Part2: Artificial Immune Systems

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- Artificial Immune System (AIS) are algorithms that try to replicate the way biological defensive/immune systems works.

Artificial immune systems were used in many areas:

- Optimization:
  - An advanced immune based strategy to obtain an optimal feasible assembly sequence (2016)
- Clustering/Classification:
  - An artificial immune system with bootstrap sampling for the diagnosis of recurrent endometrial cancers (2021)
- Robotics:
  - Clonal selection algorithm based control for two-wheeled self-balancing mobile robot (2022)
- Job shop Scheduling:
  - An artificial immune algorithm for the flexible job-shop scheduling problem(2010)
- Optimization in Assembly line balancing:
  - An Artificial Immune System Approach for Solving Type-E Assembly Line Balancing Problem with Problem-Specific Information(2020)

I. IMMUNE SYSTEM BIOLOGY

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2. Innate immune system
3. Adaptive immune system

II. AIS BASIC CONCEPT AND TECHNIQUES

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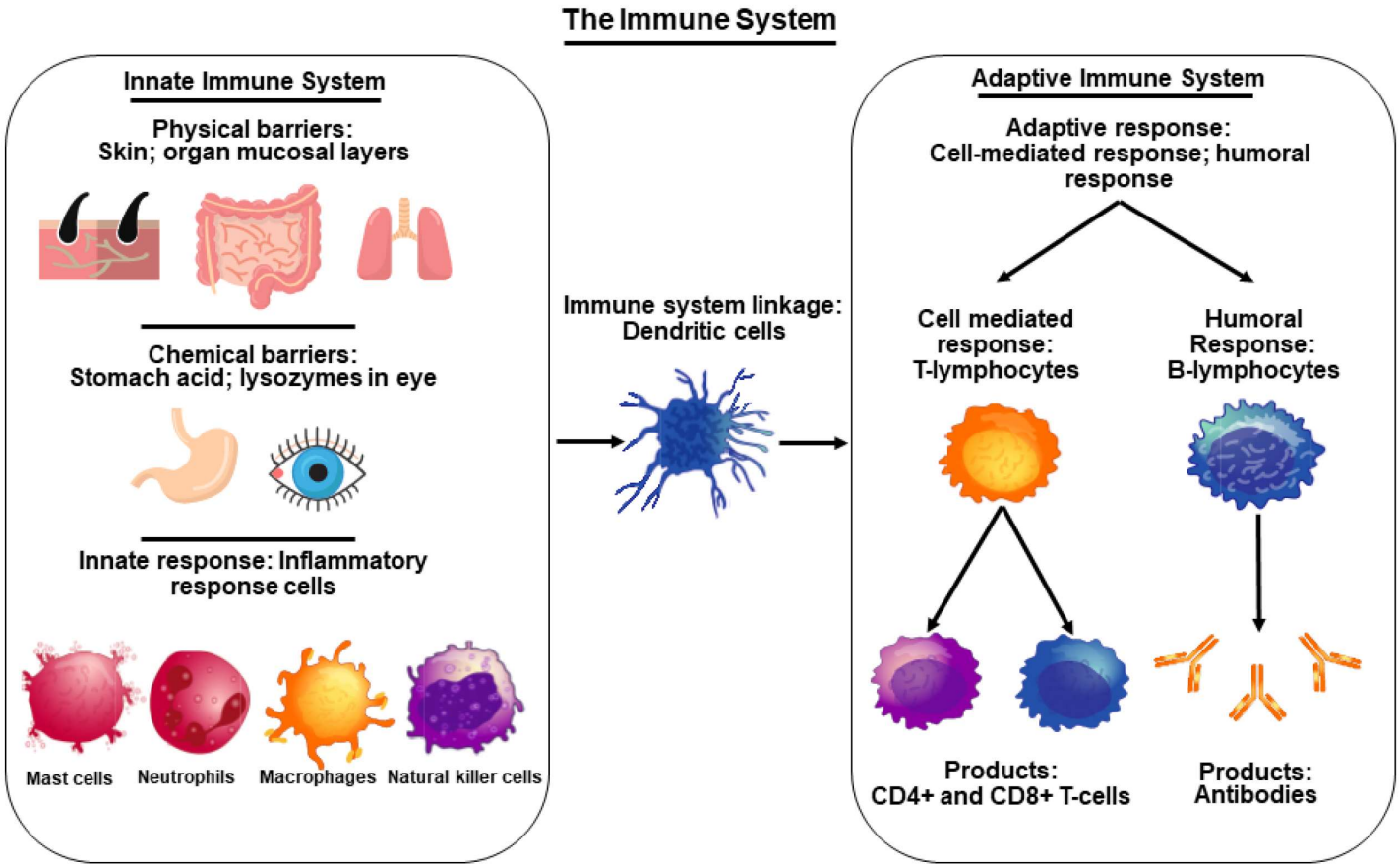
I. IMMUNE SYSTEM BIOLOGY

1. Introduction
2. Innate immune system
3. Adaptive immune system

1.Introduction

The immune system is a “team effort,” involving many different players.

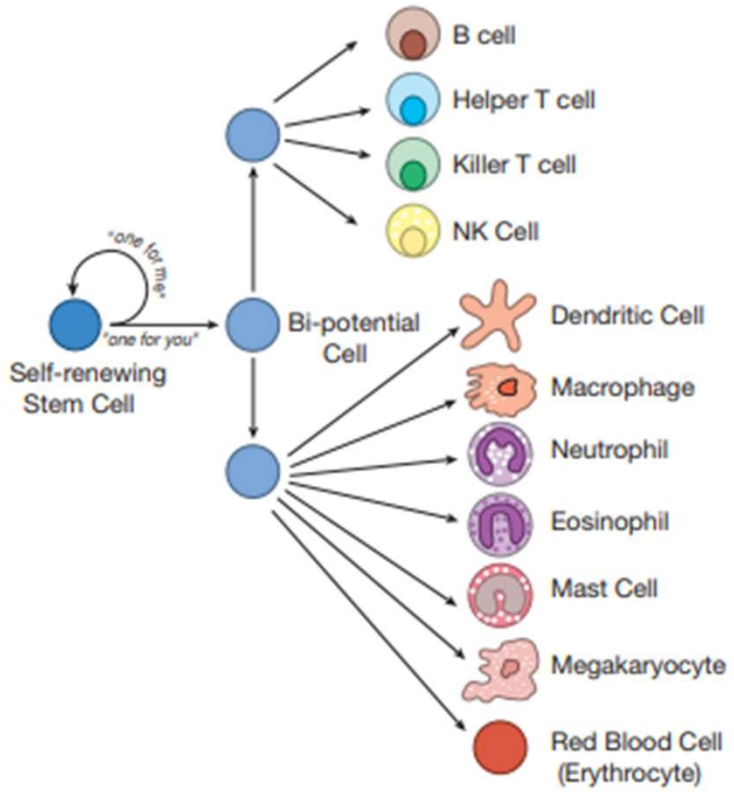
- These players can be divided roughly into two groups:
  - Members of the innate immune system team.
  - Members of the adaptive immune system.
- These two groups work together to provide a powerful defense mecanism.



Immune system

1.Introduction

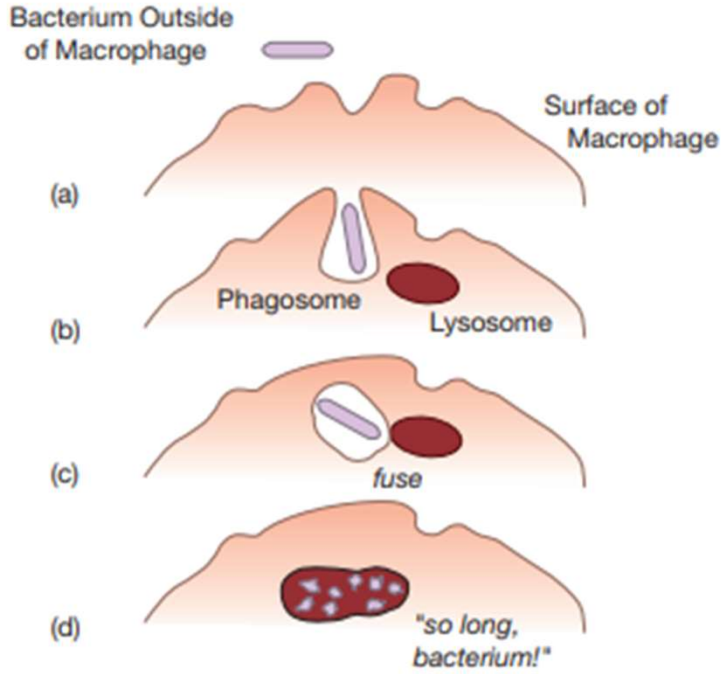
- Made in bone marrow(center of the bone),
- here some of the many different kinds of blood cells of a stem cell can become:



Type of Cells a Stem cell can become

2. Innate immune system

- “Innate” because it is a defense that all animals just naturally seem to have.
- Have been around for more than 500 million years.
- One of the most famous defender cells of the innate system that is stationed in your tissues is : the macrophage.



Macrophage killing process

3. Adaptive immune system

1) Introduction
2) Antibodies and B cells
3) Generating antibody diversity by modular design
4) Clonal selection
5) What antibodies do
6) T cells
7) Antigen presentation
8) Activation of the adaptive immune system
9) The secondary lymphoid organs
10) Immunological memory
11) Tolerance of self

3. Adaptive immune system

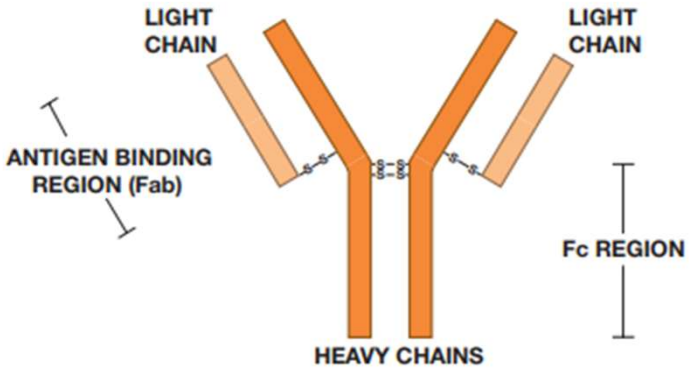
1) Introduction

- In the 1790s , physician and scientist Edward Jenner created the smallpox virus vaccine, the world's first vaccine.
- The terms vaccine and vaccination are derived from Variolae vaccinae, the term devised by Jenner to denote the virus cowpox.
- The pus caused by the virus cowpox was used as a vaccine for smallplox.

3. Adaptive immune system

2) Antibodies and B cells

- Immunity to the virus was conferred by special proteins that circulated in the blood.
- These proteins were named antibodies, the agent that caused the antibodies to be made was called an antigen (the virus).



Prototype antibody, immunoglobulin G (IgG). From Book: How the Immune System Works, 6th Edition, 2019, Lauren M. Sompayrac

3. Adaptive immune system

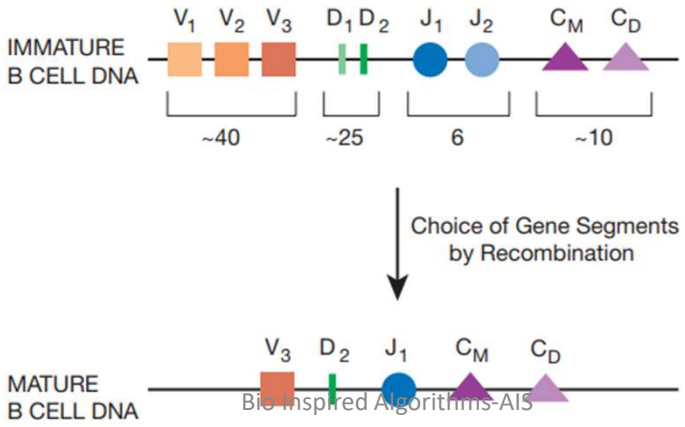
3) Generating antibody diversity by modular design

- If we want antibodies to protect us from every possible invader we need about 100 million.
- How B cells can produce the 100 million different antibodies?

3. Adaptive immune system

3) Generating antibody diversity by modular design

- In every B cell, on the chromosomes that encode the antibody heavy chain there are multiple copies of four types of DNA modules (gene segments) :V, D, J, and C.
- In humans there are about 40 different V segments, 25 D segments…
- To assemble a mature heavy chain gene, each B cell chooses (more or less at random) one of each kind of gene segment, and pastes them together.



3. Adaptive immune system

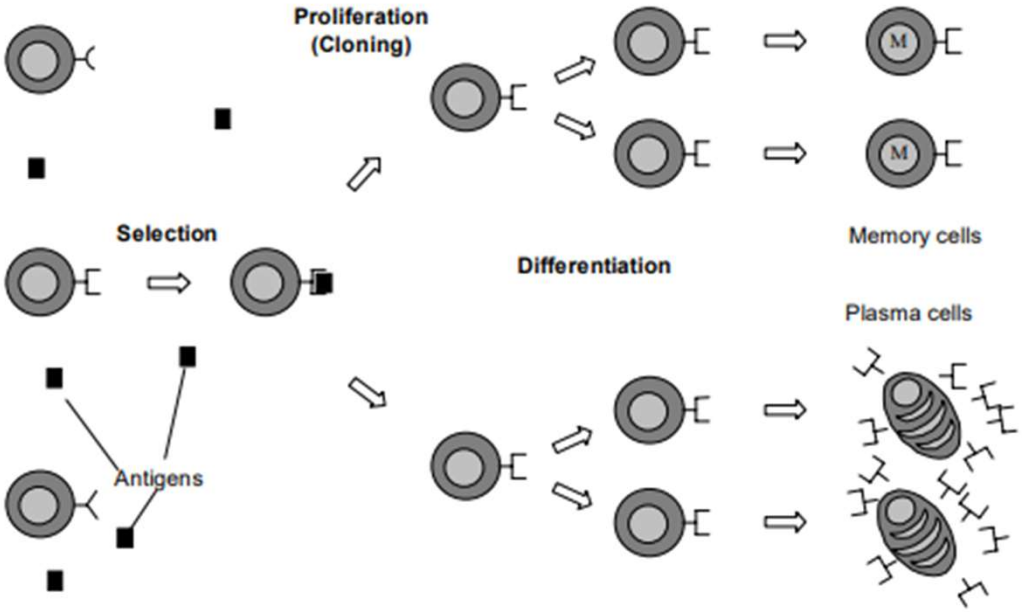
4) Clonal selection

B cells are made on demand, we start with a small number of B cells, and then:

- Select the B cells that will be useful against the “invader.”
- Produce a large clone of B cells .
- Produce antibodies
- When the invader has been eliminated, most of the B cells die

3. Adaptive immune system

4) Clonal selection

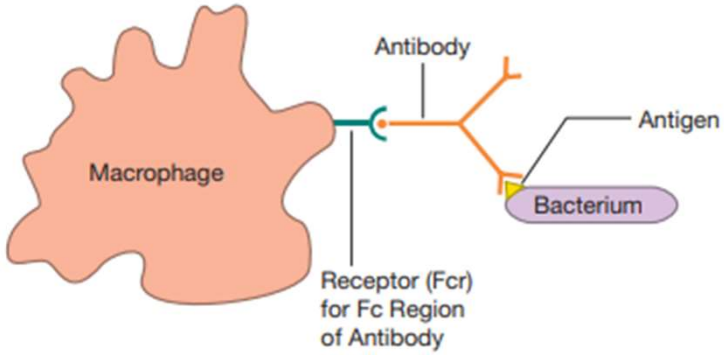


Clonal Selection principle

3. Adaptive immune system

5) What antibodies do

- They don’t kill anything, they identify invaders
- Antibodies can bind to invaders (bacteria and viruses)and tag them for destruction.



Antibodies forming a bridge between a macrophage and an invader
From Book: How the Immune System Works, 6th Edition, 2019, Lauren M. Sompayrac

3. Adaptive immune system

6) T cells

Antibodies can’t get to a virus once it is inside a cell, so the virus is safe to make thousands of copies of itself.

To deal with this problem, the immune system evolved to include another weapon: the killer T cell

3. Adaptive immune system

6) T cells

Similarity with b cells:

- Appearance.
- Produced in the bone marrow,
- In their surface they display antibody-like molecules called T cell receptors (TCRs) (BCRS for b cells
- the antibody molecules attached to its surface,
- Made by a mix-and-match, modular design strategy.
- TCRs are diverse as BCRs.
- Employ the principle of clonal selection.

3. Adaptive immune system

6) T cells

B cells	T cells
Mature in the bone marrow	Mature in the thymus (that's why they're called "T" cells)
Make antibodies that can recognize any organic molecule	Specialize in recognizing protein antigens
Can secrete its receptors in the form of antibodies	Receptors remain tightly glued to its surface
Recognize an antigen by itself	Only recognize an antigen if it is properly presented by another cell

3. Adaptive immune system

6) T cells

3 main types of T cells:

killer T cells (cytotoxic lymphocytes or CTLs),

helper T cells,

regulatory T cells.

3. Adaptive immune system

6) T cells

The killer T cell can destroy virus-infected cells.

killer T cell destroys virus-infected cells by making contact with its target and then triggering the cell to commit suicide

when an infected cell dies, the viruses within the cell die also.

the CTL solves the “hiding virus” problem

3. Adaptive immune system

6) T cells

the helper T cell (Th cell) serves as the quarterback of the immune system team.

It directs the action by secreting chemical messengers (cytokines) that have dramatic effects on other immune system cells.

helper T cells are basically cytokine factories.

3. Adaptive immune system

6) T cells

the regulatory T cell (Treg) keeps the immune system from overreacting or from reacting inappropriately.

Immunologists are still working to understand how T cells become regulatory T cells, and exactly how Tregs perform these important functions.

3. Adaptive immune system

7) Antigen presentation

The MHC complex

The T cell receptor recognizes antigens bound to a cell surface molecule called a major histocompatibility complex (MHC)

3. Adaptive immune system

7) Antigen presentation

Two major classes of MHC molecules

MHC class I (MHCI)

MHC class II (MHC-II)

3. Adaptive immune system

7) Antigen presentation

Class I molecules are found on every cell,

killer (cytotoxic) cells, interact with MHC class I.

Cytotoxic T cells recognize antigens bound to MHC-I molecules, once any cell can become virally infected.

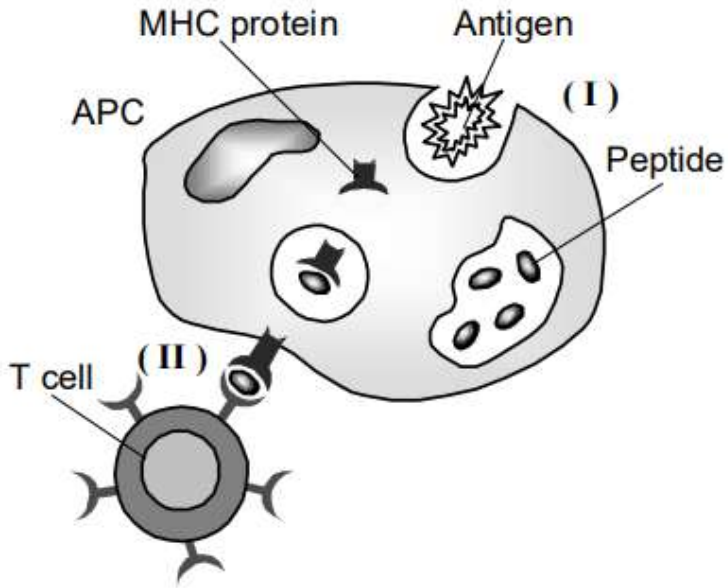
3. Adaptive immune system

7) Antigen presentation

class II molecules are found only on a subset of cells called antigen-presenting cells (APCs)(B cells, macrophages, and dendritic cells).

APCs take up protein antigens from their environment and partially digest them, cut them into smaller pieces called peptides.

Some of these peptides are then bound to an MHC-II molecule and transported to the surface of the APC, where they can interact with the helper T cell.



MHC-II molecule and T cell interaction[14]

3. Adaptive immune system

7) Antigen presentation

Both MHC classes bind peptides and present them to T cells.

The class I system specializes in presenting proteins synthesized within the cell (intracellular pathogens), such as viral proteins made by an infected cell,

class II system specializes in presenting fragments of molecules picked up from the environment.

Both systems present peptides from self molecules as well as from foreign molecules.

3. Adaptive immune system

8) Activation of the adaptive immune system

2 steps are needed

The first step in the activation of a helper T cell is

recognition of its cognate antigen (e.g., a fragment of a bacterial protein) displayed by class II MHC molecules on the surface of an antigen presenting cell.

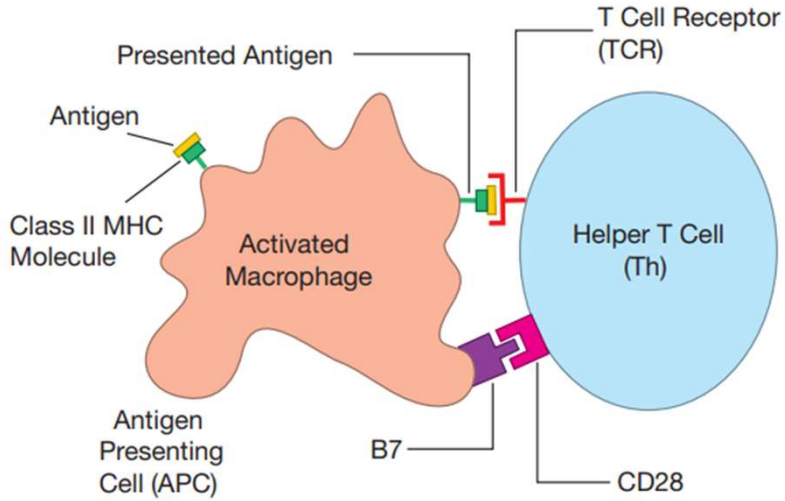
a second signal also is required for activation.

This signal is non-specific (it's the same for any antigen),

3. Adaptive immune system

8) Activation of the adaptive immune system

second signal : involves a protein (B7 in this drawing) on the surface of an antigen presenting cell that plugs into its receptor (CD28 in this drawing) on the surface of the helper T cell.



Two-key system for the activation of adaptive immune

3. Adaptive immune system

8) Activation of the adaptive immune system

Once a helper T cell is activated by this two-key system,

it builds up a clone composed of many helper T cells whose receptors recognize the same antigen.

These helper cells then mature into cells that can produce the cytokines needed to direct the activities of the immune system.

B cells and killer T cells also require two-key systems for their activation,.

3. Adaptive immune system

9) The secondary lymphoid organs

The main roles of the lymphatic system: managing the fluid levels in the body.

Without this system, our tissues would fill up with fluid.

the immune system includes “meeting places” for T cells and APC – the secondary lymphoid organs.

The best known secondary lymphoid organ is the lymph node.

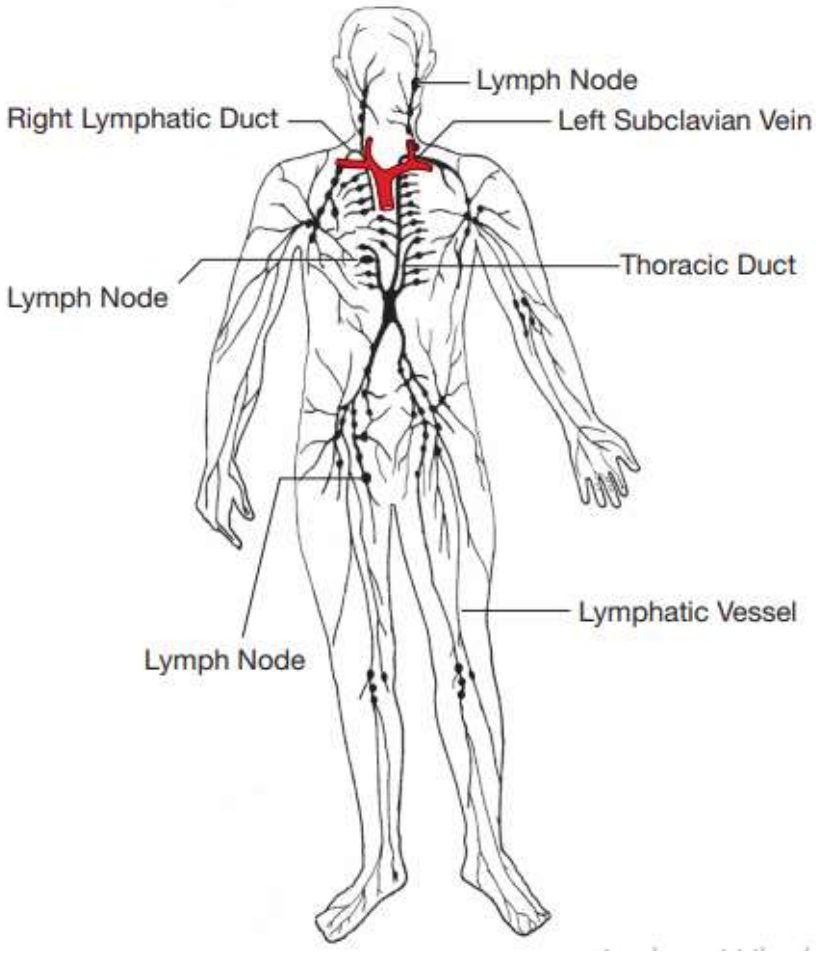
3. Adaptive immune system

9) The secondary lymphoid organs

drains fluid (called lymph) is collected from the tissues of our lower body into lymphatic vessels, and is transported, under the influence of muscular contraction, through a series of one-way valves to the upper torso.

the lymph winds it passes through a series of way stations – the lymph nodes.

B cells and T cells circulate from node to node, looking for the antigens



Lymphatic system

3. Adaptive immune system

10)Immunological memory

After B and T cells have been activated, build up clones of cells with identical antigen specificities, and have vanquished the enemy, most of them die off.

These “leftover” B and T cells are called memory cells.

In addition to being more numerous than the original,

Memory cells are easier to activate.

3. Adaptive immune system

10)Immunological memory

As a result of this immunological memory, during a second attack, the adaptive system usually can spring into action quickly that you don’t experience any symptoms.

3. Adaptive immune system

11)Tolerance of self

- B cell receptors and T cell receptors are so diverse that they should be able to recognize any invader.
- This diversity poses a potential problem,
- If B and T cell receptors recognize our own “self” molecules,

our adaptive immune system might attack our own bodies,

and we could die from autoimmune disease.

3. Adaptive immune system

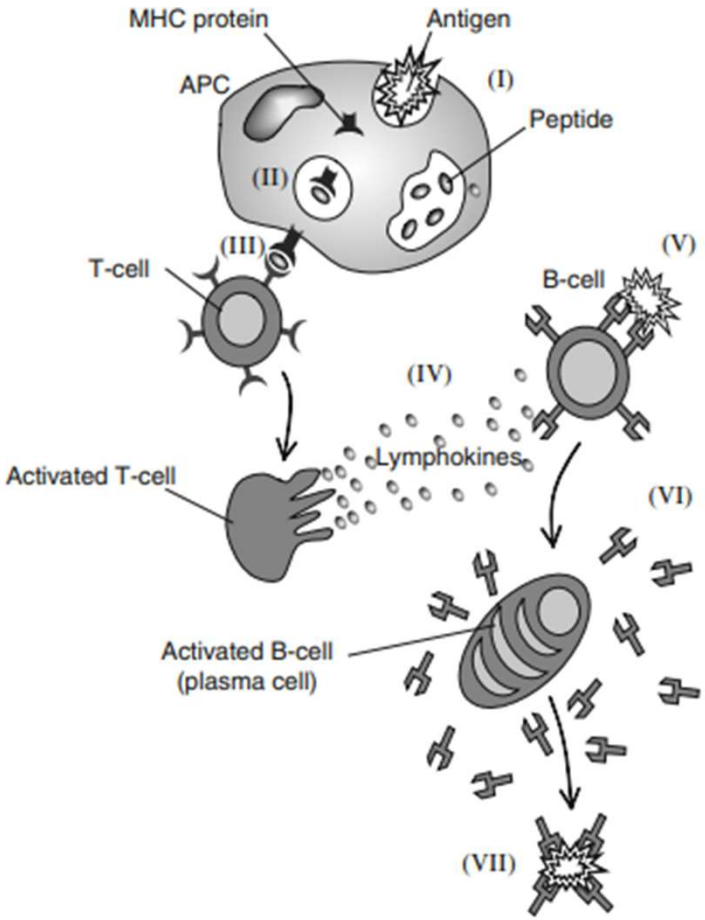
11)Tolerance of self

- B cells and T cells are “screened” to avoid autoimmunity.
- Tests are used to eliminate self-reactive B and T cells,

3. Adaptive immune syste

Conclusion

- (I)–(II) show the invade entering the body and activating T cells,
- which then in (IV) activate the B-cells,
- (V) is the antigen matching,
- (VI) the antibody production
- (VII) the antigen's destruction



How the immune system defends the body[2]

II. AIS BASIC CONCEPT AND TECHNIQUES

1. AIS Basic concept
2. AIS Techniques

1. AIS BASIC CONCEPT

1. Introduction
2. Initialisation/ Encoding
3. Similarity or Affinity Measurement
4. Negative, Clonal or Neighborhood selection
5. Somatic Hypermutation

1. Introduction

- To implement a basic Artificial Immune System we need four decisions :

1. Encoding,
2. Similarity measure,
3. Selection
4. Mutation.

- The algorithm perform selection and mutation based on the suitable similarity measure chosen,
- until stopping criteria is met.

2. Initialisation/ Encoding

- Choosing a suitable encoding is very important for the algorithm's success.
- Like genetic algorithms, there is close connection between the encoding and the fitness function (the matching/affinity function in AIS) .
- Antigens(target or solution) and antibodies (the remainder of the data) are encoded in the same way.

3. Similarity or Affinity Measurement/Matching rule

- One of the most important design choices in an Artificial Immune Systems algorithm developement.
- Closely related to the encoding scheme.
- Calculate the affinity between antibody and antigen at each generation,
- Examples of the Similarity measure:
  - Hamming distance
  - Geometrical (Euclidian) distance
  - Pearson correlation coefficient.

4. Negative, Clonal or Neighborhood selection

- Differs depending on the exact problem the Artificial Immune Systems is applied to.
- According to the affinity of the antibody in the current antibody group, the higher the fitness value of the antibody is, the more likely it is to be selected for cloning, which generates more promising antibodies

5. Somatic Hypermutation

- The mutation used in Artificial Immune Systems is similar to that found in genetic algorithms,
  - For binary strings bits are flipped,
  - For real value strings one value is changed at random,
  - For others the order of elements is swapped.
- Can produce more promising offspring, so as to form a new antibody population.
- This mechanism is often enhanced by the somatic idea: the closer the match (or the less close the match), the more (or less) disruptive the mutation.

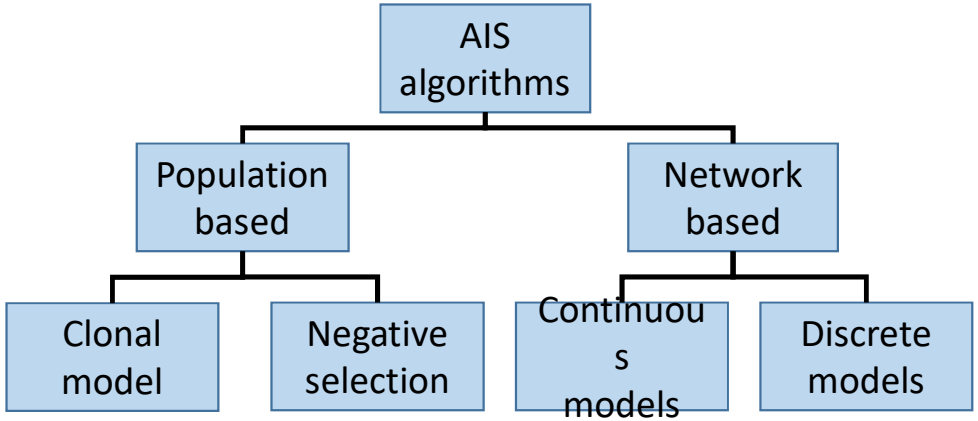
2. AIS TECHNIQUES

1. Introduction
2. Clonal Selection
3. Negative Selection
4. Immune Network Theory
5. Dendritic Cells
6. Danger Theory
7. NSA, INA, and CSA Application area

1. Introduction

In the artificial immune algorithms have been grouped into two categories[4]:

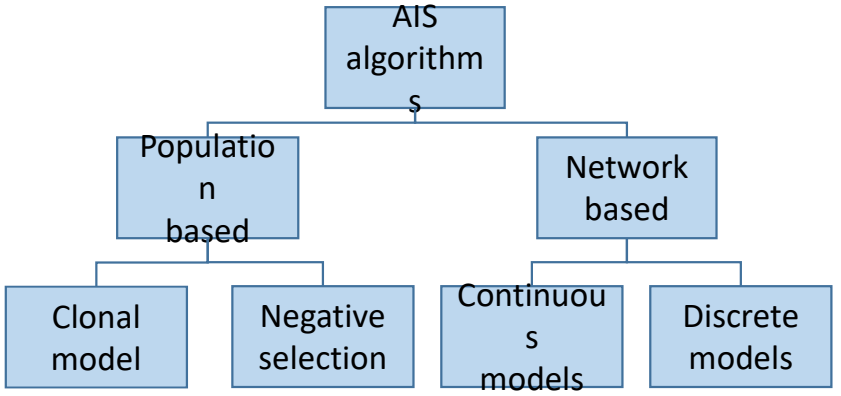
- Population based methods,
- Network based methods.



Artificial immune systems (AIS) categories

1. Introduction

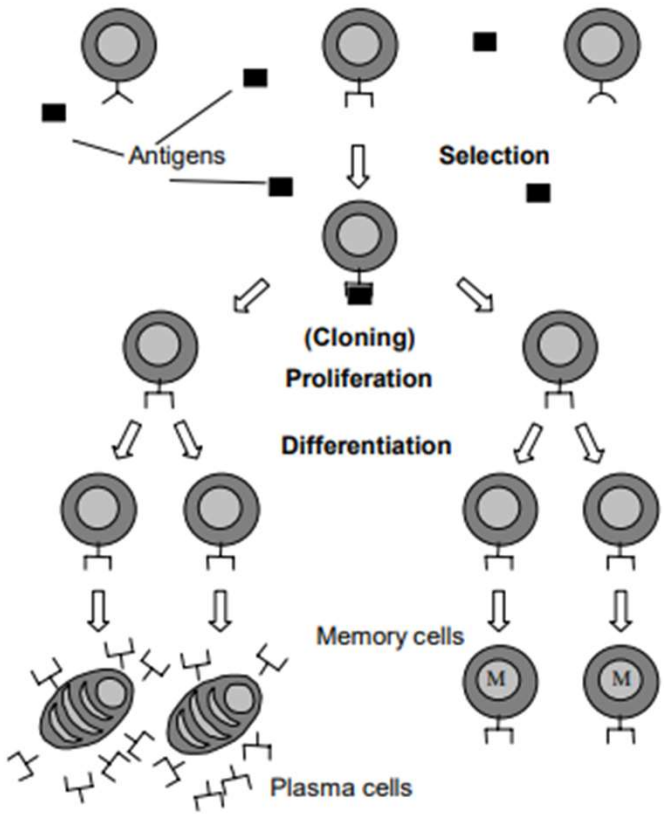
- In general,
- Clonal Model algorithm is applied to optimization problems,
- Negative Selection algorithm is applied to classification and grouping problems.
- Algorithms in the network-based categories are applied to classification problems [9]



Artificial immune systems (AIS) categories

2. Clonal Selection Algorithr

Influenced by the clonal selection hypothesis.

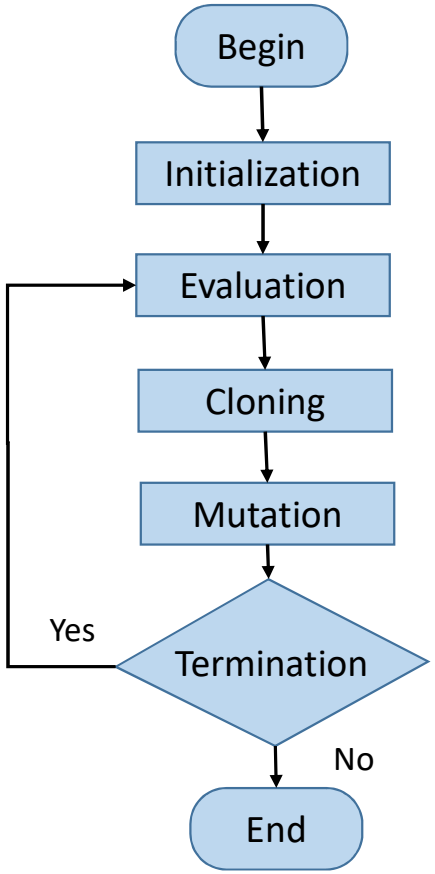


Clonal Selection Principle

2. Clonal Selection Algorithm

- The selection of the cell is influenced by antigen–antibody affinity,
- The cell is reproduces by division (clone) , and variation through somatic hyper mutation.
- Elimination of newly differentiated lymphocytes carrying self-reactive receptors;
- Proliferation and differentiation on contact of mature cells with antigens.

2. Clonal Selection Algorithm



Classical Clonal Selection Algorithm

2. Clonal Selection Algorithm

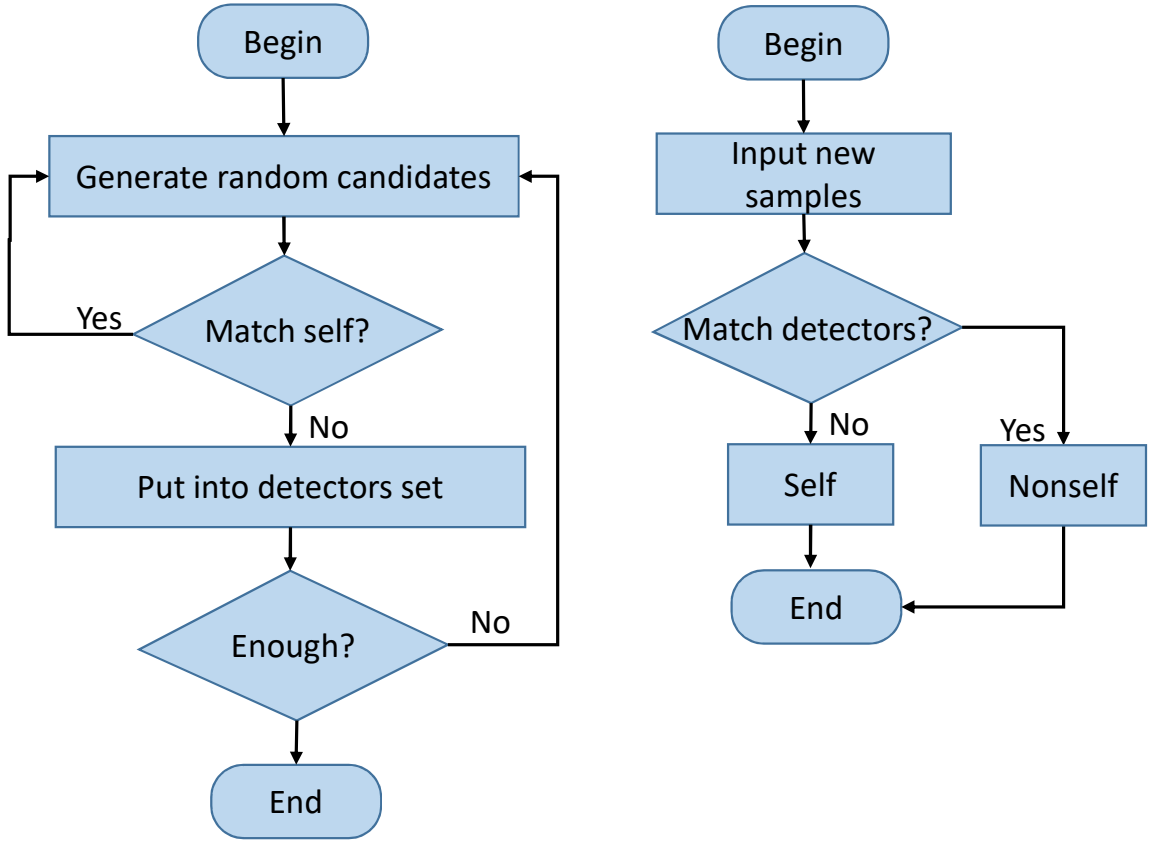
- Pseudocode of the clonal selection algorithm (CLONALG) [17].

Input: $Population_{size}$, $Selection_{size}$, $Problem_{size}$, $RandomCells_{num}$, $Clone_{rate}$, $Mutation_{rate}$
Output: Population
Population ← CreateRandomCells($Population_{size}$, $Problem_{size}$);
While ¬StopCondition() **do**
  foreach p_i∈ Population **do**
    Affinity(p_i);
  end
  $Population_{select}$ ← Select(Population, $Selection_{size}$);
  $Population_{clones}$ ← ∅;
  foreach $p_i \in Population_{select}$ **do**
    $Population_{clones}$ ← Clone(p_i, $Clone_{rate}$);
  end
  foreach $p_i \in Population_{clones}$ **do**
    Hypermutate(p_i, $Mutation_{rate}$);
    Affinity(p_i);
  end
  Population ← Select(Population, $Population_{clones}$, $Population_{size}$);
  $Population_{rand}$ ← CreateRandomCells($RandomCells_{num}$);
  Replace(Population, $Population_{rand}$);
end
return Population;

3. Negative Selection Algorithm (NSA)

- Negative selection is the process of identifying and eliminating self-reacting cells, or T cells that may select or attack own tissues.

3. Negative Selection Algorithm (NSA)



a)Generation of the Detectors

b) Detection of new instances

Flowchart of of the traditional NSA[13]

3. Negative Selection Algorithm (NSA)

- Pseudocode of the detector generation procedure for the negative selection algorithm.

```
Input: SelfData
Output: Repertoire
Repertoire ← ∅;
While ¬StopCondition() do
    Detectors ← GenerateRandomDetectors();
    foreach Detector_i ∈ Repertoire do
        If ¬Matches(Detector_i, SelfData) then
            Repetoire ← Detector_i;
        end
    end
end
return Repertoire;
```

3. Negative Selection Algorithm (NSA)

- Pseudocode of the detector application procedure for the negative selection algorithm.

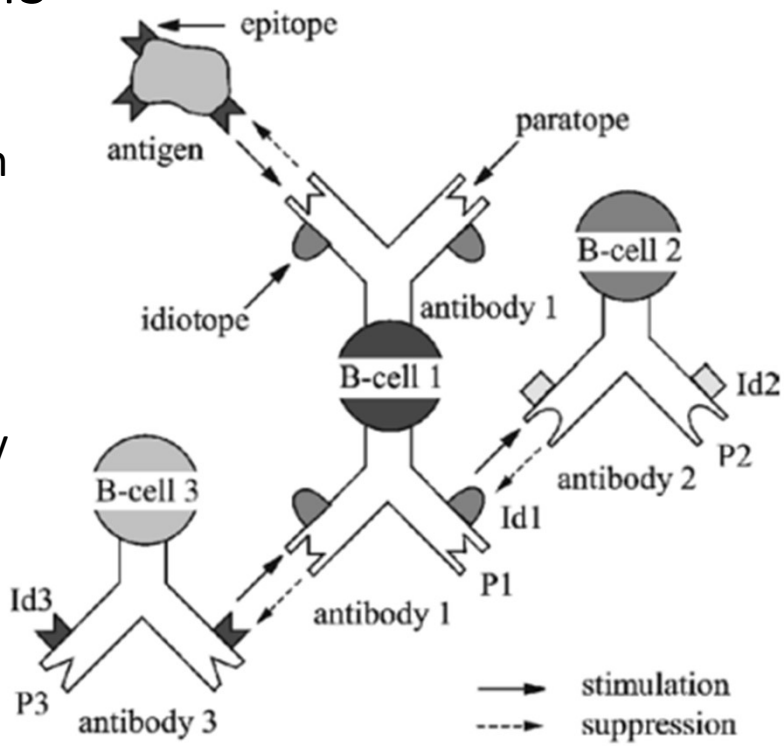
Input: InputSamples, Repertoire
for $Input_i \in$ InputSamples **do**
  $Inputi_{class} \leftarrow$ ''non-self'';
  foreach $Detector_i \in$ Repertoire **do**
    If Matches($Input_i$, $Detector_i$) **then**
      $Inputi_{class} \leftarrow$ ''self'';
      Break;
    end
  end
end

4. Immune Network Algorithms

- Algorithms based on Niels Kaj Jerne's idiotypic network theory, which describes how antiidiotypic antibodies regulate the immune system.
- The idiotypic effect builds on the premise that antibodies can match other antibodies as well as antigens.
- Anti-idiotypic antibodies are antibodies that bind to the antigen-binding site of another antibody
- The hypothesis was that the immune system maintains an idiotypic network of interconnected B-cells for antigen recognition.
- Idiotypes: the unique and characteristic parts of an antibody’s variable region, which can themselves serve as antigens

4. Immune Network Algorithms

- These cells both stimulate and suppress each other in certain ways that lead to the stabilization of the network.
- Two B-cells are connected if the affinities they share exceed a certain threshold, and the strength of the connection is directly proportional to the affinity they share.



Structure of immune network
(2009, D. Tsankova)

4. Immune Network Algorithms

- This class of algorithms focuses on network graph architectures involving antibodies as nodes, with the training method creating between nodes based on affinity.
- Immune network techniques are similar to artificial neural networks
- utilised in clustering, data visualisation, control, and optimization.

4. Immune Network Algorithms

Pseudocode of the Artificial Immune Network Optimization Algorithm (opt-aiNet) to minimize a cost function.

- aiNet is designed for the clustering unsupervised,
- the optaiNet extension was designed for pattern recognition and optimization, in particular the optimization of multimodal functions.

Input: $Population_{size}$, ProblemSize, N_{clones}, N_{random}, AffinityThreshold
Output: S_{best}
Population ← InitializePopulation($Population_{size}$, ProblemSize);
while ¬StopCondition() do
    EvaluatePopulation(Population);
    S_{best} ← GetBestSolution(Population);
    Progeny ← ∅;
    $Cost_{avg}$ ← CalculateAveragePopulationCost(Population);
    while CalculateAveragePopulationCost(Population) > $Cost_{avg}$ **do**
        foreach $Cell_i$ ∈ Population **do**
            Clones ← CreateClones($Cell_i$, N_{clones});
            foreach $Clone_i$ ∈ Clones **do**
                $Clone_i$ ← MutateRelativeToFitnessOfParent($Clone_i$, $Cell_i$);
            end
            EvaluatePopulation(Clones);
            Progeny ← GetBestSolution(Clones);
        end
    end
    SupressLowAffinityCells(Progeny, AffinityThreshold);
    Progeny ← CreateRandomCells(N_{random});
    Population ← Progeny;
end
return S_{best};

5. Dendritic Cells

- Dendritic cells (DCs) act as messengers between innate immune system and adaptive immune system, as well as mediators of various immune responses.

5. Dendritic Cells

Dendritic cells (DCs) are exposed to various molecular information/signals and antigens at their immature state in tissue.

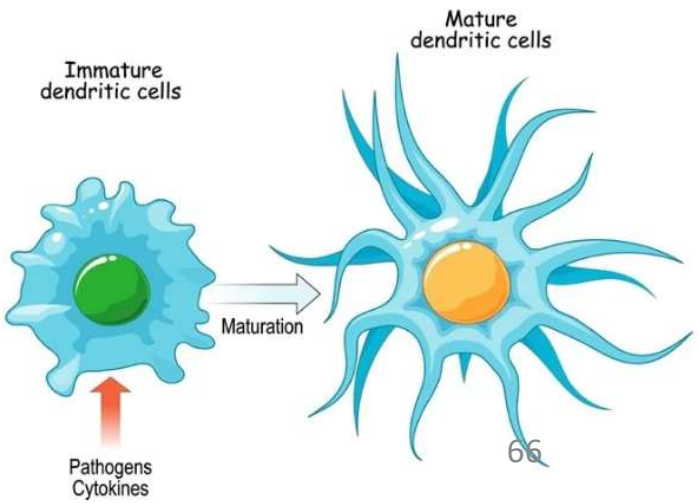
3 main types of signals:

- Pathogen(antigen)-associated molecular patterns (PAMPs),
- Danger signals derived from uncontrolled cell death (necrosis),
- Safe signals resulting from programmed cell death (apoptosis).

5. Dendritic Cells

If more PAMPs and danger signals are presented,

- DCs differentiate into fully mature state and report an anomalous status in tissue.
- If more safe signals are presented,
- DCs differentiate into semi-mature state and report a normal status in tissue.



5. Dendritic Cells

- Pseudocode for deterministic dendritic cell algorithm.

Input: InputPatterns, $iterations_{max}$, $cells_{num}$, $MigrationThresh_{bounds}$
Output: MigratedCells
ImmatureCells ← InitializeCells($cells_{num}$, $MigrationThresh_{bounds}$);
MigratedCells ← ∅;
for $i = 1$ **to** $iterations_{max}$ **do**
  P_i ← SelectInputPattern(InputPatterns);
  k_i ← ($P_{i_{danger}} - 2{\times}P_{i_{safe}}$);
  cms_i ← ($P_{i_{danger}} + P_{i_{safe}}$);
  foreach $Cell_i \in$ ImmatureCells **do**
    UpdateCellOutputSignals($Cell_i$, k_i, cms_i);
    StoreAntigen($Cell_i$, $P_{i_{antigen}}$);
    if $Cell_{i_{lifespan}} \leq 0$ ***then***
      ReInitializeCell($Cell_i$);
    else if $Cell_{i_{csm}} \geq Cell_{i_{thresh}}$ **then**
      RemoveCell(ImmatureCells, $Cell_i$);
      ImmatureCells ← CreateNewCell($MigrationThresh_{bounds}$);
      if $Cell_{i_k} < 0$ **then**
        $Cell_{i_{type}}$ ← Mature;
      else
        $Cell_{i_{type}}$ ← Semimature;
      end
      MigratedCells ← $Cell_i$;
    end
  end
end
return MigratedCells;

cms : concentration of co-stimulatory molecules (CSM)
K: abnormality of signals seen by a dendritic cell

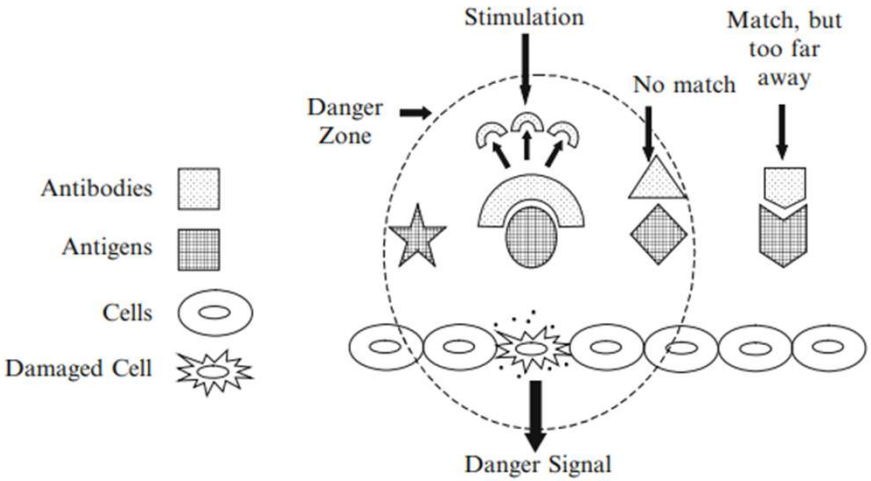
6. Danger Theory

- The central idea in the Danger Theory is that the immune system does not respond to nonself but to danger.
- This theory is borne out of the observation that there is no need to attack everything that is foreign,
- In this theory, danger is measured by damage to cells indicated by distress signals that are sent out when cells die an unnatural death.

6. Danger Theory

According to the Danger Theory (Aickelin and Cayzer 2002):

- A cell that is in distress sends out an alarm signal,
- Antigens in the neighborhood are captured by antigen presenting cells(APCs),
- APCs travel to the local lymph node and present the antigens to lymphocytes(B and T cells).
- The danger signal establishes a danger zone around itself.
- B-cells producing antibodies that match antigens within the danger zone get stimulated and produce clones.
- Those that do not match or are too far away do not get stimulated.



Danger theory illustration

6. Danger Theory

How could we use the Danger Theory in Artificial Immune Systems?

- The Danger Theory provides ideas about which data the Artificial Immune Systems should represent and deal with; dangerous (i.e. interesting) data.
- The challenge is to define a suitable danger signal, as fitness function for an evolutionary algorithm.
- The physical distance in the biological system should be translated into a suitable measure for similarity or causality in Artificial Immune Systems.

6. Danger Theory

- The Danger theory is not complete,
- there are some doubts about how much it actually changes behavior and/or structure.
- But the theory contains enough interesting ideas for Artificial Immune Systems

7. NSA, INA, and CSA Application area

	NSA	INA	CSA
Application Area	• Virus protection • Monitoring tools • Binary classification • Computer security • Rapid response detection system	• Control • Clustering/unsupervised clustering/classification • Data mining / data analysis / data visualization • DNA classification • Text classification • Pattern recognition • Optimization • Mobile-robot behavior arbitration	• Optimization/multi-modal optimization • Binary character recognition • Numeric data classification • Solving complex machine learning tasks • Alternative to genetic algorithm and evolutionary algorithm • Complex combinatorial optimization problems

3. Exploration and Exploitation

3. Exploration and Exploitation

- Exploration in AIS involves searching for new and diverse solutions to the problem at hand.
- This can be achieved through various mechanisms such as random mutation or the introduction of novel elements into the system.
- Exploration allows the system to search beyond the local optima and discover potentially better solutions.

3. Exploration and Exploitation

- Exploitation in AIS involves utilizing the knowledge and experience gained through previous exploration to improve the current solution.
- This can be achieved through mechanisms such as clonal selection or affinity maturation, which selectively amplify and refine the best solutions found during exploration.
- Exploitation allows the system to converge towards the best solutions found so far.

3. Exploration and Exploitation

- The balance between exploration and exploitation is critical in AIS.
- Too much exploration can lead to a lack of convergence towards a good solution, while too much exploitation can lead to getting stuck in local optima.

III. MULTI OBJECTIVE ARTIFICIAL IMMUNE ALGORITHM

1. Introduction
2. Basic concepts of multi-objective optimization
3. MOIA
4. MOIA categories

1. Introduction

- MOIA was used in different areas:
- SVM optimization:
  - A multi-objective artificial immune algorithm for parameter optimization in support vector machine (2009)
- With ANN to solve multiobjective programming problems:
  - Artificial immune system based neural networks for solving multi-objective programming problems(2010)
- Manufacturing industry:
  - Improved artificial immune algorithm for the flexible job shop problem with transportation time(2020)

2. Basic concepts of multi-objective optimization

1) Multi-objective optimization problems (MOPs)
2) Dynamic multi-objective optimization problems (DMOPs)
3) Constrained multi-objective optimization problems (CMOPs)
4) Pareto-dominance and Pareto-optimality

2. Basic concepts of multi-objective optimization

1) Multi-objective optimization problems (MOPs)

Optimization problems with several objectives, which may be conflicted with each other. Defined by:

$$\min_{x \in \Omega} F(x) = \left(f_1(x), f_2(x), \ldots, f_m(x)\right)^T$$

where Ω the decision space and R^m the objective space (m is the number of objectives).

The objective function $F: \Omega \rightarrow R^m$ consists of m real-valued objective functions.

2. Basic concepts of multi-objective optimization

1) Multi-objective optimization problems (MOPs)

The main goals for solving MOPs are to obtain a set of Pareto-optimal solutions (PS) with:

- Good performance on convergence that can approach the Pareto-optimal front (PF)
- Good diversity that can evenly cover the PF.

2. Basic concepts of multi-objective optimization

2) Dynamic multi-objective optimization problems (DMOPs)

Can be defined as:

$$minimize\ f(x,t) = \{f_1(x,t), f_2(x,t), \ldots, f_m(x,t)\}$$

where t means the time index, $x \in R^n$ is a vector of n-dimensional decision variables, and $\Omega \in R^n$ indicates the decision space.

2. Basic concepts of multi-objective optimization

2) Dynamic multi-objective optimization problems (DMOPs)

The DMOP includes m real-valued objective functions at each time t, continuous with respect to x over Ω.

The number of objective functions remains fixed over time.

2. Basic concepts of multi-objective optimization

2) Dynamic multi-objective optimization problems (DMOPs)

the DMOPs can be classified into four categories according to the cases whether PS or PF changes.

- PS changes over time, while PF remains fixed;
- Both PS and PF change over time;
- PF changes over time, but PS remains unchanged;
- Both PS and PF remain unchanged, while the environment may change during the evolutionary process.

2. Basic concepts of multi-objective optimization

3) Constrained multi-objective optimization problems (CMOPs)

$$\left.\begin{aligned} minimize \quad & f(x) = (f_1(x), f_2(x), \dots, f_m(x)) \\ subject\ to \quad & g_j(x) \le 0, \quad j = 1,2, \dots, \mathrm{q}; \\ & h_j(x) = 0, \quad j = \mathrm{q}+1, \dots, \mathrm{m}; \\ & x = [X_1, X_2, \dots, X_D] \in S, \quad L_i \le x_i \le U_i; \end{aligned}\right\}$$

- Where $S = \prod_{i=1}^{D}[L_i, U_i]$ the decision space, $f_i(x)$ the objective function, $g_j(x)$ inequality constraints, $h_j(x)$equality constraints

2. Basic concepts of multi-objective optimization

3) Constrained multi-objective optimization problems (CMOPs)

- The individual x is called a feasible individual if and only if it meets the constraints.
- The individual x is called an infeasible individual when it doesn't satisfy the constraints.

2. Basic concepts of multi-objective optimization

4) Pareto-dominance and Pareto-optimality

For two solutions $x_1, x_2 \in \Omega$, x_1 dominates x_2, noted by $x_1 \prec x_2$, if and only if

- $f_i(x_1) \leq f_i(x_2)$ for all $i \in \{1,2, \ldots, m\}$ and
- $f_j(x_1) \neq f_j(x_2)$ for at least one $j \in \{1,2, \ldots, m\}$.

2. Basic concepts of multi-objective optimization

4) Pareto-dominance and Pareto-optimality

For the Pareto-optimality, a solution x is said to be Pareto-optimal :

if and only if $\neg\exists y \in \Omega: \quad y \prec x$.

2. Basic concepts of multi-objective optimization

4) Pareto-dominance and Pareto-optimality

- The set of Pareto-optimal solutions (PS) is composed by all the Pareto-optimal solutions, defined as

$$PS = \{x | \neg\, \exists y \in \Omega:\ \ y \prec x\}$$

- The set of Pareto-optimal front(PF) includes the values of all the objective functions corresponding to the Pareto optimal solutions in PS, i.e.,

$$PF = \{F(x) = \left(f_1(x), f_2(x), \dots, f_m(x)\right)^T | x \in PS\}$$

3. MOIA

1) Yoo and Hajela's Algorithm,
2) I-PAES
3) Luh and Chueh's MOIA
4) MISA
5) MOCSA
6) VAIS
7) IDCMA
8) IFMOA
9) ACSAMO
10) A Common Framework for MO-AIS Algorithms

3. MOIA

1) Yoo and Hajela's Algorithm,

- The first multiobjective technique that employed AIS.
- Used a genetic algorithm, with normal selection, crossover, and mutation operators, but employing immune-based ideas for modifying the fitness values.

3. MOIA

1) Yoo and Hajela's Algorithm,

In their algorithm:

1. the memory population A(t) containing the nondominated solutions is called antigen population.
2. The online population B(t) is called antibody population.
3. One antigen is randomly selected from A(t)
4. S antibodies are randomly selected from B(t).
5. The affinity (similarity) between antigen and antibodies is calculated and the one with the highest affinity has his fitness value increased.
6. This process is repeated a given number of times.

3. MOIA

1) Yoo and Hajela's Algorithm,

- Although Yoo and Hajela's algorithm can not be considered a true MO-AIS,
- It is pioneer in using AIS ideas in multiobjective optimization.

3. MOIA

2) Immune Pareto Archived Evolution Strategy (I-PAES)

- Hybrid approach,
- Based on the PAES algorithm, with a local search phase based on the clonal selection principle.
- The original PAES is a multiobjective (1+1) local search evolution strategy, that proposes a grid-based approach for maintaining diversity in the offline population.

3. MOIA

2) Immune Pareto Archived Evolution Strategy (I-PAES)

- I-PAES modifies the variation mechanism in the original PAES(1+1) by using immune inspired operators, specifically cloning and hypermutation.
- The authors demonstrate the application of I-PAES in protein structure prediction problems.

3. MOIA

2) Immune Pareto Archived Evolution Strategy (I-PAES)

- The authors demonstrate the application of I-PAES in protein structure prediction problems.

3. MOIA

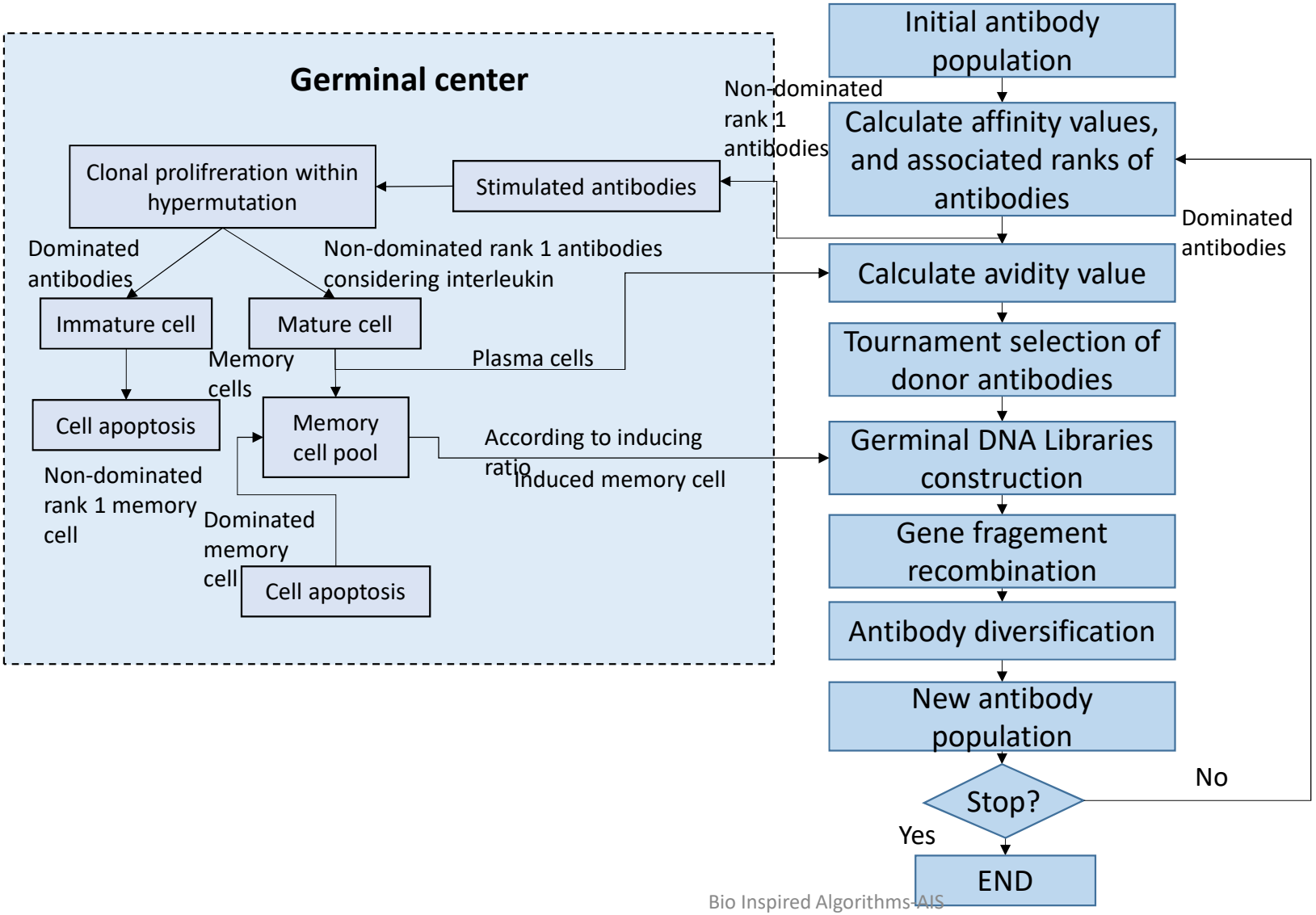
3) Luh and Chueh's MOIA

Complex algorithm with a strong biological motivation,

Based on the Clonal Selection theory, DNA library building, distinction between heavy and light protein chains in the antibodies, interleukin interactions, and a number of other immunological models.

MOIA uses binary representation of the search space, with each variable of the candidate solutions represented by a heavy chain part (the most significant bits) and a light chain (less significant bits).

This distinction is used at a certain stage of the algorithm to implement a local search procedure around the most promising solutions of the population.



Luh and Chueh's MOIA

3. MOIA

4) Multi-objective Immune System Algorithm (MISA)

MISA is an immune algorithm based on the Clonal Selection Principle with elitism.

- Uses a grid-based random generation of the initial population in the search space,
- Selection strategy for choosing the antibodies to be cloned, based both dominance and feasibility.
- The number of clones each selected antibody receives is regulated by a niching procedure in the objective space, in order to drive the evolution towards a fair sampling of the Pareto front.

3. MOIA

4) Multi-objective Immune System Algorithm (MISA)

- The performance of the MISA has shown a competitive performance when compared to NSGA-2, micro-GA, and PAES.

3. MOIA

5) Multi-Objective Clonal Selection Algorithm (MOCSA)

- Combines ideas from CLONALG and opt-AINet in a MO-AIS algorithm for real-valued optimization.
- The quality values are calculated using nondominated sorting.
- The population is sorted based on these values,
- The first Nc best solutions are selected for cloning.
- MOCSA uses real-coding and Gaussian mutation similarly to opt-AINet.
- The number of clones in the proliferation phase depends on the ranking of the individual in the nondominated fronts.

3. MOIA

5) MOCSA

- The mutated clones are evaluated and combined with the original ones.
- Sorted again using nondominated sorting and the Nc best solutions are preserved.
- MOCSA employs a diversity generation mechanism : the worst individuals, i.e., those not selected for cloning, are eliminated and substituted by randomly generated individuals.

3. MOIA

6) The Vector Artificial Immune System (VAIS)

- Multiobjective version of the opt-AINet algorithm.
- In VAIS, a multiobjective algorithm whose memory population stores the nondominated solutions.
- VAIS employs real representation of the variables and quality-proportional Gaussian mutation, as in the opt-AINet.

3. MOIA

6) The Vector Artificial Immune System (VAIS)

- To evaluate the quality values, VAIS utilizes strength values likewise in SPEA2 , but without the use of density values, since the suppression mechanism in the memory population already deals with dense regions.
- The suppression mechanism considers similarity in the objective space, not in the parameter space as in opt-AINet.

3. MOIA

7) The Immune Dominance Clonal Multi-objective Algorithm (IDCMA)

- Introduces a new similarity measure between antibodies, based on distances in the objective space: the immune differential degree.
- this similarity measure is used to reduce the size of the offline population in the update step.
- presents a different selection mechanism for cloning: one antibody is randomly selected from the offline population in the beginning of each iteration.

3. MOIA

7) The Immune Dominance Clonal Multi-objective Algorithm (IDCMA)

- The quality value of each individual in the online population is computed based on the antibody-antibody affinity
- The population is sorted based on these affinity values,
- The first Nc ones are selected for cloning.
- Finally, the solutions in the clone population undergo recombination and mutation to generate the next population.

3. MOIA

8) the Immune Forgetting Multiobjective Optimization Algorithm (IFMOA)

- Based on the clonal selection principle for the variation step.
- The scalar quality values for the solutions are calculated in the same way as in SPEA2.
- The selection for cloning is deterministic and the same number of clones is used for each solution.
- The immune forgetting operator, consists of replacing a given number of solutions from the online population, randomly selected, by individuals from the offline population, also randomly selected.
- The authors do not clarify the benefit of this operator to the algorithm

3. MOIA

9) Adaptive Clonal Selection Algorithm for Multiobjective Optimization (ACSAMO)

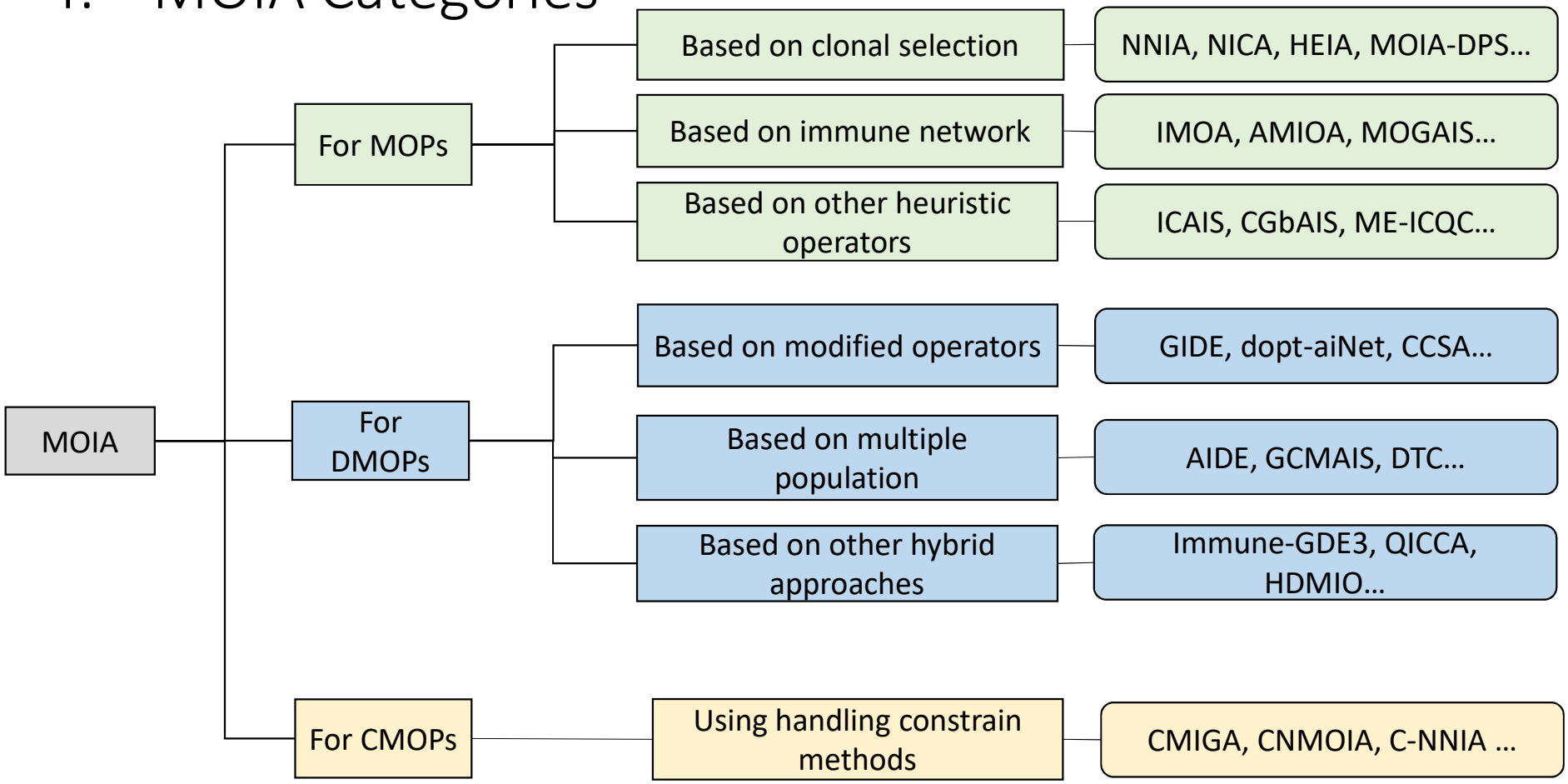
- Based on the Clonal Selection Principle I
- Proposed in 2006 by Wang and Mahfouf. ACSAMO
- Generates a fixed number of clones for all antibodies and presents a quality-proportional mutation, like in the VAIS.
- The antibody-antigen affinities are calculated by using a dynamically adjusted weighted approach, in which an evolutionary pressure in the direction of the “best so far” and “best this generation” solutions is applied over the online population.
- At each generation, the two “best” solutions are found according to a random-weight linear aggregation of objectives,

3. MOIA

10) A Common Framework for MO-AIS Algorithms based on clonal selection

```
t=0;
initializeOfflinePopulation(A(t=0));
initializeOnlinePopulation (B(t=0));
while not stop_condition do
    Ψ(t) = avidity(B(t));                                    //or Ψ(t) = affinity(B(t)
    C(t) = P(t).selectForCloning(A(t), B(t), Ψ(t) );
    D(t) = proliferationAndMutation(C(t));
    E(t) = diversification();
    A(t+1) = update(A(t), B(t));
    B(t+1)= D(t) + E(t);
    t=t+1;
end
```

4. MOIA Categories



MOIA categories