 20 - Summary of the memory cell homing algorithm

A5 – Homeostasis Algorithm

Memory cells have a longer lifetime than effector cells. Cells age with time, which may be modelled as a decay of the cells energy through time. Effector cells decay and are removed from the system relatively rapidly, whereas memory cells remain for relatively long to infinite periods of time. Naïve cells also have a relatively short lifespan and their population is continually over turned.

Step1: If Memory cell, decay very slowly or not at all
Step2: If Naïve cell, decay quickly, replenish their numbers
Step3: If Effector cell, decay relatively rapidly, no direct replenishment

Figure 21 - Summary of the varied decay properties of lymphocytes

A repertoire has a capacity-equilibrium when unstimulated, and the population consists of a mixture or naïve cells, memory cells that are in recirculation, and any remaining effector cells from past exposures. This capacity increases rapidly (instantly) when the system is exposed to pathogen.

VII. SERIES OF EXPERIMENTS

Unlike the previous work [7] in realizing a clonal selection algorithm in a piece-wise fashion, this work realises multiple instances of the clonal selection algorithm as a multiple repertoire system of algorithms. The system itself is composed of a number of localised processes, which provide the intended high-level functionalities via emergence. Each of these algorithms requires independent investigation in the context of the principle system effects. The following table suggests some future investigations:

Algorithm	Relevant Principle Effects
A1 – Recirculation Algorithm	Information dispersal
A2 – Germinal Centre Algorithm	Maturation of the response
A3 – Inflammation Algorithm	Recruitment Spatial self-organization
A4 – Homing Algorithm	Spatial self-organization Recirculation
A5 – Homeostasis Algorithm	Short and long-term memory

Table 6 - Summary of the independent algorithm investigations

Study 1: Spatial Self-Organization

Spatial self-organization is the emergent effect of the system to localise a response to a pathogen exposure, and more than that, to exploit the resources of the system in that localization effect. This localization effect is at odds with the 'consistency of response' effect, although is also facilitated by that effect. Some concerns with regard to investigating the spatial self-organization effect include the following (see Figure 22).

Speed: The length of time it takes from the time of exposure until the system finishes organizing a response (when all that remains is dissemination)
Size: The amount of resources allocated at the point of exposure, this may be broken down into the different sources of lymphocytes
Quality: The usefulness (with regard to the pathogen) of lymphocytes in the vicinity of the exposure. This includes cells (1) located in the site at the time of exposure (2) cells created via the maturation process, (3) cells recruited from the recirculating pool, (4) cells homing in from other locations

Figure 22 - Summary of the concerns in investigating the spatial self-organization effect

Study 2: Consistency of Response

The consistency of the response refers to the dissemination of acquired knowledge throughout the system such that repertoires that were not directly exposed to the pathogen have immunity to the pathogen. Some areas of concern in investigating this effect include the following (see Figure 23).

Speed: How quickly the acquired immunity is available throughout the system
Coverage: The physical locations of where the acquired immunity is available after dissemination
Movement: The on-going movement behaviour of the acquired immunity after dissemination
Accretion: The effects of accruing memory for the pathogen over multiple exposures
Variability: The acquisition of different variations of a pathogen and generalizing the knowledge

Figure 23 - Summary of the concerns of investigating the consistency of response effect

VIII. DISCUSSION

This work has laid the foundation for a multiple repertoire algorithm (system) as a collective of lymphoid and cellular inspired architectural components and migration inspired processes. The series of algorithms proposed may be investigated independently, although still within the context of the defined broader principles of the system, namely: (1) spatial self-organization, and (2) consistency of response. Further, this work reviled that, although may interesting architectural and behavioural properties had been defined for the series of discrete repertoire adaptive models, that a singular system underlies that work, providing a means of ruthless attrition. Further, it highlights that the previously realized clonal selection algorithm is but one component in this realized multiple repertoire system, which may be used as the baseline algorithm for the independent investigation of the multiple-repertoire algorithms.

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