Information Processing with a Lymphoid Tissue Architecture

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***Abstract*-The lymphatic system provides the context for the immune system cells and setting for their interactions as described by immunological theory. A previously defined and elaborated lymphoid tissue model is proposed as a general lymphoid-tissue inspired information processing architecture, with specific information processing and information transmission constraints imposed on different tissue types. The lymphoid tissue architecture is applied in the proposal of three different immune-inspired lymphoid tissue models, which incorporate a plethora of previously defined immune cell and cell trafficking algorithms.**

Keywords- Lymphoid Tissue, Artificial Immune System, Clonal Selection Algorithm, Information Processing

I. INTRODUCTION

The field of artificial immune systems (AIS) exploits theories from immunology and models from theoretical immunology toward information processing ends (for example optimization, adaptive, and cognitive models). Those theories that are popular in the field of AIS are concerned with the information processing properties of immune cells (lymphocytes) and collections of cells, for example clonal selection, negative selection and network theory. This work raises the level of abstraction from the cell level to the tissue level, proposing the lymphoid tissues of the host as the context for the information processing properties of models inspired by immune cell theories. The lymphatic system consists of a series of tissues and organs responsible for filtering the blood and the lymph for antigen, and coordinating immune response. The tissues and organs of the lymphatic system may be categorised into primary, secondary, and tertiary. Within the context of immune cells, the primary lymphoid tissue is responsible for the formation of lymphocytes (for example the bone marrow and the thymus), secondary tissues are responsible for the presentation of antigen and coordination of immune response and lymphocyte maturation (for example the spleen and the lymph nodes). The tertiary lymphoid tissues are the non-lymphatic tissues of the host organism in which immune cells may patrol. See [2] for a more detailed treatment.

A basic lymphoid tissue model has been proposed previously in the context of lymphocyte migration in discrete repertoire models [1], and in more depth [3,4]. In a more recent work [7] a separate lymphoid tissue model was proposed as an information processing architecture with distinct properties from that of lymphocyte migration models. In that work, (as in the previous works) the various tissue types imposed constraints on the nature of the cell-based information processing that may occur of the immune cells housed within each tissue. In addition, the model proposed two information transmission properties of the architecture: (1) information streaming from tertiary to secondary lymphoid tissue, and (2) information couriering from tertiary to secondary lymphoid tissue. The earlier models proposed the following information processing properties of tissues: (3) recirculation of cells between secondary tissues, (4) the migration native cells from primary to secondary and (5) the homing of effector cells from secondary tissues to sites of infection in tertiary tissues.

This work elaborates the lymphoid tissue model as standalone information processing architecture and model (not a model of the immune system). Section II provides a general treatment of the lymphoid tissue architecture (previously the lymphoid tissue model), highlighting the inter-tissue information transmission concerns. Section III provides some general comments as to the architecture as an information processing model, and proposes three applications of the architecture as tissue-based artificial immune system models.

II. LYMPHOID TISSUE RESPONSIBILITIES

There are many different cell types, with different behaviours and information processing capabilities. Cells may be divided into three casts: (1) *naïve* cells that have not demonstrated their usefulness to the system. (2) *memory* cells, which are the product of naïve cells that have demonstrated their usefulness to the system. (3) *effector* cells, which are created in the same manner as memory cells, although in larger numbers and with shorter lifespan to address immediate needs. In previously proposed single repertoire models that do not take the context of lymphoid tissue into account, these cell types (or casts) are formed implicitly in the population, emergent as a result of the cells interactions with the environment and each other [5].

This section describes a lymphoid tissue model in which the tissue types constrain the cell-based

information processing that may occur to the cells housed within the tissue. In a similar manner to automatic formation of cell types in the single population clonal selection algorithm, the constraints imposed by the different tissues result in emergent cell casts. Tissues are considered the units of adaptation that may receive or transmit information. Cells are the substrate for tissues knowledge representation, communication, and adaptation. This section describes a number of tissue-tissue interactions.

A. ***Cell Formation***

Naïve lymphocytes are created in primarily lymphoid tissue. A naïve lymphocyte is generated in a quasi-random manner. It represents an untested guess of a unit of information that may be useful to the system. A naïve cell may be created in one primarily lymphoid tissue and migrate to another for specialisation, similar to the migration of pre-lymphocyte cells from the bone marrow to the thymus to become naïve T-cells. Those cells that remain in the bone marrow become B-cells.

Principle*: Naïve cells are only created in the primary lymphoid tissue, although may migrate between primary lymphoid tissue for preparation purposes*

The primary tissues may condition the formed naïve cells. For example, the cells may be subjected to a negative and positive selection process such as that subjected to T cells in the thymus. The result of such a process is the assessment and ultimate judgement of the feasibility of the proposed information guesses that the cells represent.

Principle*: Naïve cells may be subjected to feasibility assessment and judgement after generation via the application of prior domain knowledge*

In addition to the migration of naïve cells between primary lymphoid tissue for maturation, naïve cells may unidirectionally migrate from primary to secondary lymphoid tissue. This represents an upgrade in status for the cell from un-prepared to prepared naïve cells, ready for information processing in the secondary tissue. As an interaction between primary and secondary lymphoid tissue it represents a transmission of feasible quasi-random information that may be useful to the system.

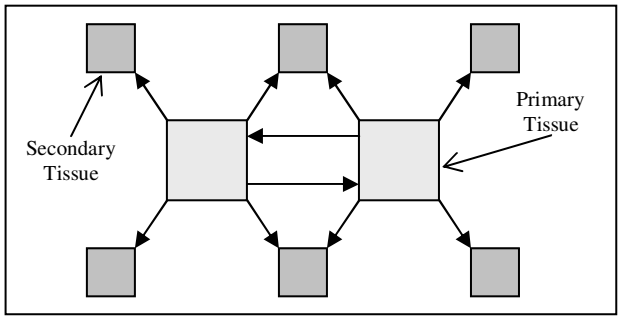

Figure 1 - Depiction of the relationship between primary and secondary lymphoid tissues

Principle*: Once prepared, naïve cells migrate from primary to secondary tissues, ready for secondary information processing; this migration represents a one-way transmission from primary to secondary levels*

B. ***Cell Maturation***

Secondary tissues house many naïve lymphocytes as well as some memory cells and effectors if available. The tissue accepts a steady stream of naïve lymphocytes from primary tissue and integrates them into the cell population. Secondary tissue is responsible for exposing resident cells to antigen and facilitating any immune response that occurs as a result.

Principle*: Secondary tissue presents antigen to resident lymphocytes and facilitates the response*

Exposure is selection of cognate receptors for a given antigen, and response is the clonal selection process or similar as outlined in previous models. The result of the response are memory cells which have demonstrated their usefulness, and effector cells for addressing the immediate concerns of the antigen. Effector cells may or may not be given an impression of the tissue origin of the antigen (site of infection), as proposed by T-cell homing [6]. Memory cells, and non-homing effector cells recirculate between secondary tissues (lymph nodes for example), using the vascular system as the transport mechanism.

Principle*: Effector cells created in the secondary tissue may home to the site of infection in tertiary tissue, memory and effector cells recirculate between secondary lymphoid tissues.*

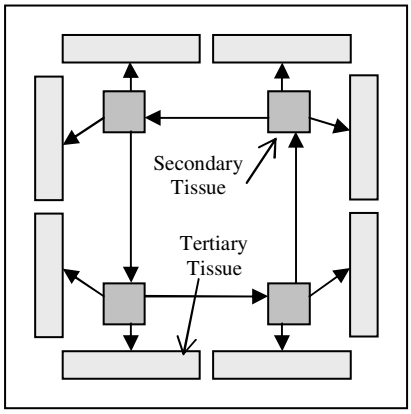

Figure 2 - Depiction of the relationship between secondary tissues and secondary and tertiary tissues

The recirculation of memory and effector cells between secondary lymphoid tissue represents a transmission of acquired information regarding the environment. Portions of acquired information (individual cells) are shared between secondary tissues such that the information may be available for application or further maturation. Acquired information in the form of effector cells is transmitted from the location of maturation in the secondary tissue, to the location of application in the tertiary tissue.

C. ***Cell Application***

Tertiary tissues accept and house many effector cells. The tissues accept a steady stream of effectors from locally connected secondary tissues, which are integrated into the population. Tertiary tissues are responsible for being receptive to pathogenic infection, thus may be considered receptive fields for information from the environment.

***Principle**: Tertiary tissues are directly exposed to pathogen, acting as receptive fields for information from the environment*

The effector cells are employed at the sites of infection as needed, addressing the major function of their lifecycle: application. Samples of the antigen may be taken from the site of infection in the tertiary tissue and transported into secondary tissue by courier cells, taking in addition information as to where the antigen was collected (to facilitate homing).

***Principle**: Antigen may be sampled from the site of infection and transported by courier cells back into secondary tissue for presentation*

Samples of antigen and some effector cells may be drained back into locally connected secondary tissue. This draining effect is facilitated by the lymph fluid that permeates tertiary tissues. The secondary tissue collections and filters the lymph for antigen, which are presented to resident lymphocytes

***Principle**: A stream of samples of antigen is provided to secondary tissue from locally connected tertiary tissue tertiary tissue, transported by the lymph.*

Pathogen exposure to tertiary tissue represent samples of the environment collected by the system. Different tertiary tissues may collect samples in different ways (for example skin, food, respiratory). The couriering and streaming of samples of pathogen back to secondary tissue provides a transmission of sensory information from the environment to areas of the system that can be adapted to address it.

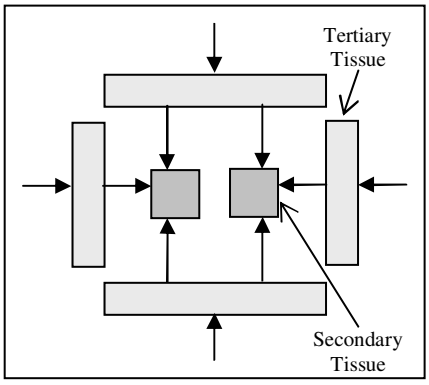

Figure 3 – Depiction of the relationship between tertiary and secondary tissues and tertiary tissues and the environment

III. INTEGRATED MODELS

The aggregation of all three tissue types describes an integrated model with layered information processing. From the inside out, the information availability increases in maturation (usefulness). The tertiary tissue contains no other cells than those known to be immediately useful, the primary tissue contains no other cells than those whose usefulness is unknown. The secondary tissues act as the mediator between these two extremes, providing the testing and maturation processes for information acquisition. The outward flow of knowledge through the layers of the system, information about the environment flows inward. Principle pathogen exposures occur in the tertiary tissue where it may be addressed by resident effectors. If sufficiently large or novel, samples of the pathogen find their way into secondary tissue (courier or stream) for presentation to the learning mechanisms of the system.

Flow of Information	**Examples**
Outward	Untested generated data points Acquired knowledge for memory Acquired knowledge for application
Inward	Principle pathogen exposures for response Samples of pathogen exposures for learning

Table 1 - Summary of the information flow between the layers of the lymphoid tissue architecture

The information properties of the system have been described with regard to the transmission of the information substrate (immune cells) between the layers and within the layers. Algorithms for within layer information processing have been defined in previous works. The following lists the algorithms required to meet the information processing needs outlined for the architecture.

Tier	**Information Processing**	**Algorithm**
1	Generation and feasibility testing	Negative Selection
2	Maturation	Clonal Selection
2	Homeostasis	Elaborated Clonal Selection
2	Recirculation	Recirculation Algorithm
2/3	Courier/Homing	Homing Algorithm
2/3	Exposures/Streaming	Pathogenic Exposure

Table 2 - Summary of information processing needs, and proposed algorithms that meet those needs

The information processing constraints of each tissue type, outline a clear responsibility for each tier of the architecture. Primary tissue is concerned with information generation and the pre-processing of information before it is employed in a learning process. Secondary tissue is responsible for learning, for identifying which internal information is presently useful and attempting to improve it (maturation), whilst at the same time applying it (effectors). The second tier is also responsible for the generation and maintenance of longer term memory, and the selective application of acquired memory. The tertiary tissue is responsible for providing an interface to the environment, mediating the application of acquired knowledge to sensory signals, with the filtering of temporally novel signals to secondary tissues for response generation.

Tissue Type (Tier)	**Responsibility**
Primary Tissue	Information generation (preparation)
Secondary Tissue	Information maturation (learning and memory)
Tertiary Tissue	Information application (sensory)

Table 3 - Summary of the principle responsibility of each tier of the architecture

All of the interesting information processing occurs in the secondary lymphoid tissue. The other two layers may be easily incorporated into the secondary tissue, providing only conceptual attributes of the tissue model. This compression of responsibility has been implicit in previously proposed clonal selection, negative selection, and other cell-theory based algorithms. Given that the tissues may be compressed, it is important to consider the utility of separating the proposed responsibilities into a dependant hierarchy of layers.

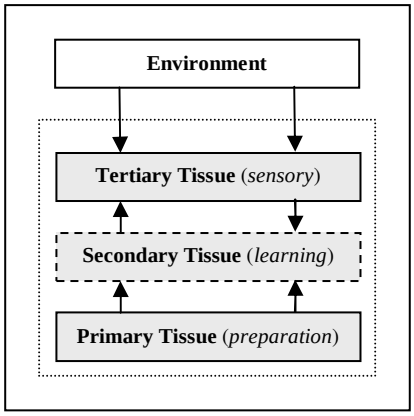

Figure 4 - Depiction of the layered information processing properties of the lymphoid tissue architecture

This section proposes three different models that employ the proposed lymphoid tissue architecture. Each model is inspired by a different aspect of the acquired immune system, from a lymphatic system (tissue) perspective. The principles for separated responsibility are (1) the centralised generation of naïve cells facilitating centralised prior knowledge, (2) consolidated secondary tissue for a networked learning architecture large enough to meet the needs of the system, (3) a large host consisting predominantly of tertiary tissue, which provides a distributed sensor platform for receiving and responding to environmental signals.

A. ***Filter Model***

The filter model is inspired by the specialisation of the lymphatic system at the primary entry points for exogenous antigen (pathogen). Examples include the tonsils and related tissues for addressing pathogen that enter the host via the respiratory system, the Peyer's patch tissues in the intestines that addressing pathogen that enter the host via the digestive system, and the spleen that filters the blood for pathogen. The model contains a single point of entry for pathogen (tertiary tissue), which is monitored by one or a small collection of secondary lymphoid tissues. The secondary tissue is supported by a single source of naïve cells (primary tissue).

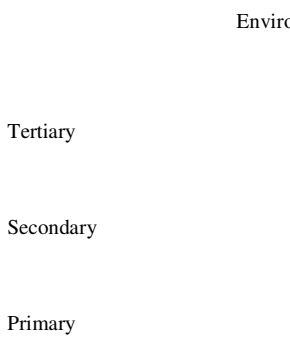

Figure 5 - Depiction of the simple filter model

Although the model is called 'the filter model' (the basis for its inspiration) it is not restricted to filtering information processing tasks. The focus of this model is on the system possessing a single point of entry for pathogen (sensory signals) although at a high load (many signals), and one or a small number of specialised secondary tissues to address the needs of the tertiary tissue.

Tissue Type	Configuration
Primary	Single tissue feeding the secondary tissue
Secondary	Single (or a small number of) secondary tissues with high capacity of cells
Tertiary	Single point of entry for the system to monitor

Table 4 - Configuration of the architecture for the filter model

B. ***Lymph Node Model***

The lymph node model is inspired by the network of lymph nodes, connected by the vascular system, and that receive antigen as a stream in the lymph. The model is more complex than the filter model as it contains a network of moderate sized secondary lymphoid tissues that recirculate memory and effector cells. Further, unlike the filter model, it has a large receptive field of tertiary tissue, which provides a single broad sensory system.

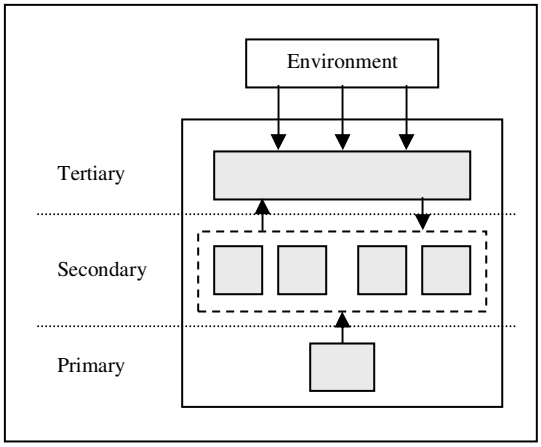

Figure 6 - Depiction of the lymph node model

The focus in this model is the large tertiary tissue receptive field, and the network of secondary tissues (lymph nodes), in particular the capabilities of the lymph nodes to recirculate mature cells (share acquired information), and their capabilities in trafficking effectors into tertiary tissues (applying acquired information).

Tissue Type	Configuration
Primary	Single tissue feeding the secondary tissue
Secondary	A consolidated network of moderate sized secondary tissues
Tertiary	A large and uniform receptive field for input signals

Table 5 - Configuration of the architecture for the lymph node model

C. ***Host Model***

The host model is an integration of one or more filter models with the lymph node model. The resultant model is a larger-scale tissue architecture that may be equated to a lymphatic system of a host. The model is composed of a variety of different tertiary tissue types and thus different means for the secondary tissue to be provided with antigen to present to resident cells. In addition, the

secondary tissue is made of a core network of lymph nodes, as well as collections of specialised lymphoid tissue to address principle pathogen penetration areas. Finally, the system has one or more primary lymphoid tissues for the creation and dissemination of naïve cells to secondary tissues.

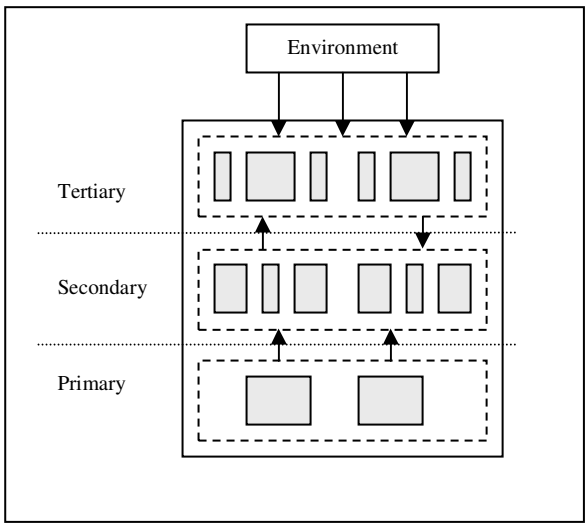

Figure 7 - Depiction of the host model

The focus of the model is the integration of the lymph node network (and related method for sampling antigen from tertiary tissue) with a number of filter-based models centred around primary pathogen access points. This host model represents a hybrid integration of the two sub-types of tissue architectures, and culminating (pinnacle in complexity) lymphatic tissue model.

Tissue Type	Configuration
Primary	Single tissue feeding the secondary tissue
Secondary	A backbone of a consolidated network as well as specialised regions for each major entry point (diverse)
Tertiary	Multiple tertiary tissues of varied size and scope (diverse)

Table 6 - Configuration of the architecture for the host model

IV. Discussion

The lymphoid tissue architecture provides the context for the previously defined adaptive models inspired by theories concerning immune cells, and a context for the cell migration algorithms previously proposed. The applications of the architecture in the proposed lymphoid tissue models provides three specific settings for integrated lymphoid tissue-based information processing. Although the algorithms and tissue principles had been previously articulated, integrated models that employed the principles and algorithms had not. This work suggests at the potential for tissue-based artificial immune system algorithms as a scale above cell-based artificial immune system algorithms.

Two algorithms were commented on although have not been proposed in the context of the framework. These algorithms are as follows:

1) ***Negative Selection***: An implementation of the negative selection algorithm in the context of the framework as a cell-based algorithm for feasibility-testing generated naïve lymphocytes
2) ***Tertiary Migration***: An algorithm for migrating effector cells from secondary tissue to locally connected tertiary tissue. Although a homing algorithm has been proposed, no general trafficking algorithm for effectors has been proposed.

An interesting aspect of future work highlighted in the proposed lymphoid tissue models is their relation to evolutionary algorithms in the next tier (Species) of the broader framework (Cell, Host, Species). Evolutionary algorithms may be used to adapt many aspects of the lymphoid tissue architecture. An important aspect, that does not naturally facilitate adaptation is the prior knowledge employed in the generation of naïve cells. This prior knowledge could be acquired (rather than by other means such as hard coded, or inducted from other systems), using an evolutionary process.

Acknowledgments

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