

Peptide Computing – Universality and Complexity

M.Sakthi Balan

Kamala Krithivasan

Y.Sivasubramanyam

Department of Computer Science and Engineering,

Indian Institute of Technology, Madras, India

Organization

Natural Computing

Biological Computing

DNA Computing

Peptide Computing

Solving HPP

Solving Exact 3-cover set problem

Universality Result

Conclusion

Natural Computing

Biological Computing

Quantum Computing

Biological Computing

DNA Computing

Peptide Computing

DNA Computing

Uses DNA strands and Watson-Crick Complementarity as operation

Highly *non-deterministic*

Massive *parallelism*

Solves NP-Complete Problems quite efficiently

Peptide Computing

Uses peptides and antibodies

Operation – binding of antibodies to epitopes in peptides

Epitope – The site in peptide recognized by antibody

Highly *non-deterministic*

Massive *parallelism*

Peptide Computing Contd..

Peptides – sequence of amino acids

Twenty amino acids. Example – Glycine, Valine

Connected by covalent bonds

Peptide Computing Contd..

Antibodies recognizes epitopes by binding to it

Binding of antibodies to epitopes has associated power called *affinity*

Higher priority to the antibody with larger affinity power

Computing DNA Vs Peptide

Four building blocks

Adenine (A),
Guanine (G), Cytosine
(C), Thiamine (T)

Only one reverse
complement –

Watson-Crick
Complement

Complement (A) = T
and Complement (G)

Twenty building
blocks (20 amino
acids)

Example: Glycine,
Valine

Different antibodies
can recognize
different epitopes

Binding affinity of

antibodies can be 9

different

Peptide Computing Model

Peptides represent sample space of the problem

Antibodies are used to select the correct solution of the problem (i.e. peptides)

Definition

For finite sequence $M = m_1, m_2, \dots, m_n$
the *doubly duplicated sequence* is

$$MM = m_1, m_1, m_2, m_2, \dots, m_n, m_n$$

Doubly duplicated permutation of a
finite set S is

$\{mm \mid m \text{ is a permutation of the set } S\}$

Hamiltonian Path Problem

$G = (V, E)$ is a directed graph

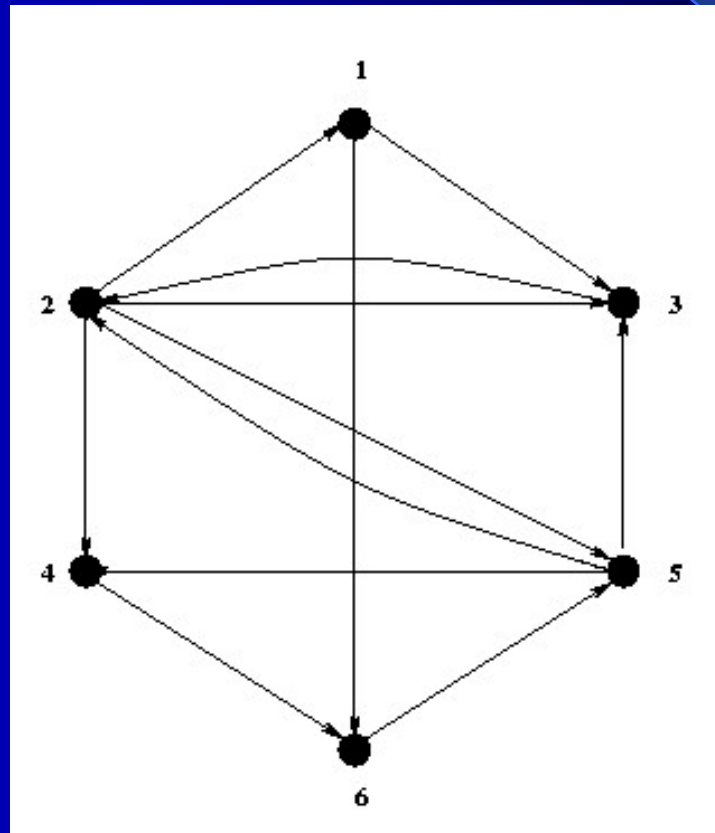
$V = \{v_1, v_2, \dots, v_n\}$ is the vertex set

$E = \{e_{ij} \mid v_i \text{ is adjacent to } v_j\}$ is the edge set

v_1 - source vertex, v_n - end vertex

Problem – Test whether there exists a Hamiltonian path between v_1 and

Graph G



Peptides Formation

Each vertex v_i has a corresponding epitope ep_i

Each peptide has ep_1 on one extreme and ep_n on the other extreme

All doubly duplicated permutations of

$\{ep_2, \dots, ep_{n-1}\}$ are formed in each of the peptide in between ep_1 and ep_n

Antibody Formation

Form antibodies A_{ij} – site = $ep_i ep_j$
s.t. v_j is adj. to v_i

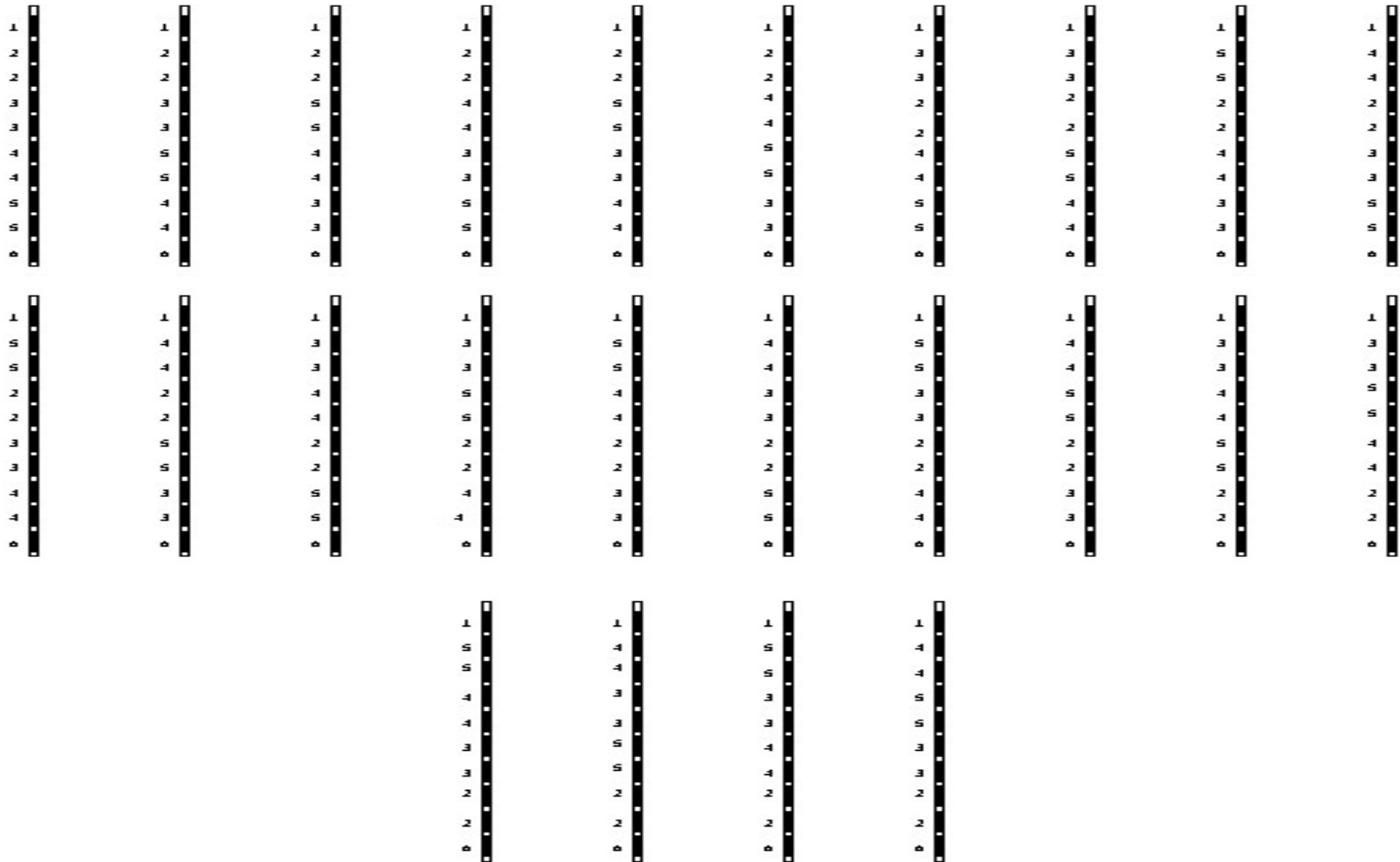
Form antibodies B_{ij} – site = $ep_i ep_j$ s.t.
 v_j is not adj. to v_i

Form antibody C – site is whole of
peptide

$\text{Affinity}(B_{ij}) > \text{Affinity}(C)$

$\text{Affinity}(C) > \text{Affinity}(A_{ij})$

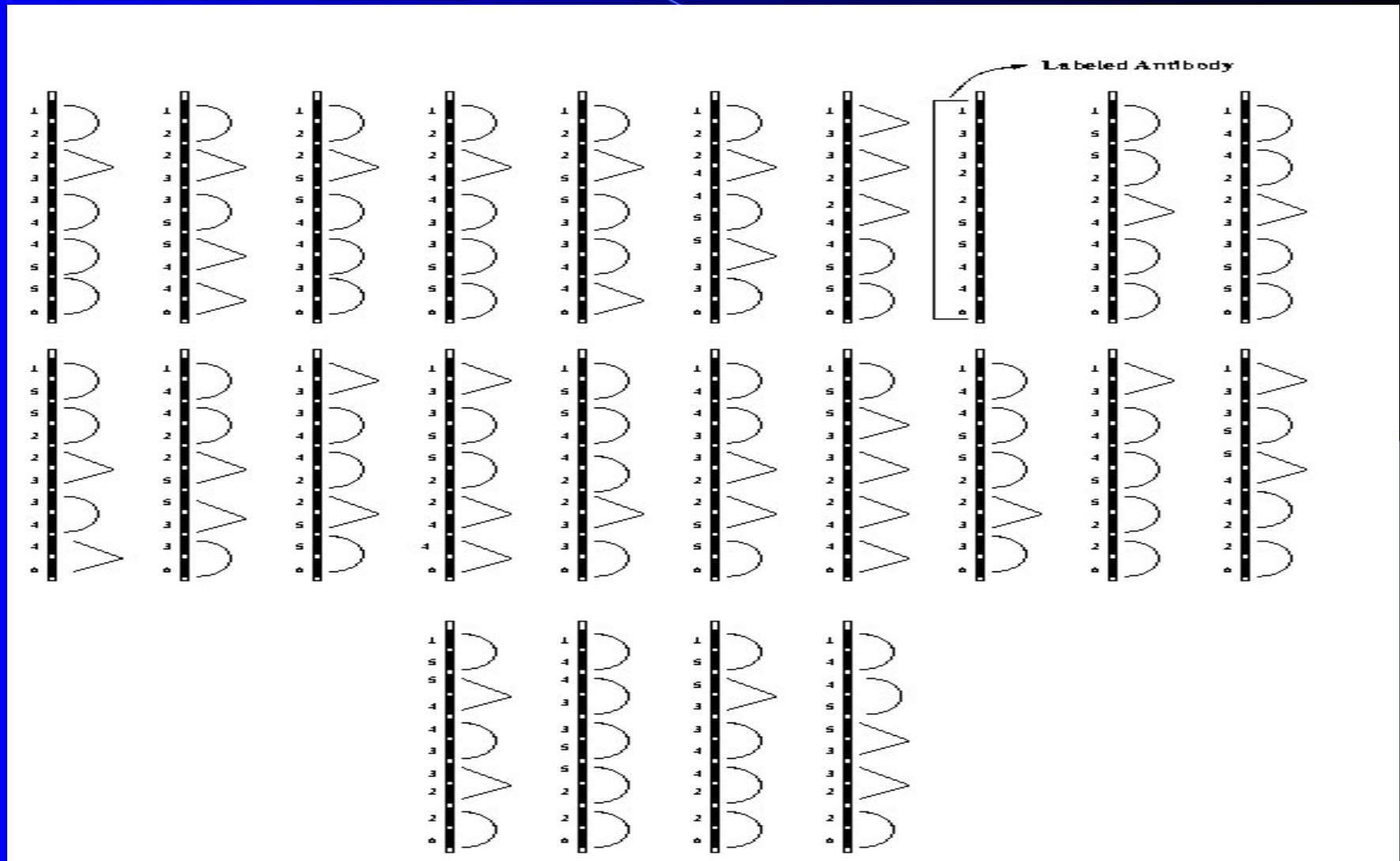
Peptide Solution Space



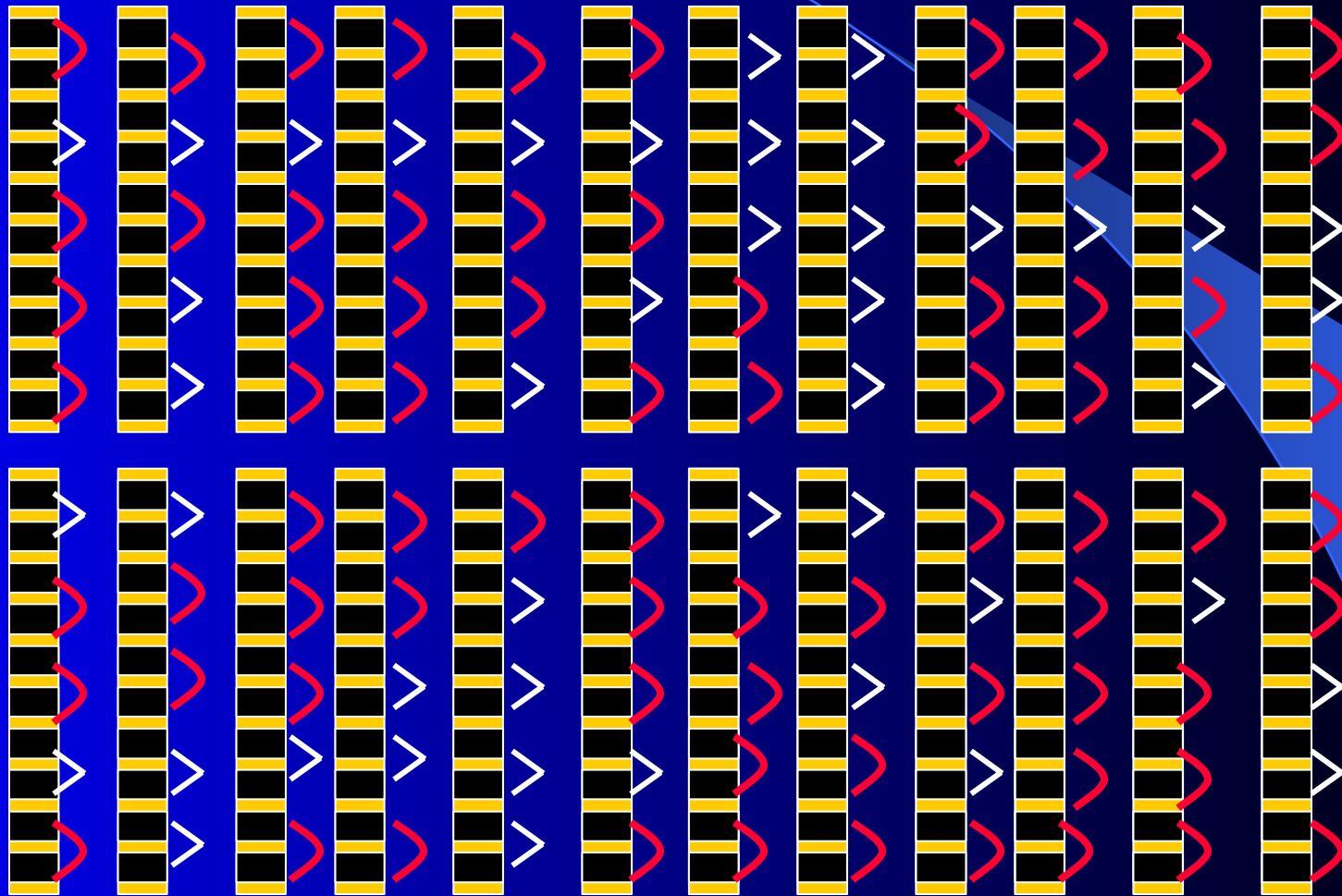
Algorithm

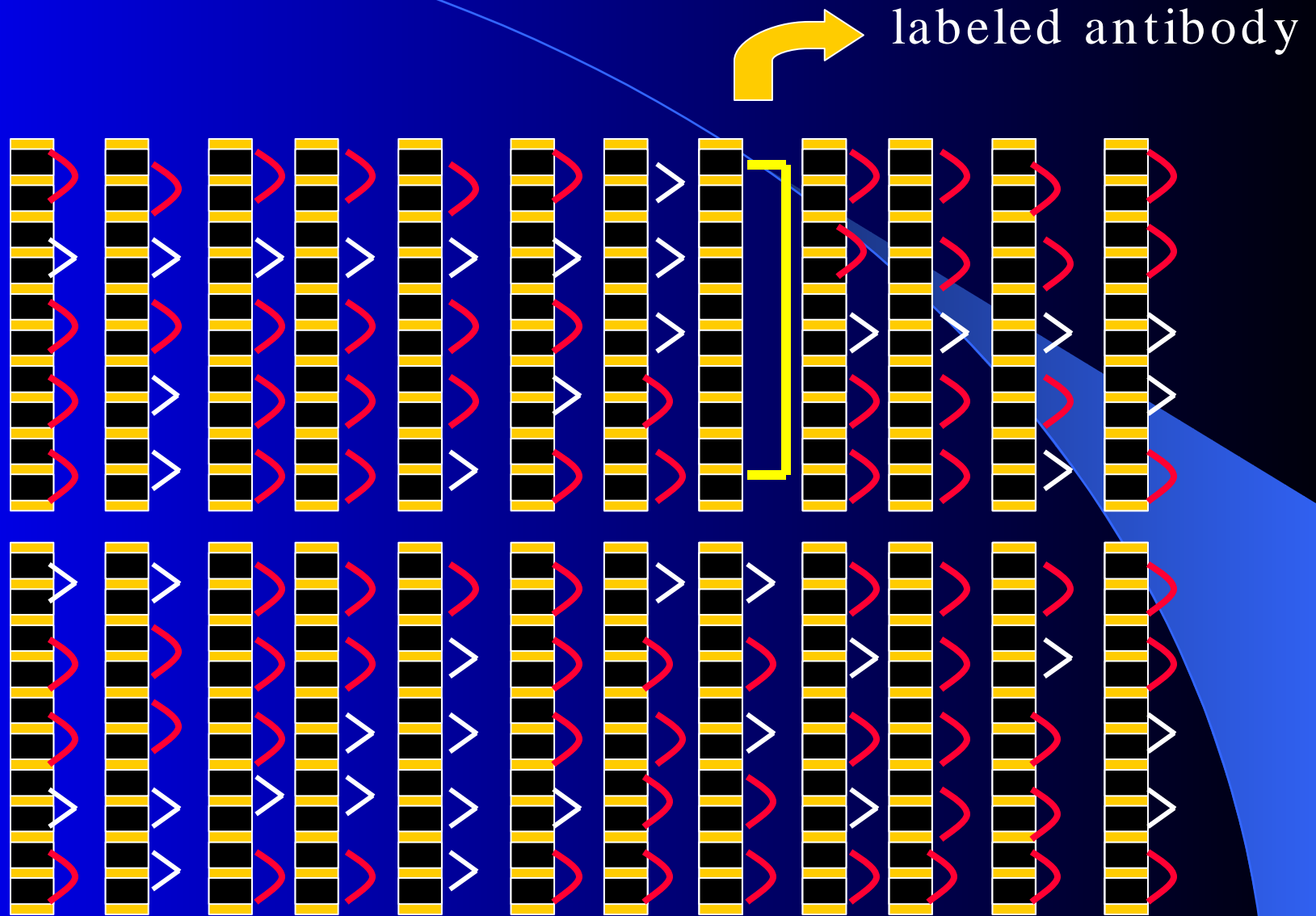
1. Take all the peptides in an aqueous solution
2. Add antibodies A_{ij}
3. Add antibodies B_{ij}
4. Add labeled antibody C
5. If fluorescence is detected answer is *yes* or else the answer is *no*

Peptides with Antibodies



Peptide with Antibodies





Complexity

Number of peptides = $(n-2)!$

Length of peptides = $O(n)$

Number of antibodies = $O(n^2)$

Number of Bio- steps is
constant

Exact Cover by 3- Sets Problem

Instance: A finite set $X = \{x_1, x_2, \dots, x_n\}$,
 $n = 3q$ and a collection C of 3-
elements subsets of X

Question: Does C contain an *Exact Cover* for X

Peptide Formation

For each x_i a specific epitope ep_i is chosen

For every permutation of the set $\{ep_i\}$ a peptide is chosen *s.t.* every subsequence of $ep_i ep_j ep_k$ is followed by the epitope ep_{ijk}

Example

$$X = \{x_1, x_2, \dots, x_9\}$$

For permutation

$$x_1, x_7, x_9, x_2, x_6, x_4, x_3, x_5, x_8$$



Antibody Formation

Form antibodies A_{ijk} , site = $ep_i ep_j ep_k$ if $\{x_i, x_j, x_k\}$ is in C

Form antibodies B_{ijk} , site = $ep_i ep_j ep_k$ if $\{x_i, x_j, x_k\}$ is not in C

Form colored antibody C , site is whole of peptide

$\text{Affinity}(B_{ijk}) > \text{Affinity}(C)$

$\text{Affinity}(C) > \text{Affinity}(A_{ijk})$

Algorithm

Take all the antibodies in an aqueous solution.

Add antibodies A_{ijk}

Add antibodies B_{ijk}

Add antibody C

If fluorescence is detected the answer is *yes* otherwise *no*

Complexity

Number of peptides = $n!$

Length of peptides = $O(n)$

Number of Antibodies = $O(n^3)$

Number of Bio- steps is *constant*

Peptide Computing is Computationally Complete

A Turing Machine can be
simulated by a Peptide
System

Assumptions

Turing Machine halts when it reaches a final state

Let $s(n)$ be the space complexity of the Turing Machine

Assume that $s(n)$ is apriori known

Universality Result

Turing machine, $M = (Q, \Sigma, \delta, s_0, F)$

$$Q = \{q_1, q_2, \dots, q_m\}$$

$$\Sigma = \{a_1, a_2, \dots, a_l\}$$

B is the blank symbol

Universality Result Contd..

Form $s(n)$ epitopes,

$$E_Q = \{ep_i^Q \mid 1 < i < s(n)\}$$

Form $s(n)$ epitopes,

$$E_\Sigma = \{ep_i^\Sigma \mid 1 < i < s(n)\}$$

Universality Result Contd..

Form $s(n)*m$ antibodies,

$$A_Q = \{A_i^q \mid 1 < i < s(n), q \in Q\}$$

Form $s(n)*l$ antibodies,

$$A_\Sigma = \{A_i^a \mid 1 < i < s(n), a \in \Sigma \cup \{b\}\}$$

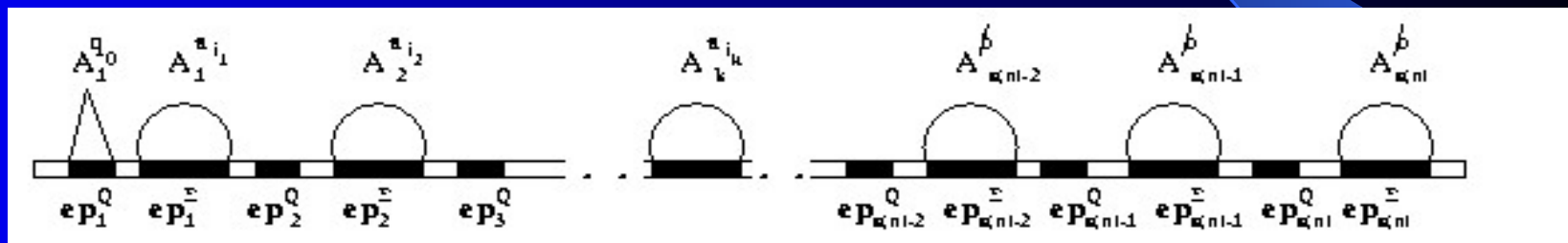
- The antibodies $A_{i_f}^q$ are labeled

Universality Result Contd..

Peptide without antibodies



Initial Configuration of Peptide



Simulating the Right Move

M moves from $a_i q a_j a_j$ to $a_i a_j q' a_j$

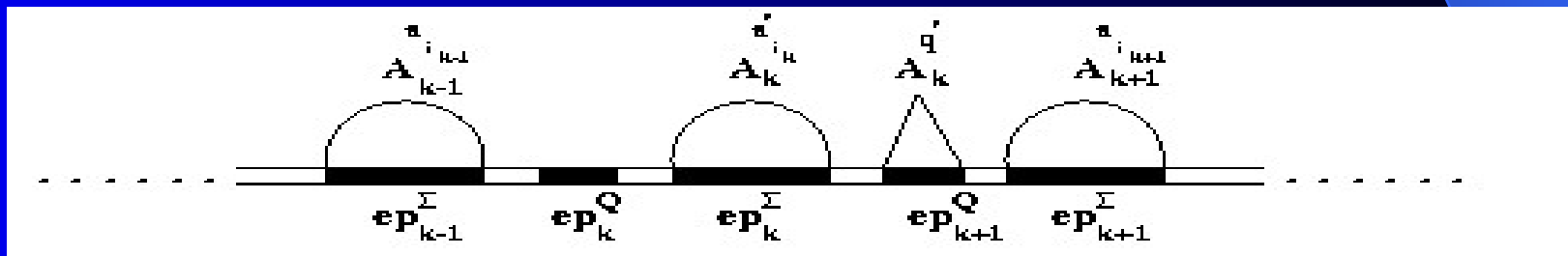
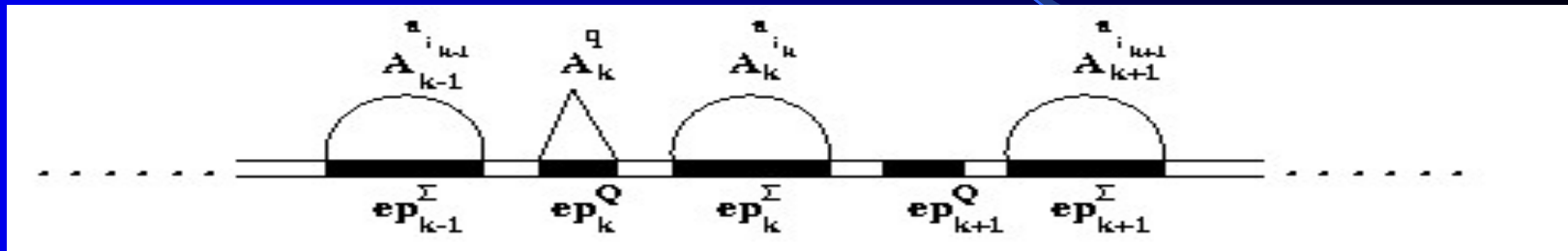


Add excess of free epitopes ep_k^Σ and ep_k^Q

Add antibodies $A_k^{a_j}$ and $A_{k+1}^{q'}$

k is the position of the head prior to the right move

Simulating the Right Move Contd..



Simulating the Left Move

M moves from $a_i q a_j a_j$ to $q' a_i a_j a_j$



Add excess of free epitopes ep_k^Σ and ep_k^Q

Add antibodies $A_k^{a_j}$ and $A_{k-1}^{q'}$

k is the position of the head prior to the right move

Complexity

Peptide system takes $O(t(n))$ time

Length of the peptide is $O(s(n))$

Number of peptide is *one*

Amount of antibodies is

$$O(m.s(n) + l.(s(n)))$$

What Next...

Complexity Issues

Cost effectiveness

Implementation Difficulties

Theoretical Model

The image features the words "Thank You" in a large, 3D, orange-yellow font with a slight gradient. The text is positioned diagonally across the center of the frame. The background is a solid dark blue, with a lighter blue curved band or arc sweeping from the top left towards the bottom right, passing behind the text.

Thank You