AGENT ENABLED MINING OF DISTRIBUTED PROTEIN DATA BANKS

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ABSTRACT

Mining biological data is an emergent area at the intersection between bioinformatics and data mining (DM). The intelligent agent based model is a popular approach in constructing Distributed Data Mining (DDM) systems to address scalable mining over large scale distributed data. The nature of associations between different amino acids in proteins has also been a subject of great anxiety. There is a strong need to develop new models and exploit and analyze the available distributed biological data sources. In this study, we have designed and implemented a multi-agent system (MAS) called Agent enriched Quantitative Association Rules Mining for Amino Acids in distributed Protein Data Banks (AeQARM-AAPDB). Such globally strong association rules enhance understanding of protein composition and are desirable for synthesis of artificial proteins. A real protein data bank is used to validate the system.

KEYWORDS

Knowledge Discovery, Association Rules, Intelligent Agents, Multi-Agent System, Bioinformatics.

1. INTRODUCTION

Data Mining (DM) is a process to automatically extract some interesting and valid data patterns or trends representing knowledge, implicitly stored in large databases [1], [2]. Distributed Data Mining (DDM) is concerned with application of classical DM procedures in a distributed computing environment trying to make the best of the available resources. In DDM, DM takes place both locally at each geographically distributed site and at a global level where the local knowledge is merged in order to discover global knowledge. A DDM system is a very complex entity that is comprised of many components; mining algorithms; communication subsystems; resources management; task scheduling; user interface etc. It should provide efficient access to both distributed data and computing resources; monitor the entire mining procedure; and present results to users in appropriate formats. A successful DDM system is also flexible enough to adapt to various situations [3], [4], [5], [6], [7].

Intelligent software agent technology is an interdisciplinary technology. The motivating idea of this technology is the development and efficient utilization of autonomous software objects called agents, which have access to geographically distributed and heterogeneous information resources to simplify the complexities of distributed computing. They are autonomous, adaptive, reactive, pro-active, social, cooperative, collaborative and flexible. They also support temporal continuity and mobility within the network. An intelligent agent with mobility feature is known as Mobile Agent (MA). MA migrates from node to node in a heterogeneous network without losing its operability. It can continue to function even if the user is disconnected from the network. On reaching at a node MA is delivered to an Agent Execution Environment (AEE) where its executable parts are started running. Upon completion of the desired task, it delivers the results to
the home node. With MA, a single serialized object is transmitted over the network carrying the small amount of resultant data only thus reducing the consumption of network bandwidth, latency (response time delay) and network traffic. An AEE or Mobile Agent Platform (MAP), is server application that provides the appropriate functionality to MAs to authenticate, execute, communicate (with other agents, users, and other platforms), migrate to other platform, and use system resources in a secure way. A Multi Agent System (MAS) is distributed application comprised of multiple interacting intelligent agent components [8].

Table 1. Single Letter codes for Amino Acids

| Sr. No. | Amino Acid Name | Single Letter Code | Three Letter Code |
|---------|-----------------|--------------------|-------------------|
| 1       | Alanine         | A                  | Ala               |
| 2       | Cysteine        | C                  | Cys               |
| 3       | Aspartic Acid   | D                  | Asp               |
| 4       | Glutamic Acid   | E                  | Glu               |
| 5       | Phenylalanine   | F                  | Phe               |
| 6       | Glycine         | G                  | Gly               |
| 7       | Histidine       | H                  | His               |
| 8       | Isoleucine      | I                  | Ile               |
| 9       | Lysine          | K                  | Lys               |
| 10      | Leucine         | L                  | Leu               |
| 11      | Methionine      | M                  | Met               |
| 12      | Asparagine      | N                  | Asn               |
| 13      | Proline         | P                  | Pro               |
| 14      | Glutamine       | Q                  | Gln               |
| 15      | Arginine        | R                  | Arg               |
| 16      | Serine          | S                  | Ser               |
| 17      | Threonine       | T                  | Thr               |
| 18      | Valine          | V                  | Val               |
| 19      | Tryptophan      | W                  | Trp               |
| 20      | Tyrosine        | Y                  | Tyr               |

Bioinformatics or computational molecular biology aims at automated analysis and the management of high-throughput biological data as well as modelling and simulation of complex biological systems. Bioinformatics has very much changed since the first sequence alignment algorithms in 1970s [9]. Today in-silico analysis is a fundamental component of biomedical research. Bioinformatics has now encompasses a wide range of subject areas from structural biology, genomics to gene expression studies [10], [11]. The post-genomic era has resulted into availability of the enormous amount of distributed biological data sets that require suitable tools and methods for modelling and analyzing biological processes and sequences. The bioinformatics research community feels a strong need to develop new models and exploit and analyze the available genomes [12]. The protein sequences are made up of 20 types of Amino Acids (AA). Each AA is represented by a single letter alphabet as shown in Table 1. Unique 3-dimensional structure of each protein is decided completely by its amino-acid sequence. Proteins are important constituents of cellular machinery of any organism and the functioning of proteins heavily depends upon its AA sequence. A slight change in the sequence might completely change the functioning of the protein. Therefore, the nature of associations between different amino acids has been a subject of great anxiety. In [20], authors mine the association rules among amino acids in protein sequences. As per the literature available, no researcher has applied the agent technology to mine association rules for amino acids from distributed protein data sets. The amalgamation of
the DDM and MAS provides rewarding solution in terms of security, scalability, storage cost, computation cost and communication cost. Mining biological data is an emerging area and continues to be an extremely important problem, both for DM and for biological sciences [21]. State of the art in use of agent technology in bioinformatics is reviewed in [22].

The rest of the paper is organised as follows. Section 2 discusses the distributed association rule mining and preliminary notations used in this paper. A running environment for the proposed system is present in Section 3 along with algorithms used for various components and protein data banks used in this study. The layout and working of various agents involved in the proposed system and their algorithms are also discussed. System is implemented in Java and its performance is studied in Section 4 and finally the article is concluded in Section 5.

2. DISTRIBUTED ASSOCIATION RULE MINING

Let \( DB = \{T_j, j = 1 \ldots D\} \) be a transactional dataset of size \( D \) where each transaction \( T \) is assigned an identifier (\( TID \)) and \( I = \{d_i, i = 1 \ldots m\} \), total \( m \) data items in \( DB \). A set of items in a particular transaction \( T \) is called itemset or pattern. An itemset, \( P = \{d_i, i = 1 \ldots k\} \), which is a set of \( k \) data items in a particular transaction \( T \) and \( P \subseteq I \), is called \( k \)-itemset. Support of an itemset, \( \text{sup}(P) = \frac{\text{No.of.T.containing.P}}{D} \% \) is the frequency of occurrence of itemset \( P \) in \( DB \), where No_of_T_containing_P is the support count (sup_count) of itemset \( P \). Frequent Itemsets (FIs) are the itemset that appear in \( DB \) frequently, i.e., if \( \text{sup}(P) \geq \text{min.th.sup} \) (given minimum threshold support), then \( P \) is a frequent \( k \)-itemset. Finding such FIs plays an essential role in miming the interesting relationships among itemsets. Frequent Itemset Mining (FIM) is the task of finding the set of all the subsets of FIs in a transactional database. It is CPU and input/output intensive task, mainly because of the large size of the datasets involved [2].

Association Rules (ARs) first introduced in [13], are used to discover the associations (or co-occurrences) among item in a database. AR is an implication of the form \( P \Rightarrow Q \) [support,confidence] where, \( P \subseteq I, Q \subseteq I \) and \( P \) and \( Q \) are disjoint itemsets, i.e., \( P \cap Q = \emptyset \). An AR is measured in terms of its support (\( s \)) and confidence (\( c \)) factors. An AR \( P \Rightarrow Q \) is said to be strong if \( \text{support}(P \Rightarrow Q) \geq \text{min.th.sup} \) (given minimum threshold support) and \( \text{confidence}(P \Rightarrow Q) \geq \text{min.th.conf} \) (given minimum threshold confidence). Association Rule Mining (ARM) today is one of the most important aspects of DM tasks. In ARM all the strong ARs are generated from the FIs. The ARM can be viewed as two step process [14], [15].

1. Find all the frequent \( k \)-itemsets (\( L_k \))
2. Generate Strong ARs from \( L_k \)
   a. For each frequent itemset, \( l \in L_k \), generate all non empty subsets of \( l \).
   b. For every non empty subset \( s \) of \( l \), output the rule “\( s \Rightarrow (l - s) \)”, if
      \[
      \frac{\text{sup_count}(l)}{\text{sup_count}(s)} \geq \text{min.th.conf}
      \]

Distributed Association Rule Mining (DARM) generates the globally strong association rules from the global FIs in a distributed environment. Because of an intrinsic data skew property of the distributed database, it is desirable to mine the global rules for the global business decisions and
the local rules for the local business decisions. Comparative analysis of existing agent based DARM systems can be found in [23].

Few preliminaries notations and definitions required for defining DARM and to make this study self contained are as follows:

- \( S = \{ S_i, i = 1 \ldots n \} \), \( n \) distributed sites.
- \( S_{CENTRAL} \), Central Site.
- \( PDB_i = \{ PR_m, m = 1 \ldots X_i \} \), Protein Data Bank of \( X_i \) protein records at site \( S_i \), each \( PR_m \) has two main parts; first part is the description headers (PD) for structural classification of protein and the second part contains protein sequence (PS), i.e., the chain of amino acids. Snapshot of \( PDB_i \) is shown in Appendix A.1.
- \( FPDB_i = \{ PR_k, k = 1 \ldots D_i \} \), Filtered Protein Data Bank of \( D_i \) protein records at site \( S_i \), where length of \( PS \) in each \( PR \) is in the range \( \geq 50 \) and \( < 400 \). Snapshot of \( FPDB_i \) is shown in Appendix A.2.
- \( AAF_i \), Data bank of amino acids frequency for each \( PR \in FPDB \) at site \( S_i \). \( AAF_i \) is shown in Appendix A.3. \( AAF_i \) and \( AAF_j \) are not shown due to space constraint.
- \( BDB_i \), Boolean Data Bank that contains a value ‘1’ if the frequency of an amino acid lies in the specific range and ‘0’ otherwise at site \( S_i \). Snapshot of \( BDB_i \) is shown in Appendix A.5.
- \( IDB_i \), Itemset Data Bank of frequency partition items to map boolean value ‘1’ with its frequency partition item number at site \( S_i \). Snapshot of \( IDB_i \) is shown in Appendix A.6.
- \( FFI_k(i) \), Local frequent \( k \)-itemsets at site \( S_i \).
- \( FISC_k(i) \), List of support count \( \forall Itemset \in FFI_k(i) \).
- \( LSAR_i \), List of locally strong association rules at site \( S_i \).
- \( L^{TLSAR}_i = \bigcup_{k=1}^{n} L^{LSAR}_k \), List of total locally strong association rules.
- \( L^{TFI}_k = \bigcup_{i=1}^{n} L^{FI}_k(i) \), List of total frequent \( k \)-itemsets.
- \( L^{GFI}_k = \bigcap_{i=1}^{n} L^{FI}_k(i) \), List of global frequent \( k \)-itemsets.
- \( GSAR_{CENTRAL} \), List of Globally strong association rule.

Local Knowledge Base (LKB), at site \( S_i \), comprises of \( L^{FI}_k(i) \), \( L^{FISC}_k(i) \) and \( L^{LSAR}_k \) which can provide reference to the local supervisor for local decisions. Global Knowledge Base (GKB), at \( S_{CENTRAL} \), comprises of \( L^{TLSAR}_k \), \( L^{TFI}_k \), \( L^{GFI}_k \) and \( L^{GSAR}_{CENTRAL} \) for the global decision making. Like ARM, DARM task can also be viewed as two-step process [15]:

1. Find the global frequent \( k \)-itemset (\( L^{GFI}_k \)) from the distributed Local frequent \( k \)-itemsets (\( L^{FI}_k(i) \)) from the partitioned datasets.
2. Generate globally strong association rules (\( L^{GSAR}_{CENTRAL} \)) from \( L^{GFI}_k \).
3. Proposed AEQARM-AAPDB System

3.1. Environment for the proposed system

Every MAS needs an underlying AEE to provide running infrastructure on which agents can be deployed and tested. A running environment has been designed in Java to execute all the DM agents involved in the proposed system. Various attributes of the MA are encapsulated within a data structure known as AgentProfile. AgentProfile contains the name of MA (AgentName), version number (AgentVersion), entire byte code (BC), list of nodes to be visited by MA, i.e., itinerary plan ($L^{NODES}$), type of the itinerary (ItinType) which can be serial or parallel, a reference of current execution state (AObject) and an additional data structure known as Briefcase that acts as a result bag of MA to store final resultant knowledge (Result_S) at a particular site. Computational time (CPUTime) taken by a MA at a particular site is also stored in Briefcase. In addition to results, Briefcase also contains the system time for start of agent journey ($TripTime_{start}$), system time for end of journey ($TripTime_{end}$) and total round trip time of MA ($TripTime$) calculated using the formula $TripTime_{end} - TripTime_{start}$. This environment consists of the following three components:

- **Data Mining Agent Execution Environment (DM_AEE):** It is the key component that acts as a Server. DM_AEE is deployed on any distributed sites $S_i$ and is responsible for receiving, executing and migrating all the visiting data mining (DM) agents. It receives the incoming AgentProfile at site $S_i$, retrieves the entire BC of agent and save it with AgentName.class in the local file system of the site $S_i$ after that execution of the agent is started using AObject. Steps are shown in Algorithm 1.

- **Agent Launcher (AL):** It acts a Client at agent launching station ($S_{CENTRAL}$) and launches the goal oriented DM agents on behalf of the user through a user interface to the DM_AEE running at the distributed sites. Agent Pool (or Zone) at $S_{CENTRAL}$ is a repository of all mobile as well as stationary agents (SAs). AL first reads and stores AgentName in AgentProfile. The entire BC of the AgentName is loaded from the Agent Pool and stored in AgentProfile. $L^{NODES}$ and ItinType are retrieved and stored in AgentProfile. $TripTime_{start}$ is maintained in Briefcase which is further added to AgentProfile. In case of parallel computing model, i.e., if ItinType = Parallel AL creates $L^{NODES}$ number of clones of the specific MA and dispatches each clone in parallel to all the sites listed in $L^{NODES}$. Here $L^{NODES}$ number of threads are created to dispatch the MAs in parallel. Each clone has AgentVersion starting from 1 to size of $L^{NODES}$, which is used to identify each clone on the network. Before dispatching the clone of a MA to DM_AEE, the current state of the newly created ith clone object (AObject[i]) is also stored in AgentProfile. AL also contacts the Result Manager (RM) for processing the Briefcase of an agent. Detailed steps are given in Algorithm 2.

- **Result Manager (RM):** It manages and processes the Briefcase of all MAs. RM is either contacted by a MA for submitting its results or by AL for processing the results of the specific MA. On completion of itinerary, each DM agent submits its results to RM which computes total round trip time ($TripTime$) of that MA and saves it in the Briefcase of that agent. If ItinType = Parallel then it saves the AgentProfile of all the clones of the agent with AgentName in a collection $[ AgentProfiles ]_{/AgentName}$. It is assumed that all the clones report
their results to RM. RM may be equipped with the feature of non reporting clones by issuing an alert to AL for that clone with specific AgentVersion. AL then launch a new clone for the specific AgentVersion for the specific site. When it is contacted by AL for processing the results of a specific agent it sends back a collection $L_{AgentName}^{AllProfiles}$ for all the clones of that agent. Steps are defined in Algorithm 3.

**Algorithm 1 DATA MINING AGENT EXECUTION ENVIRONMENT (DM_AEE)**

```plaintext
1: procedure DM_AEE()
2:  while TRUE do
3:  AgentProfile ← listen and receive AgentProfile at $S_i$
4:  AgentName ← get AgentName from AgentProfile
5:  BC ← retrieve the BC of agent from AgentProfile
6:  save the BC with AgentName.class in the local file system of $S_i$
7:  $AObject \leftarrow \text{get } AObject \text{ from AgentProfile}$
8:  $AObject.run()$ \hspace{1cm} \triangleright \text{current state}
9:  end while
10: end procedure
```

**Algorithm 2 AGENT LAUNCHER (AL) FOR AEQARM-AAPDB**

```plaintext
1: procedure AL()
2:  option ← read option (dispatch / result)
3:  switch option do
4:  case dispatch \hspace{1cm} \triangleright \text{dispatch the mobile agent to DM_AEE}
5:  AgentName ← read Mobile Agent’s name
6:  BC ← load entire byte code of AgentName from AgentPool
7:  add AgentName and BC to AgentProfile
8:  $L_{NODES}^N$ ← read itinerary (IP addresses) of mobile agent
9:  ItinType ← read ItinType (Serial / Parallel)
10: add ItinType to AgentProfile
11: if ItinType = ”Parallel” then \hspace{1cm} \triangleright \text{Parallel Itinerary}
12:  $AObject[L_{NODES}.size]$ \hspace{1cm} \triangleright \text{Array of Agent Objects for clone references}
13:  $TripTime_{start}$ ← get system time for start of the agent journey
14:  add $TripTime_{start}$ to Briefcase
15:  add Briefcase to AgentProfile
16: switch AgentName do
17:  case PDBFA \hspace{1cm} \triangleright \text{for each node in the itinerary}
18:    for $i \leftarrow 1, L_{NODES}.size$ do
19:      AgentVersion ← $i$
20:      add AgentVersion to AgentProfile
21:      $NodeAddress \leftarrow L_{NODES}.get(i)$ \hspace{1cm} \triangleright \text{get an IP address}
22:      $AObject[i] \leftarrow \text{new PDBFA(AgentProfile)}$
23:      Add $AObject[i]$ to AgentProfile \hspace{1cm} \triangleright \text{clone’s state}
24:    Transfer AgentProfile to DM_AEE at $NodeAddress$
25:    end for
26: end switch
27: end if
28: end switch
29: end procedure
```
end case

case AAFFA
    for i ← 1..L_{NODES}.size do ▷ for each node in the itinerary
        AgentVersion ← i
        add AgentVersion to AgentProfile
        NodeAddress ← L_{NODES}.get(i) ▷ get an IP address
        AObject[i] ← new AAFFA(AgentProfile)
        Add AObject[i] to AgentProfile ▷ clone’s state
        Transfer AgentProfile to DM_AEE at NodeAddress
    end for
end case

case FMIDBGA
    max_freq ← read maximum frequency range for amino acids
    for i ← 1..L_{NODES}.size do ▷ for each node in the itinerary
        AgentVersion ← i
        add AgentVersion to AgentProfile
        NodeAddress ← L_{NODES}.get(i) ▷ get an IP address
        AObject[i] ← new FMIDBGA(AgentProfile, max_freq)
        Add AObject[i] to AgentProfile ▷ clone’s state
        Transfer AgentProfile to DM_AEE at NodeAddress
    end for
end case

case LKGA_P
    min_s ← read minimum threshold support
    min_c ← read minimum threshold confidence
    for i ← 1..L_{NODES}.size do ▷ for each node in the itinerary
        AgentVersion ← i
        add AgentVersion to AgentProfile
        NodeAddress ← L_{NODES}.get(i) ▷ get an IP address
        AObject[i] ← new LKGA_P(AgentProfile, min_s, min_c)
        Add AObject[i] to AgentProfile ▷ clone’s state
        Transfer AgentProfile to DM_AEE at NodeAddress
    end for
end case

case LKCA_P
    for i ← 1..L_{NODES}.size do ▷ for each node in the itinerary
        AgentVersion ← i
        add AgentVersion to AgentProfile
        NodeAddress ← L_{NODES}.get(i) ▷ get an IP address
        AObject[i] ← new LKCA_P(AgentProfile)
        Add AObject[i] to AgentProfile ▷ clone’s state
        Transfer AgentProfile to DM_AEE at NodeAddress
    end for
end case

case GKDA_P
    L^{GKDA}_{CENTRAL} ← load L^{GKDA}_{CENTRAL} generated by GKGA at S_{CENTRAL}
end case
add $\text{GSAR}_\text{CENTRAL}$ to Briefcase

add updated Briefcase to AgentProfile

for $i \leftarrow 1, L_{\text{NODES}}.\text{size}$ do
  AgentVersion $\leftarrow i$
  add AgentVersion to AgentProfile
  NodeAddress $\leftarrow L_{\text{NODES}}.\text{get}(i)$  \(\triangleright\) get an IP address
  $\text{AObject}[i] \leftarrow \text{new GKDA}_P(\text{AgentProfile})$
  Add $\text{AObject}[i]$ to AgentProfile  \(\triangleright\) clone’s state
  Transfer AgentProfile to DM_AEE at NodeAddress
end for

end case
end switch
end if
end case

\(\triangleright\) process the results of mobile agent

AgentName $\leftarrow$ read mobile agent’s name

ItinType $\leftarrow$ read mobile agent’s itinerary type

add AgentName and ItinType to $L_{\text{Agentinfo}}$

if ItinType = "Parallel" then

$L_{\text{AllProfile}}_{\text{AgentName}} \leftarrow$ contact RM for $L_{\text{Agentinfo}}$

switch AgentName do
  case PDBFA
  for all $\text{AgentProfile} \in L_{\text{AllProfile}}_{\text{AgentName}}$ do
    Briefcase $\leftarrow$ retrieve Briefcase from AgentProfile
    process the Briefcase of PDBFA clone
  end for
  end case

  case AAFPA
  for all $\text{AgentProfile} \in L_{\text{AllProfile}}_{\text{AgentName}}$ do
    Briefcase $\leftarrow$ retrieve Briefcase from AgentProfile
    process the Briefcase of AAFPA clone
  end for
  end case

  case FMIDBGA
  for all $\text{AgentProfile} \in L_{\text{AllProfile}}_{\text{AgentName}}$ do
    Briefcase $\leftarrow$ retrieve Briefcase from AgentProfile
    process the Briefcase of FMIDBGA clone
  end for
  end case

  case LKGA_P
  for all $\text{AgentProfile} \in L_{\text{AllProfile}}_{\text{AgentName}}$ do
    Briefcase $\leftarrow$ retrieve Briefcase from AgentProfile
    process the Briefcase of LKGA_P clone
  end for
  end case

  case LKCA_P
  call RIGKGA($L_{\text{AllProfile}}_{\text{AgentName}}$)  \(\triangleright\) stationary agent
end switch
end case

case GKDA_P

for all AgentProfile ∈ \(L_{\text{AgentName}}\) do // for each clone
  Briefcase ← retrieve Briefcase from AgentProfile
  process the Briefcase of GKDA_P clone
end for
end case
end switch
end if
end case
end switch
end procedure

---

**Algorithm 3 RESULT MANAGER(RM)**

1: procedure RM( )
2: while TRUE do
3:   listen and receive the incoming request
4:   if contacted by a mobile agent for submitting results from site \(S_i\) then
5:     AgentProfile ← receive the incoming AgentProfile from site \(S_i\),
6:     ItinType ← retrieve ItinType from AgentProfile
7:     Briefcase ← retrieve mobile agent’s Briefcase from AgentProfile
8:     TripTime\(_{\text{start}}\) ← retrieve TripTime\(_{\text{start}}\) from Briefcase
9:     TripTime\(_{\text{end}}\) ← retrieve TripTime\(_{\text{end}}\) from Briefcase
10:    TripTime ← TripTime\(_{\text{end}}\) – TripTime\(_{\text{start}}\)
11:    add TripTime to Briefcase
12:    add updated Briefcase to AgentProfile
13:    if ItinType = ”Parallel” then
14:      AgentName ← retrieve AgentName from AgentProfile
15:      AgentVersion ← retrieve AgentVersion from AgentProfile
16:     if AgentVersion = 1 then
17:       add AgentProfile to \(L_{\text{AgentName}}\)
18:       save \(L_{\text{AgentName}}\) at \(S_{\text{CENTRAL}}\)
19:      end if
20:     if AgentVersion > 1 then
21:       retrieve \(L_{\text{AgentName}}\) from \(S_{\text{CENTRAL}}\)
22:       add AgentProfile to \(L_{\text{AgentName}}\)
23:       save updated \(L_{\text{AgentName}}\) at \(S_{\text{CENTRAL}}\)
24:      end if
25:    end if
26:  end if
27: end if
28: end if
29: if contacted by AgentLauncher for processing the results then
30:   AgentName ← retrieve AgentName from AgentProfile
31:   ItinType ← retrieve ItinType from incoming \(L_{\text{Itin}}\)
32:   if ItinType = ”Parallel” then
33:     \(L_{\text{AgentName}}\) ← load \(L_{\text{AgentName}}\) from \(S_{\text{CENTRAL}}\)
32: \[\text{dispatch } L_{\text{AllProfiles}} \text{ to AgentLauncher}\]
33: \[\text{end if}\]
34: \[\text{end if}\]
35: \[\text{end while}\]
36: \[\text{end procedure}\]

![Diagram of AeQARM-AAPDB MAS]

Figure 1. AeQARM-AAPDB MAS

### 3.2. Protein Data Bank

AeQARM-AAPDB system is tested on a real dataset of protein sequences, the Astral SCOP [16], [17] version 1.75 genetic domain sequence subsets, based on PDB SEQRES records with less than 40% identity to each other [18]. There are total of 10569 Protein records in this dataset. This single PDB is divided into 3 units (\(PDB_1\), \(PDB_2\), and \(PDB_3\)) of 3523 protein records in each and are stored at three distributed sites. Each \(PDB_i\) is further filtered to generate \(FPDB_i\) for \(PS\) length range \(\geq 50\) and \(\leq 400\). A total of only 9633 (3341 \((FPDB_1)\) + 3253 \((FPDB_2)\) + 3039 \((FPDB_3)\)) such filtered records are considered for the mining. The frequencies of 20 amino acids in each protein sequence are retrieved and stored in \(AAF_i\) which is further mapped into \(BDB_i\) for
each amino acid having 15 frequency ranges (partitions) resulting into 300 amino acids \(\{\text{attribute, value}\}\) pairs as shown in Appendix A.4.

### 3.3. Layout and working of AeQARM-AAPDB system

AeQARM-AAPDB MAS is shown in Figure 1. This MAS consists of total seven agents, clones of six MAs in serial number 1 to 6 are dispatched from \(S_{CENTRAL}\) with parallel itinerary migration and one at serial number 7 is an intelligent stationary agent (SA) running at \(S_{CENTRAL}\) to perform the different tasks. The CPU time taken by a MA while processing on each site along with some other specific information is carried back in the result bag at \(S_{CENTRAL}\). Relationship among these agents and their working behaviour are given as follows.

1. **Protein Data Bank Filtering Agent (PDBFA)**: Clones of this MA is dispatched in parallel to each distributed site by AL. It carries the AgentProfile along with it and filters \(PDB_i\) to generate \(FPDB_i\) at each site \(S_i\). PDBFA carries back the computational time (\(\text{CPUTime}\)) at each site \(S_i\) and \(\text{TripTime}_{end}\).

2. **Amino Acids Frequency Finder Agent (AAFFA)**: Every clone of this MA carries the AgentProfile along with it and finds the frequencies of each amino acids in every protein sequence record in \(FPDB_i\) to create \(AAF_i\) at each site \(S_i\). AAFFA carries back the computational time (\(\text{CPUTime}\)) at each site \(S_i\) and \(\text{TripTime}_{end}\).

3. **Frequency Mapping and Itemset Data Bank Generator Agent (FMIDBGA)**: Every clone of this MA carries the AgentProfile and \(\text{maxfrq}\) (the given maximum frequency range for amino acids) along with it. It divides the frequencies of each amino acids in \(AAF_i\) into intervals and maps the frequencies into Boolean values to create \(BDB_i\) for frequency intervals and further maps it to \(IDB_i\) for frequency interval items.

4. **Local Knowledge Generator Agent with Parallel Itinerary (LKGA\_P)**: Every cloned LKGA\_P carries the AgentProfile, \(\text{min\_th\_sup}\) and \(\text{min\_th\_conf}\) along with it. This agent is embedded with Apriori algorithm [19] for generating all the frequent k-itemset lists. This agent may be equipped with decision making capability to select other FIM algorithms based on the density of the dataset at a particular site. It first performs the FIM to generate and store \(L^{FI}_{k\{0\}}\) and \(L^{FISC}_{k\{0\}}\) at site \(S_i\) by scanning the local \(IDB_i\) at that site with the constraint of \(\text{min\_th\_sup}\). It then performs the ARM applying the constraint of \(\text{min\_th\_conf}\) to generate and store \(L_i^{LSAR}\) by using the \(L^{FI}_{k\{0\}}\) and \(L^{FISC}_{k\{0\}}\). \(L_i^{LSAR}\) list also contains support and confidence for a particular association rule along with site name. It carries back the computational time (\(\text{CPUTime}\)) at each site \(S_i\) and \(\text{TripTime}_{end}\).

5. **Local Knowledge Collector Agent with Parallel Itinerary (LKCA\_P)**: Every cloned LKGA\_P carries the AgentProfile and collects the list of local frequent k-itemset (\(L^{FI}_{k\{i\}}\)) and list of locally strong association rules (\(L_i^{LSAR}\)) generated by LKGA\_P. It carries back these distributed results in the result bag to RM at \(S_{CENTRAL}\) where these results are integrated with the help of a RIA stationary agent. In addition to this resultant knowledge it also carries back the computational time (\(\text{CPUTime}\)) at each site \(S_i\) and \(\text{TripTime}_{end}\).

6. **Global Knowledge Dispatcher Agent with Parallel Itinerary (GKDA\_P)**: Every cloned GKDA\_P carries AgentProfile containing global knowledge (\(L^{GSAR}_{CENTRAL}\)) for further
decision making and comparing with local knowledge at that site. It carries back the computational time \( CPUTime \) at each site \( S_i \) and \( TripTime_{end} \).

7. **Result Integration and Global Knowledge Generator Agent (RIGKGA):** It is a stationary agent at \( S_{CENTRAL} \), mainly used for processing the result bags of all clones of LKCA_P. It creates a list of total frequent k-itemset \( L_{\text{TFI}} \), a list of global frequent itemset \( L_{\text{GFI}} \) and a list of total locally strong association rules \( L_{\text{TLSAR}} \). \( L_{\text{TFI}} \) and \( L_{\text{TLSAR}} \) are further processed to generate and store \( L_{\text{GSAR}} \) list.

![Control Panel of AeQARM-AAPDB](image)

**Figure 2. Control Panel of AeQARM-AAPDB**

**Table 2. Network Configuration**

| Site Name | Processor | OS     | LAN Configuration |
|-----------|-----------|--------|-------------------|
| \( S_{CENTRAL} \) | Intel \(^b\) | MS \(^c\) | 192.168.46.5 NW \(^d\) |
| \( S_1 \) | Intel \(^b\) | MS \(^c\) | 192.168.46.212 NW \(^d\) |
| \( S_2 \) | Intel \(^b\) | MS \(^c\) | 192.168.46.189 NW \(^d\) |
| \( S_3 \) | Intel \(^b\) | MS \(^c\) | 192.168.46.213 NW \(^d\) |

- \(^a\) IP address with Mask: 255.255.255.0 and Gateway 192.168.46.1
- \(^b\) Intel Pentium Dual Core (3.40 GHz, 3.40 GHz) with 512 MB RAM
- \(^c\) Microsoft Windows XP Professional ver. 2002
- \(^d\) Network Speed: 100 Mbps and Network Adaptor: 82566DM-2 Gigabit NIC

**4. IMPLEMENTATION AND PERFORMANCE STUDY**

All the agents as well as Control Panel of the system, as shown in Figure 2, are implemented in Java. The required configuration for the deployment of the system is shown in Table 2 with additional deployment of DM_AEE at each distributed site and AL and RM at \( S_{CENTRAL} \).
Figure 7. Globally strong association rules for globally frequent 2-itemsets

| Sr. No. | L         | AR (support/confidence) | Site                  |
|--------|-----------|-------------------------|-----------------------|
| 1      | [16, 92]  | [192 168 46 169]        | 192 168 46 212        |
| 2      | [16, 10]  | [192 168 46 169]        | 192 168 46 169        |
| 3      | [16, 15]  | [192 168 46 169]        | 192 168 46 169        |
| 4      | [16, 21]  | [192 168 46 169]        | 192 168 46 169        |
| 5      | [16, 27]  | [192 168 46 169]        | 192 168 46 169        |
| 6      | [16, 37]  | [192 168 46 169]        | 192 168 46 169        |
| 7      | [16, 22]  | [192 168 46 169]        | 192 168 46 169        |
| 8      | [16, 33]  | [192 168 46 169]        | 192 168 46 169        |
| 9      | [16, 39]  | [192 168 46 169]        | 192 168 46 169        |
| 10     | [16, 27]  | [192 168 46 169]        | 192 168 46 169        |

Figure 8. Globally strong association rules for frequent 2- amino acids

| Sr. No. | L         | AR (support/confidence) | Site                  |
|--------|-----------|-------------------------|-----------------------|
| 1      | {<C.2>,<H.3, P>} | [192 168 46 169] | 192 168 46 212 |
| 2      | {<C.2>,<H.3, P>} | [192 168 46 169] | 192 168 46 212 |
| 3      | {<C.2>,<H.3, P>} | [192 168 46 169] | 192 168 46 212 |
| 4      | {<C.2>,<H.3, P>} | [192 168 46 169] | 192 168 46 212 |
| 5      | {<C.2>,<H.3, P>} | [192 168 46 169] | 192 168 46 212 |
| 6      | {<C.2>,<H.3, P>} | [192 168 46 169] | 192 168 46 212 |
| 7      | {<C.2>,<H.3, P>} | [192 168 46 169] | 192 168 46 212 |
| 8      | {<C.2>,<H.3, P>} | [192 168 46 169] | 192 168 46 212 |
| 9      | {<C.2>,<H.3, P>} | [192 168 46 169] | 192 168 46 212 |
| 10     | {<C.2>,<H.3, P>} | [192 168 46 169] | 192 168 46 212 |

$L_{k(i)}^{FI}$ and $L_{k(i)}^{FISC}$ at site $S_i$ generated by LKGA_P agent with 20% min_th_sup are shown in Appendix B.1. Locally strong association rules ($L_{1}^{LSAR}$) generated by LKGA_P for frequent item numbers at site $S_i$ are shown in Appendix B.2 and the same for their corresponding amino acids frequency range are shown in Appendix B.3. Globally strong association rules ($L_{CENTRAL}^{GSAR}$) for the globally frequent itemsets generated by RIGKGA are shown in Figure 7. When these item numbers are mapped with their corresponding amino acids frequency ranges then globally strong
quantitative association rules for frequent 2 amino acids are obtained and shown in Figure 8. The results, as shown in Figure 8, reveals that:

- < Cysteine: 0..2 > is strongly associated with < Histidine: 3..5 >, < Methionine:0..2 >, < Methionine: 3..5 >, < Tryptophan: 0..2 >, and < Tyrosine:3::5 >
- < Tryptophan: 0..2 > is strongly associated with < Histidine: 0..2 >, <Histidine: 3..5 >, < Methionine: 0..2 >, < Methionine: 3..5 >, < Glutamine: 3..5 > and < Tyrosine: 3..5 >

5. CONCLUSION

Mobile agents strongly qualify for designing distributed applications. DDM, when clubbed with the agent technology, makes a promising alliance that gives favourable results and provides a rewarding solution in managing Big Data with ever increasing size. In this study, a MAS called AeQARM-AAPDB to mine the strong quantitative association rules among amino acids present in primary structure of the proteins from the distributed proteins data sets using intelligent agents is presented. Such globally strong association rules are used in understanding of protein composition and are desirable for synthesis of artificial proteins. Agent-based bio-data mining leaves the technical details of choosing mining algorithms, forming hybrid system, and preparing specific data format to the intelligent system itself because such requirements are unreasonable for most biologists. It alleviates the technical difficulty while enhance the reusability of the mining algorithms and available datasets. By applying multi-agent based distributed bio-data mining, the computing load can be balanced and the computational effort can be achieved in a parallel and scalable manner.

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APPENDIX A – DATASETS USED FOR AEQARM-AAPDB SYSTEM

A.1 PDB$_1$ at site $S_1$

This is a real dataset of protein sequences, the Astral Structural Classification of Proteins (SCOP) [16], [17] version 1.75 genetic domain sequence subsets, based on PDB SEQRES records with less than 40% identity to each other. SCOP database is comprehensive ordering of all proteins of known structure, according to their evolutionary and structural relationships. Protein domains in the SCOP are grouped into species and hierarchically classified into families, superfamilies, folds and classes. In this dataset each protein record starts with greater than (‘>') character followed by protein description headers according to SCOP. An additional hash ('#') character is inserted as a separator character between protein description headers and protein sequence of amino acids. A total of 3523 protein records are stored in this protein data bank (PDB$_1$) at site $S_1$.

A.2 FPDB$_1$ at site $S_1$

PDB$_1$ shown in Appendix A.1 is further filtered to generate FPDB$_1$ for the protein sequence length range $\geq 50$ and $< 400$. A total of 3341 such filtered protein records are obtained.
A.4 Amino acids frequency ranges (15 ranges for each amino acid)

Item No. column represents Serial No. from 1 to 300. Data in the AA Frequency Range column represents single letter code of an amino acid along with a frequency range. Frequency of each amino acid is divided into 15 partitions (ranges) resulting into 300 items for 20 amino acids. For example if frequency of amino acid Alanine (A) in a protein sequence record is 22 it lies at Item No. 8.
This Boolean data bank ($BDB_1$) is created using $AAF_i$ as shown in Appendix A.3 and amino acids frequency range table as shown in Appendix A.4. Each column heading represents an Item No. as shown in Appendix A.4. Each amino acid has 15 frequency partitions and for each amino acid, a boolean value ‘1’ is put under that Item No. in which frequency of amino acid lies in a particular protein record otherwise a value ‘0’ is considered. For example it clear from $AAF_i$ that the frequency of amino acid Alanine (A) in the 1st protein record is 22 and this frequency lies at Item No. 8 in frequency range table as shown in Appendix A.4, so a boolean value ‘1’ is put under Item No. 8 in the 1st protein record in $BDB_1$. 

| Item No. | AA Frequency Range | Item No. | AA Frequency Range | Item No. | AA Frequency Range | Item No. | AA Frequency Range | Item No. | AA Frequency Range | Item No. | AA Frequency Range |
|----------|---------------------|----------|---------------------|----------|---------------------|----------|---------------------|----------|---------------------|----------|---------------------|
| 1        | <A3.2>             | 61       | <F6.2>              | 121      | <K9.2>              | 214      | <T9.2>              |
| 2        | <A3.5>             | 62       | <F9.5>              | 122      | <K9.5>              | 215      | <T9.2>              |
| 3        | <A9.8>             | 63       | <F6.8>              | 123      | <K6.8>              | 216      | <T6.8>              |
| 4        | <A9.11>            | 64       | <F9.11>             | 124      | <K9.11>             | 217      | <T9.11>             |
| 5        | <A12.14>           | 65       | <F12.14>            | 125      | <K12.14>            | 218      | <T12.14>            |
| 6        | <A15.17>           | 66       | <F15.17>            | 126      | <K15.17>            | 219      | <T15.17>            |
| 7        | <A18.20>           | 67       | <F18.20>            | 127      | <K18.20>            | 220      | <T18.20>            |
| 8        | <A21.30>           | 68       | <F21.30>            | 128      | <K21.30>            | 221      | <T21.30>            |
| 9        | <A31.40>           | 69       | <F31.40>            | 129      | <K31.40>            | 222      | <T31.40>            |
| 10       | <A41.50>           | 70       | <F41.50>            | 130      | <K41.50>            | 223      | <T41.50>            |
| 11       | <A51.60>           | 71       | <F51.60>            | 131      | <K51.60>            | 224      | <T51.60>            |
| 12       | <A61.70>           | 72       | <F61.70>            | 132      | <K61.70>            | 225      | <T61.70>            |
| 13       | <A71.80>           | 73       | <F71.80>            | 133      | <K71.80>            | 226      | <T71.80>            |
| 14       | <A81.90>           | 74       | <F81.90>            | 134      | <K81.90>            | 227      | <T81.90>            |
| 15       | <A91.400>          | 75       | <F91.400>           | 135      | <K91.400>           | 228      | <T91.400>           |
| 16       | <A101.3>           | 76       | <F101.3>            | 136      | <K101.3>            | 229      | <T101.3>            |
| 17       | <A111.4>           | 77       | <F111.4>            | 137      | <K111.4>            | 230      | <T111.4>            |
| 18       | <A121.5>           | 78       | <F121.5>            | 138      | <K121.5>            | 231      | <T121.5>            |
| 19       | <A131.6>           | 79       | <F131.6>            | 139      | <K131.6>            | 232      | <T131.6>            |
| 20       | <A141.7>           | 80       | <F141.7>            | 140      | <K141.7>            | 233      | <T141.7>            |
| 21       | <A151.8>           | 81       | <F151.8>            | 141      | <K151.8>            | 234      | <T151.8>            |
| 22       | <A161.9>           | 82       | <F161.9>            | 142      | <K161.9>            | 235      | <T161.9>            |
| 23       | <A171.0>           | 83       | <F171.0>            | 143      | <K171.0>            | 236      | <T171.0>            |
| 24       | <A181.1>           | 84       | <F181.1>            | 144      | <K181.1>            | 237      | <T181.1>            |
| 25       | <A191.2>           | 85       | <F191.2>            | 145      | <K191.2>            | 238      | <T191.2>            |

...
A.6 $IDB_1$ at site $S_1$

This Itemset data bank ($IDB_1$) is created using $BDB_1$ as shown in Appendix A.4. Each record in this dataset consist of 20 Item Numbers, one for each of amino acids for which a boolean value ‘1’ is stored in $BDB_1$.

$$
\begin{array}{cccccccccccccccccccc}
1) & 8 & 16 & 32 & 47 & 63 & 79 & 91 & 107 & 121 & 138 & 151 & 168 & 181 & 198 & 212 & 227 & 245 & 260 & 271 & 286 \\
2) & 6 & 16 & 35 & 49 & 63 & 79 & 93 & 106 & 124 & 140 & 152 & 167 & 181 & 197 & 213 & 226 & 243 & 259 & 271 & 287 \\
3) & 5 & 16 & 33 & 48 & 63 & 80 & 92 & 108 & 122 & 140 & 152 & 166 & 183 & 197 & 213 & 228 & 243 & 260 & 271 & 287 \\
4) & 5 & 16 & 34 & 50 & 63 & 78 & 92 & 107 & 121 & 140 & 152 & 166 & 182 & 197 & 216 & 228 & 242 & 258 & 271 & 288 \\
5) & 4 & 16 & 32 & 50 & 63 & 78 & 93 & 107 & 122 & 141 & 152 & 167 & 184 & 197 & 213 & 227 & 243 & 257 & 271 & 287 \\
6) & 8 & 16 & 33 & 47 & 62 & 80 & 93 & 107 & 124 & 138 & 151 & 168 & 181 & 197 & 211 & 228 & 241 & 258 & 271 & 287 \\
7) & 7 & 16 & 35 & 47 & 63 & 79 & 91 & 108 & 126 & 140 & 152 & 169 & 181 & 198 & 212 & 228 & 243 & 260 & 271 & 287 \\
8) & 8 & 16 & 33 & 47 & 64 & 81 & 91 & 106 & 124 & 139 & 153 & 168 & 182 & 197 & 211 & 229 & 242 & 258 & 272 & 286 \\
9) & 5 & 16 & 33 & 50 & 63 & 78 & 94 & 109 & 125 & 139 & 152 & 167 & 182 & 197 & 212 & 228 & 244 & 259 & 271 & 287 \\
10) & 8 & 16 & 33 & 48 & 62 & 83 & 92 & 108 & 124 & 139 & 152 & 167 & 182 & 197 & 212 & 230 & 241 & 259 & 271 & 287 \\
11) & 6 & 16 & 33 & 50 & 63 & 79 & 95 & 109 & 127 & 142 & 151 & 166 & 182 & 197 & 212 & 228 & 242 & 258 & 271 & 287 \\
12) & 8 & 16 & 33 & 47 & 66 & 79 & 91 & 107 & 124 & 139 & 152 & 169 & 183 & 196 & 212 & 230 & 241 & 259 & 271 & 286 \\
13) & 6 & 16 & 34 & 47 & 65 & 79 & 92 & 109 & 124 & 138 & 152 & 167 & 182 & 197 & 212 & 229 & 244 & 259 & 271 & 286 \\
14) & 8 & 16 & 33 & 50 & 63 & 78 & 92 & 109 & 125 & 140 & 151 & 168 & 182 & 197 & 211 & 229 & 243 & 261 & 272 & 286 \\
15) & 6 & 17 & 33 & 49 & 63 & 77 & 94 & 107 & 124 & 142 & 151 & 169 & 182 & 197 & 212 & 228 & 243 & 259 & 271 & 287 \\
16) & 5 & 16 & 34 & 47 & 62 & 78 & 92 & 109 & 125 & 140 & 152 & 167 & 183 & 196 & 212 & 230 & 242 & 259 & 271 & 287 \\
17) & 5 & 16 & 33 & 49 & 64 & 78 & 93 & 108 & 126 & 140 & 151 & 167 & 181 & 199 & 212 & 228 & 243 & 260 & 271 & 287 \\
18) & 6 & 16 & 35 & 47 & 63 & 79 & 93 & 109 & 124 & 140 & 152 & 168 & 182 & 197 & 212 & 229 & 243 & 259 & 271 & 288 \\
19) & 3 & 16 & 36 & 47 & 64 & 77 & 93 & 109 & 125 & 139 & 152 & 166 & 182 & 198 & 213 & 228 & 244 & 260 & 272 & 287 \\
20) & 3 & 16 & 33 & 49 & 64 & 77 & 91 & 111 & 127 & 140 & 151 & 168 & 183 & 190 & 211 & 230 & 242 & 258 & 271 & 287 \\
\end{array}
$$

APPENDIX B – RESULTANT KNOWLEDGE OF AEQARM-AAPDB SYSTEM

B.1 $L_{k(1)}^{FI}$ and $L_{k(1)}^{FISC}$ at site $S_1$

List of frequent k-itemset, i.e., $L_{k(1)}^{FI}$ is represented by column L and column SC shows the support count of the corresponding frequent k-itemset, i.e., $L_{k(1)}^{FISC}$ at site $S_1$. These frequent itemsets and their support counts are obtained by processing the Itemset Data Bank ($IDB_1$) as shown in Appendix A.6.
Column $L$ represents frequent k-itemset and column $AR(support, confidence)$ shows the list of locally strong association rules, i.e., $L_{S_1}^{LSAR}$ at site $S_1$. Each strong rule has its associated support and confidence factor. The minimum threshold support is taken as 20% and minimum threshold confidence as 50% for generating the strong rules by making use of the data as shown in Appendix B.1.
**B.3 $LSAR$ for corresponding Amino acid frequency ranges at site $S_1$**

Replace Item No. in Appendix B.2 data with its corresponding Amino acid frequency range as shown in table Appendix A.4.

| Sr. No. | Strong A4s for frequent 4-Itemsets | Strong A4s for frequent 3-Itemsets | Strong A4s for frequent 2-Itemsets |
|---------|-------------------------------------|-------------------------------------|-------------------------------------|
|         | L | All(support, confidence)           | L | All(support, confidence)           | L | All(support, confidence)           |
| 1       | [16, 91, 151, 271] (26%, 58%)      | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 2       | [16, 91] (26%, 58%)                | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 3       | [16, 91, 151] (26%, 58%)           | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 4       | [16, 91, 151] (26%, 58%)           | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 5       | [16, 91, 151] (26%, 58%)           | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 6       | [16, 91, 151] (26%, 58%)           | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 7       | [16, 91, 151] (26%, 58%)           | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 8       | [16, 91, 151] (26%, 58%)           | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 9       | [16, 91, 151] (26%, 58%)           | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 10      | [16, 91, 151] (26%, 58%)           | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 11      | [16, 91, 151] (26%, 58%)           | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 12      | [16, 91, 151] (26%, 58%)           | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 13      | [16, 91, 151] (26%, 58%)           | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 14      | [16, 91, 151] (26%, 58%)           | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 15      | [16, 91, 151] (26%, 58%)           | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 16      | [16, 91, 151] (26%, 58%)           | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 17      | [16, 91, 151] (26%, 58%)           | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 18      | [16, 91, 151] (26%, 58%)           | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 19      | [16, 91, 151] (26%, 58%)           | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 20      | [16, 91, 151] (26%, 58%)           | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 21      | [16, 91, 151] (26%, 58%)           | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |
| 22      | [16, 91, 151] (26%, 58%)           | [16, 32, 271] (21%, 25%)           | [16, 32, 271] (21%, 72%)           |

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