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Mourtada et al.

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(45) **Date of Patent: Aug. 12, 2025**

(54) **VISUAL REPRESENTATIONS OF PEPTIDE SEQUENCES**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 1084 days.

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(86) PCT No.: **PCT/US2019/047884**
§ 371 (c)(1),
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PCT Pub. Date: **Feb. 27, 2020**

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Related U.S. Application Data

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(51) **Int. Cl.**
G16B 15/20 (2019.01)
G16B 15/00 (2019.01)
G16C 20/30 (2019.01)

(52) **U.S. Cl.**
CPC ***G16B 15/20*** (2019.02); ***G16B 15/00*** (2019.02); ***G16C 20/30*** (2019.02)

(58) **Field of Classification Search**
CPC G16B 15/20; G16B 15/00; G16C 20/30
See application file for complete search history.

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Assistant Examiner — Mary C Leverett
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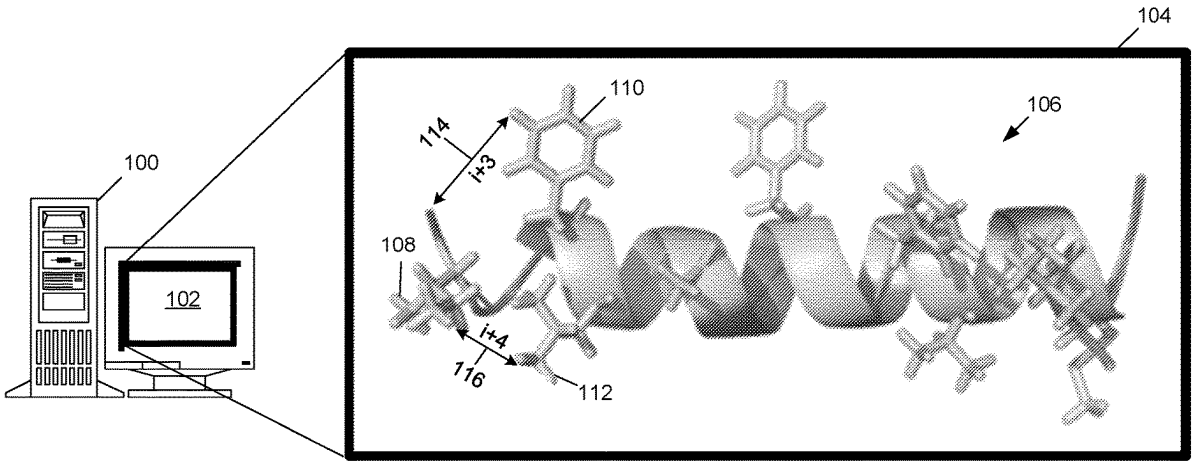
(57) **ABSTRACT**

A system for visually representing peptide sequences includes a memory configured to store instructions and a processor to execute the instructions to perform operations. The operations include receiving data representing a peptide sequence. The data includes an index representing a position for each amino acid in the peptide sequence. The operations further include categorizing each amino acid in the peptide sequence and assigning each amino acid a value associated with the category. The operations additionally include determining relationship groups, each group including two amino acids in the peptide sequence, based upon a geometrical structure of the peptide sequence. The operations also include filtering the relationship groups to remove groups based upon the category of at least one of the two amino acids that make up the group; and producing a visual representation that includes a representation of each amino acid of the filtered relationship groups.

12 Claims, 16 Drawing Sheets

Specification includes a Sequence Listing.



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Mourtada, "Engineering Membrane-Selective Antibiotic Peptides to Combat Multidrug Resistance," Dissertation for the degree of Doctor of Philosophy in Medical Engineering and Medical Physics, Massachusetts Institute of Technology, Jun. 2018, 189 pages.

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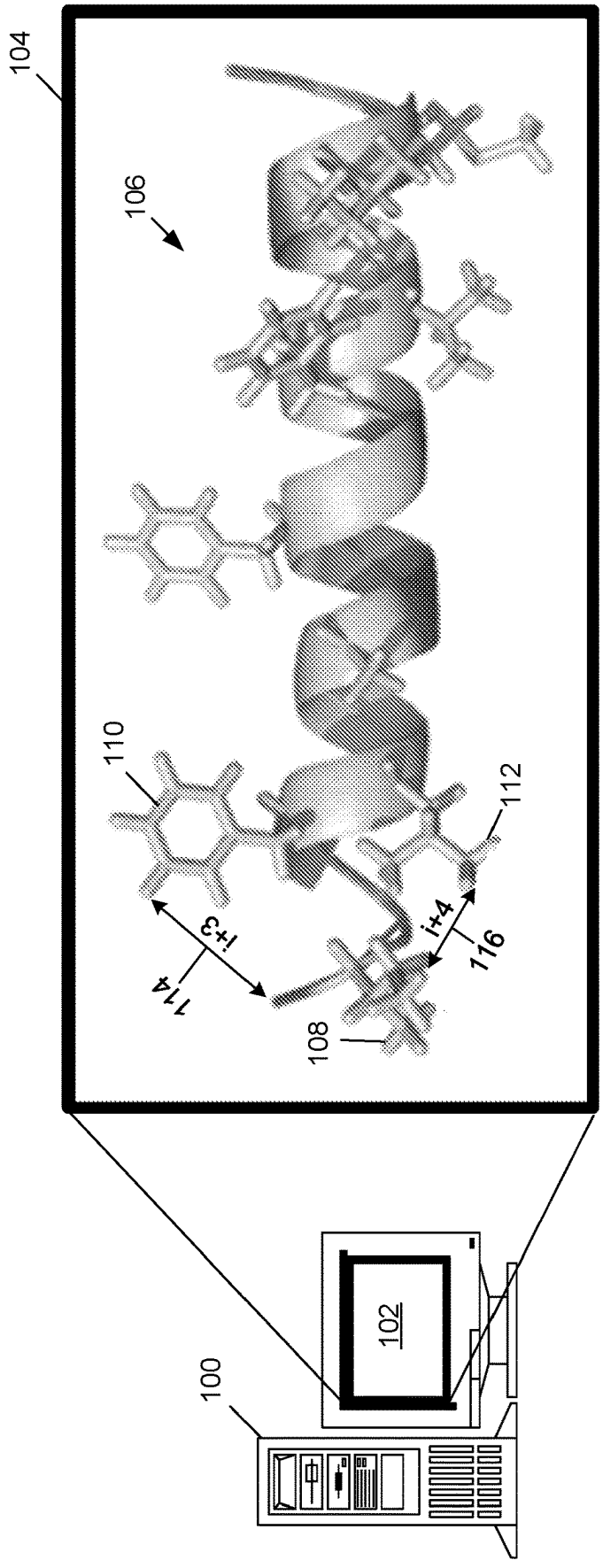

FIG. 1

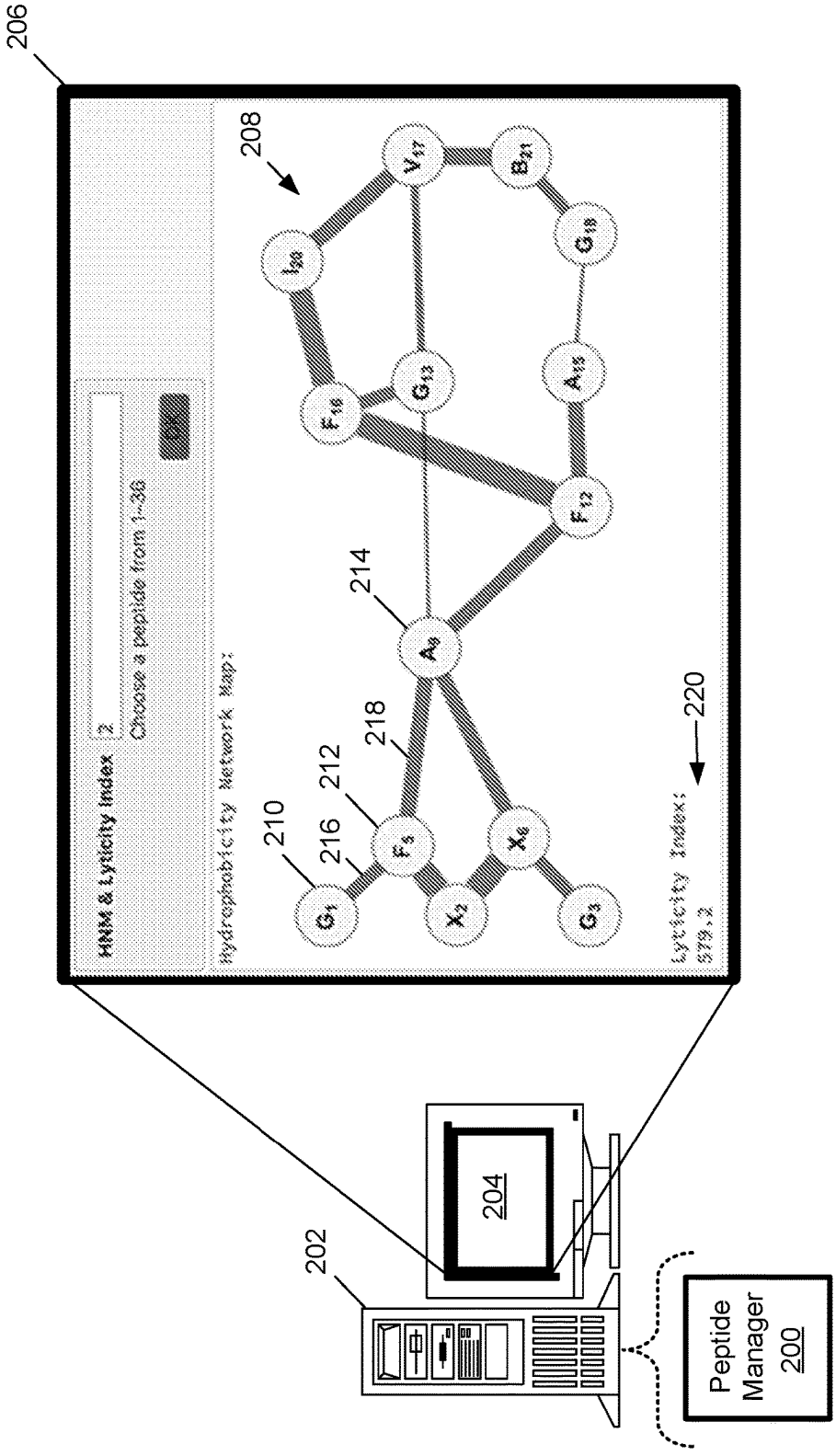
206
208
HNM & Lyticity Index
2
Choose a peptide from 1-36
OK
Hydrophobicity Network Map:
214
210
216
212
218
220
Lyticity Index:
879.2
204
202
Peptide Manager
200

FIG. 2

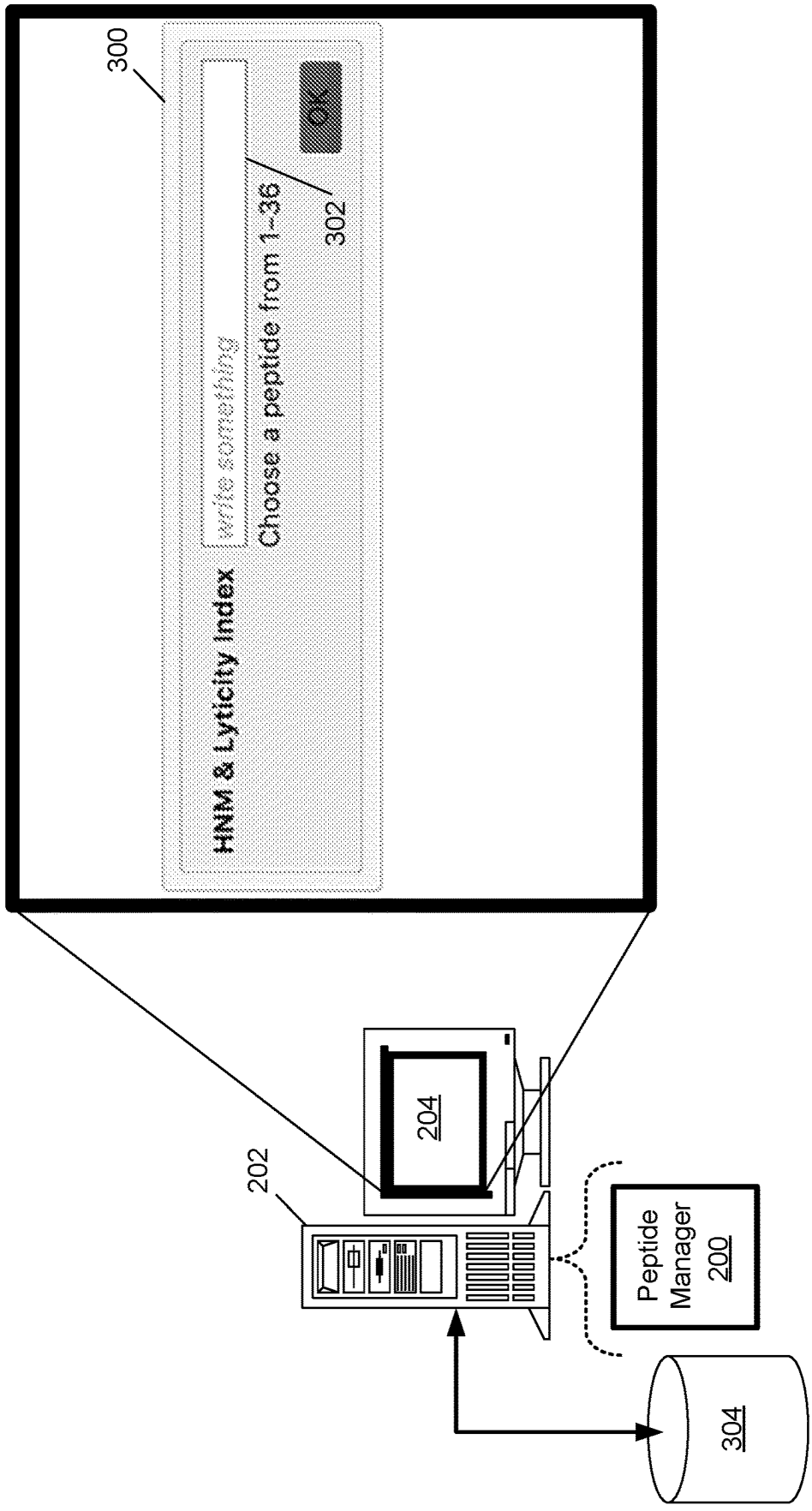
300
HNM & Lyticity Index
write something
Choose a peptide from 1-36
302
OK
204
202
Peptide Manager 200
304

FIG. 3

Amino Acid Hydrophobicities

402

{"X", "I", "G", "K", "X", "L", "H", "S", "A", "K", "K", "F", "G", "K", "A", "F", "V", "G", "E", "I", "B", "N", "S"}

404

{29.5, 22.4, 0., -1.1, 29.5, 24.2, 3.4, 0.5, 3.9, -1.1, -1.1, 29.9, 0., -1.1, 3.9, 29.9, 14.4, 0., -0.9, 22.4, 25.6, 0.5, 0.5}

```
FileNames["*.xls", NotebookDirectory[]];
raw = Import[FileNameJoin[{NotebookDirectory[], "Data Set.xls"}]];
secondSheet = Part[raw, 2];
rows = Part[secondSheet, Span[5, 40]];
pephydro = rows[[All, 3 ;; 25]];
firstSheet = raw[[1]];
rows2 = firstSheet[[5 ;; 40]];
pepsSeq = rows2[[All, 4 ;; 26]];
```

400

FIG. 4

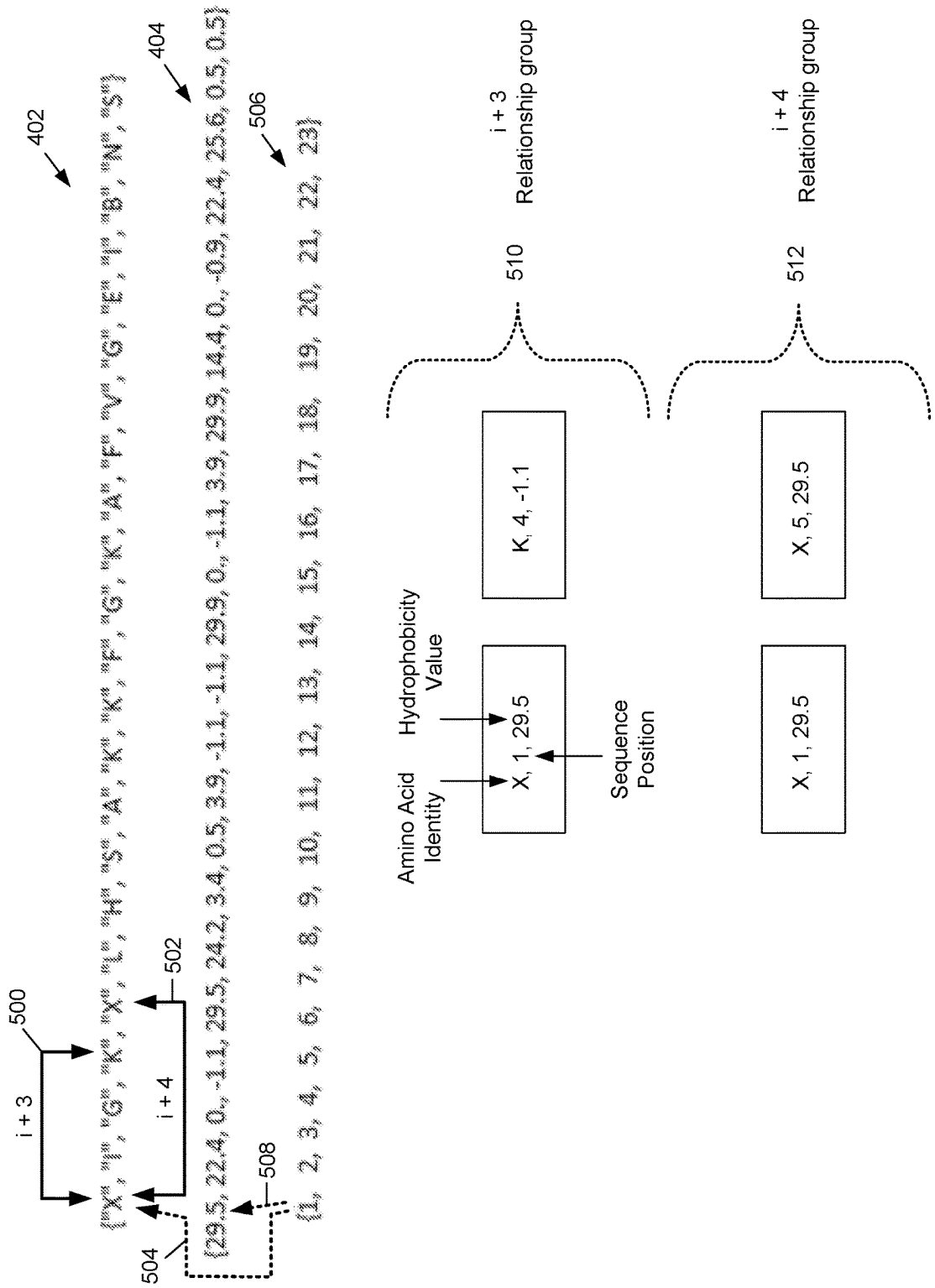
402
404
506
500
502
504
508
i + 3
i + 4
{"X", "1", "G", "K", "X", "L", "H", "S", "A", "K", "K", "F", "G", "K", "A", "F", "V", "G", "E", "1", "B", "N", "S"}
{29.5, 22.4, 0., -1.1, 29.5, 24.2, 3.4, 0.5, 3.9, -1.1, -1.1, 29.9, 0., -1.1, 3.9, 29.9, 14.4, 0., -0.9, 22.4, 25.6, 0.5, 0.5}
{1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23}
i + 3
Relationship group
i + 4
Relationship group
510
512
Amino Acid Identity
Hydrophobicity Value
Sequence Position
X, 1, 29.5
K, 4, -1.1
X, 1, 29.5
X, 5, 29.5

FIG. 5

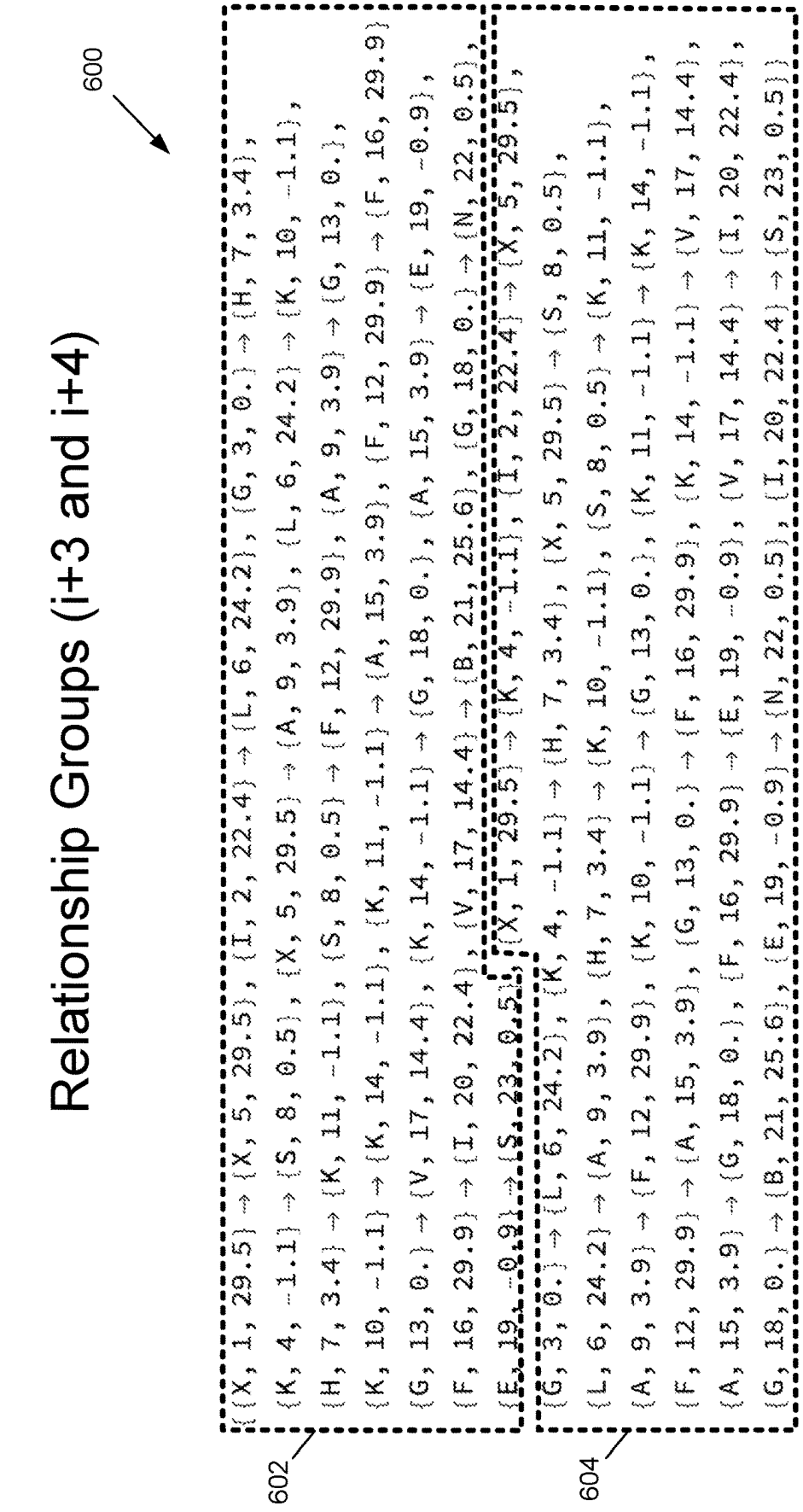
600
Relationship Groups (i+3 and i+4)
602
604
{X, 1, 29.5} → {X, 5, 29.5}, {I, 2, 22.4} → {L, 6, 24.2}, {G, 3, 0.} → {H, 7, 3.4},
{K, 4, -1.1} → {S, 8, 0.5}, {X, 5, 29.5} → {A, 9, 3.9}, {L, 6, 24.2} → {K, 10, -1.1},
{H, 7, 3.4} → {K, 11, -1.1}, {S, 8, 0.5} → {F, 12, 29.9}, {A, 9, 3.9} → {G, 13, 0.},
{K, 10, -1.1} → {K, 14, -1.1}, {K, 11, -1.1} → {A, 15, 3.9}, {F, 12, 29.9} → {F, 16, 29.9}
{G, 13, 0.} → {V, 17, 14.4}, {K, 14, -1.1} → {G, 18, 0.}, {A, 15, 3.9} → {E, 19, -0.9},
{F, 16, 29.9} → {I, 20, 22.4}, {V, 17, 14.4} → {B, 21, 25.6}, {G, 18, 0.} → {N, 22, 0.5},
{E, 19, -0.9} → {S, 23, 0.5}, {X, 1, 29.5} → {K, 4, -1.1}, {I, 2, 22.4} → {X, 5, 29.5},
{G, 3, 0.} → {L, 6, 24.2}, {K, 4, -1.1} → {H, 7, 3.4}, {X, 5, 29.5} → {S, 8, 0.5},
{L, 6, 24.2} → {A, 9, 3.9}, {H, 7, 3.4} → {K, 10, -1.1}, {S, 8, 0.5} → {K, 11, -1.1},
{A, 9, 3.9} → {F, 12, 29.9}, {K, 10, -1.1} → {G, 13, 0.}, {K, 11, -1.1} → {K, 14, -1.1},
{F, 12, 29.9} → {A, 15, 3.9}, {G, 13, 0.} → {F, 16, 29.9}, {K, 14, -1.1} → {V, 17, 14.4},
{A, 15, 3.9} → {G, 18, 0.}, {F, 16, 29.9} → {E, 19, -0.9}, {V, 17, 14.4} → {I, 20, 22.4},
{G, 18, 0.} → {B, 21, 25.6}, {E, 19, -0.9} → {N, 22, 0.5}, {I, 20, 22.4} → {S, 23, 0.5}}

FIG. 6

Hydrophilic Amino Acids:

```
wamino = {"Q", "N", "S", "C", "R", "D", "H", "K", "E"};
```

700

704

```
{{X, 1, 29.5} → {X, 5, 29.5}, {I, 2, 22.4} → {L, 6, 24.2}, {G, 3, 0.} → {H, 7, 3.4},
 {K, 4, 1.1} → {S, 8, 0.5}, {X, 5, 29.5} → {A, 9, 3.9}, {L, 6, 24.2} → {K, 10, 1.1},
 {H, 7, 3.4} → {K, 11, 1.1}, {S, 8, 0.5} → {F, 12, 29.9}, {A, 9, 3.9} → {G, 13, 0.},
 {K, 10, 1.1} → {K, 14, 1.1}, {K, 11, 1.1} → {A, 15, 3.9}, {F, 12, 29.9} → {F, 16, 29.9},
 {G, 13, 0.} → {V, 17, 14.4}, {K, 14, 1.1} → {G, 18, 0.}, {A, 15, 3.9} → {E, 19, 0.9},
 {F, 16, 29.9} → {I, 20, 22.4}, {V, 17, 14.4} → {B, 21, 25.6}, {G, 18, 0.} → {N, 22, 0.5},
 {E, 19, 0.9} → {S, 23, 0.5}, {X, 1, 29.5} → {K, 4, 1.1}, {I, 2, 22.4} → {X, 5, 29.5},
 {G, 3, 0.} → {L, 6, 24.2}, {K, 4, 1.1} → {H, 7, 3.4}, {X, 5, 29.5} → {S, 8, 0.5},
 {L, 6, 24.2} → {A, 9, 3.9}, {H, 7, 3.4} → {K, 10, 1.1}, {S, 8, 0.5} → {K, 11, 1.1},
 {A, 9, 3.9} → {F, 12, 29.9}, {K, 10, 1.1} → {G, 13, 0.}, {K, 11, 1.1} → {K, 14, 1.1},
 {F, 12, 29.9} → {A, 15, 3.9}, {G, 13, 0.} → {F, 16, 29.9}, {K, 14, 1.1} → {V, 17, 14.4},
 {A, 15, 3.9} → {G, 18, 0.}, {F, 16, 29.9} → {E, 19, 0.9}, {V, 17, 14.4} → {I, 20, 22.4},
 {G, 18, 0.} → {B, 21, 25.6}, {E, 19, 0.9} → {N, 22, 0.5}, {I, 20, 22.4} → {S, 23, 0.5}}
```

702

```
For[i = 1, i ≤ Dimensions[wamino][[1]], i++, {ii = DeleteCases[ii, {wamino[[i]], _, _} → _]
   ii = DeleteCases[ii, _ → {wamino[[i]], _, _}]}];
```

FIG. 7

Filtered Data Structure

800


```
{{X, 1, 29.5} → {X, 5, 29.5}, {I, 2, 22.4} → {L, 6, 24.2},
 {X, 5, 29.5} → {A, 9, 3.9}, {A, 9, 3.9} → {G, 13, 0.}, {F, 12, 29.9} → {F, 16, 29.9},
 {G, 13, 0.} → {V, 17, 14.4}, {F, 16, 29.9} → {I, 20, 22.4}, {V, 17, 14.4} → {B, 21, 25.6},
 {I, 2, 22.4} → {X, 5, 29.5}, {G, 3, 0.} → {L, 6, 24.2}, {L, 6, 24.2} → {A, 9, 3.9},
 {A, 9, 3.9} → {F, 12, 29.9}, {F, 12, 29.9} → {A, 15, 3.9}, {G, 13, 0.} → {F, 16, 29.9},
 {A, 15, 3.9} → {G, 18, 0.}, {V, 17, 14.4} → {I, 20, 22.4}, {G, 18, 0.} → {B, 21, 25.6}}
```

FIG. 8

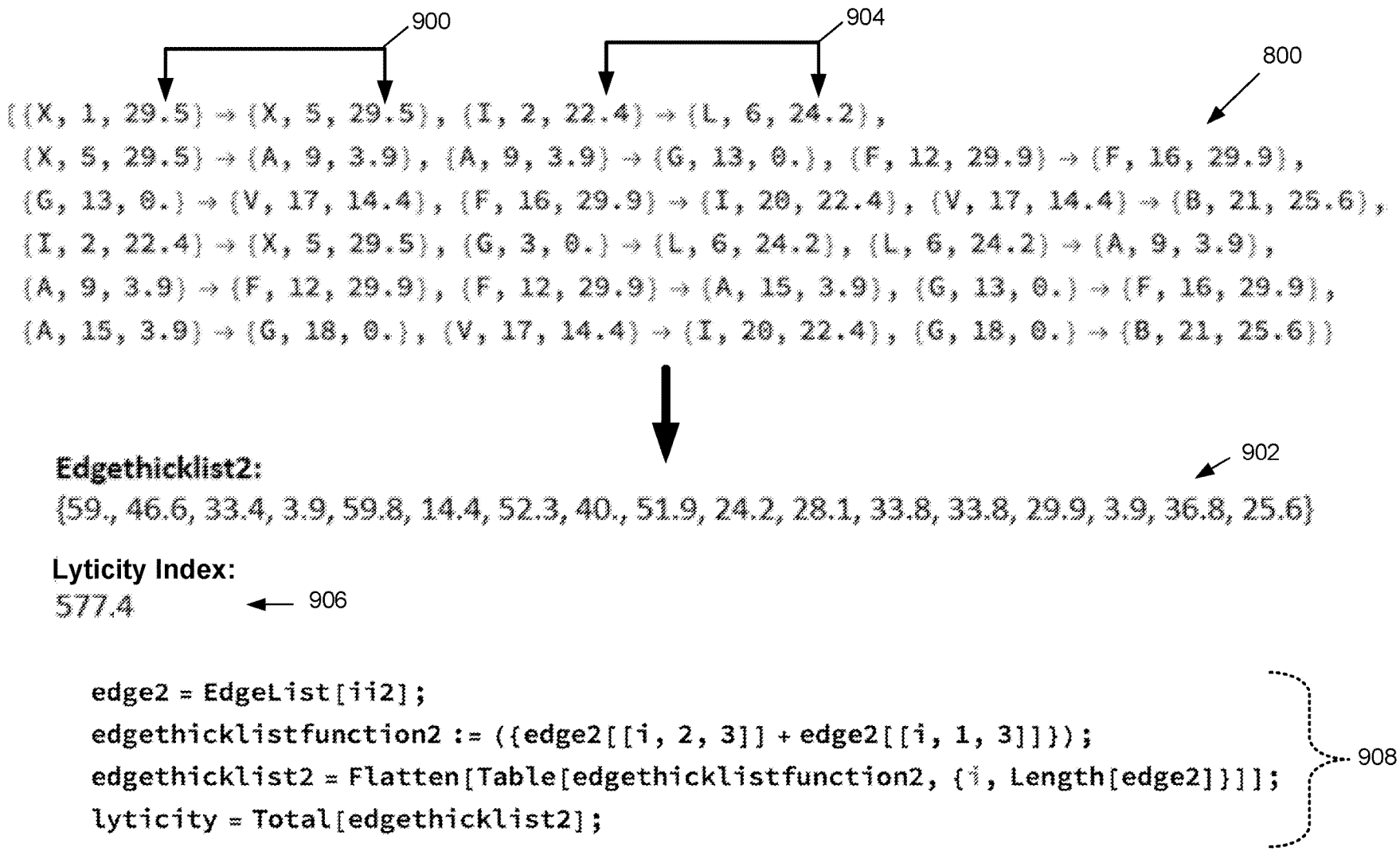
900
904
800
{{X, 1, 29.5} → {X, 5, 29.5}, {I, 2, 22.4} → {L, 6, 24.2},
{X, 5, 29.5} → {A, 9, 3.9}, {A, 9, 3.9} → {G, 13, 0.}, {F, 12, 29.9} → {F, 16, 29.9},
{G, 13, 0.} → {V, 17, 14.4}, {F, 16, 29.9} → {I, 20, 22.4}, {V, 17, 14.4} → {B, 21, 25.6},
{I, 2, 22.4} → {X, 5, 29.5}, {G, 3, 0.} → {L, 6, 24.2}, {L, 6, 24.2} → {A, 9, 3.9},
{A, 9, 3.9} → {F, 12, 29.9}, {F, 12, 29.9} → {A, 15, 3.9}, {G, 13, 0.} → {F, 16, 29.9},
{A, 15, 3.9} → {G, 18, 0.}, {V, 17, 14.4} → {I, 20, 22.4}, {G, 18, 0.} → {B, 21, 25.6}}
Edgethicklist2:
902
{59., 46.6, 33.4, 3.9, 59.8, 14.4, 52.3, 40., 51.9, 24.2, 28.1, 33.8, 33.8, 29.9, 3.9, 36.8, 25.6}
Lyticity Index:
577.4
906
edge2 = EdgeList[ii2];
edgethicklistfunction2 := ({edge2[[i, 2, 3]] + edge2[[i, 1, 3]]});
edgethicklist2 = Flatten[Table[edgethicklistfunction2, {i, Length[edge2]}]];
lyticity = Total[edgethicklist2];
908

FIG. 9

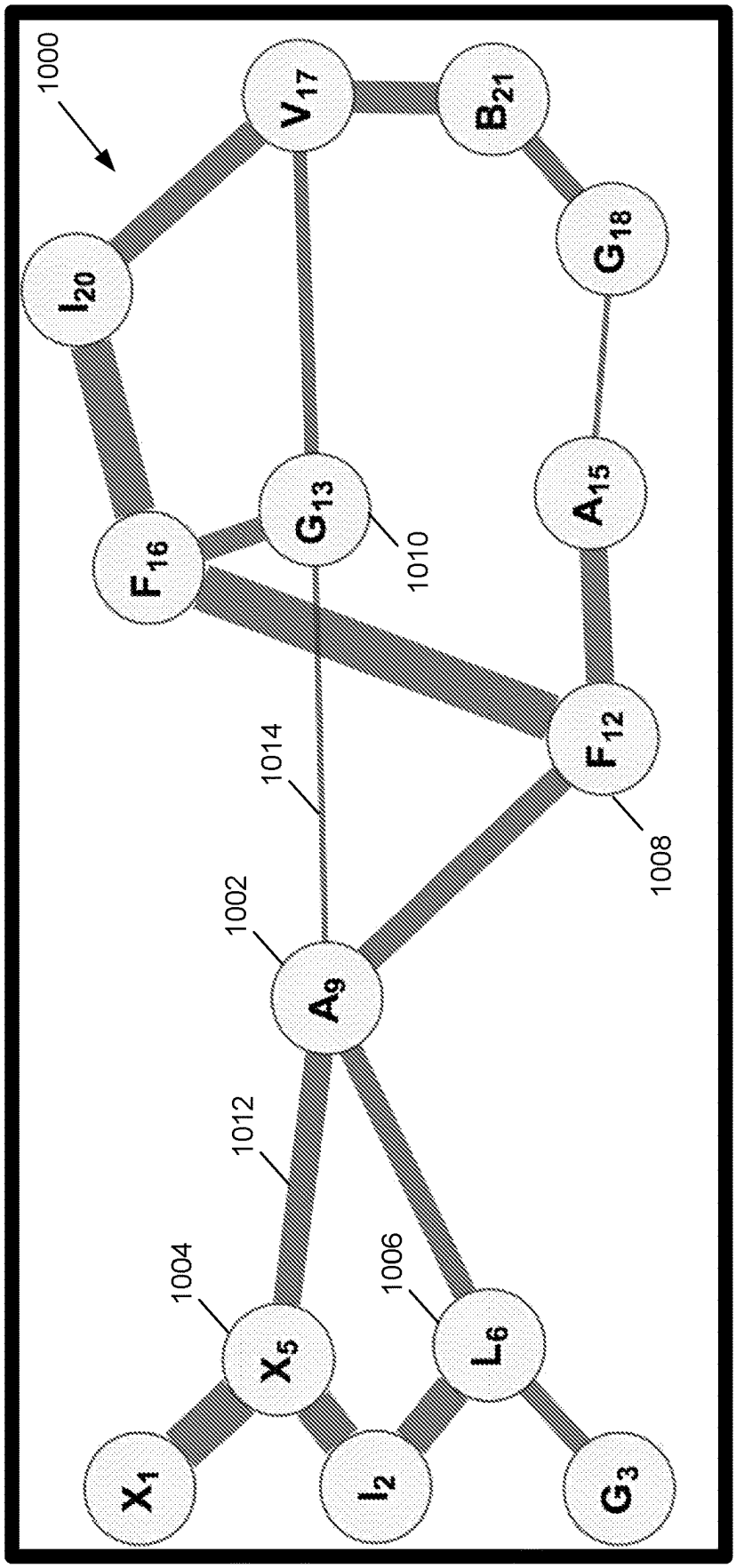
1000
V17
B21
I20
G18
G13
A15
F16
1010
F12
1014
1008
1002
A9
1012
1004
1006
X5
L6
X1
I2
G3

FIG. 10

1100

```
labels = Table[fat[[i, 1]], {i, Length[fat]}];
labels = labels /. {"Z" → "K"};
labelsubscript = Table[fat[[i, 2]], {i, Length[fat]}];
labelfull = Table[Subscript[labels[[i]], labelsubscript[[i]]], {i, Length[fat]}];
vlabel = Table[fat[[i]] → Placed[labelfull[[i]], Center], {i, Length[fat]}];

(*Setting the properties of the graph with coordinate and vertex rules*)
g1 = Graph[ii, VertexCoordinates → newcoord, EdgeWeight → edgethicklist,
   DirectedEdges → False, VertexSize → 0.7, ImageSize → Large,
   VertexLabelStyle → Directive[Black, Bold, 15], VertexLabels → vlabel,
   VertexStyle → LightYellow];
(*Color Vertices with K in Blue*)
g2 = SetProperty[g1, VertexStyle → {{"Z", _, _} → RGBColor[0.87, 0.94, 1]}];
(*Making edge thickness weighted according to how hydrophobic the vertices are*)
ew = PropertyValue[g1, EdgeWeight];
el = EdgeList[g1];
edgestylea =
  Thread[
   el →
    (Directive[CapForm["Round"], Thickness[Rescale[#, Through@{Min, Max}@ew, {0.004, .03}]],
       RGBColor[0.5`, 0.`, 0.`]] & /@ ew)];
(*Graphing the map with weighted edges and if K is present change those edges*)
g1a = SetProperty[g2, EdgeStyle → edgestylea];

g1b =
  SetProperty[g1a,
   EdgeStyle →
    {"Z", _, _} ↔ _ →
     (Directive[CapForm["Round"], Thickness[0.006], RGBColor[0.2, 0.25, 0.56], Dashed])];
Column[{"Hydrophobicity Network Map:", g1b, "", "Lyticity Index:", lyticity}]
```

FIG. 11

1200
Function Call
FormPage[
{"HMM & Lyticity Index" → <|"Interpreter" → Restricted["Integer", {1, 36}],
"Control" → InputField, "Help" → "Choose a peptide from 1-36",
"Hint" → "write something"|>}, hydrophobicitynetworkmap[#"HMM & Lyticity Index"] &]

FIG. 12

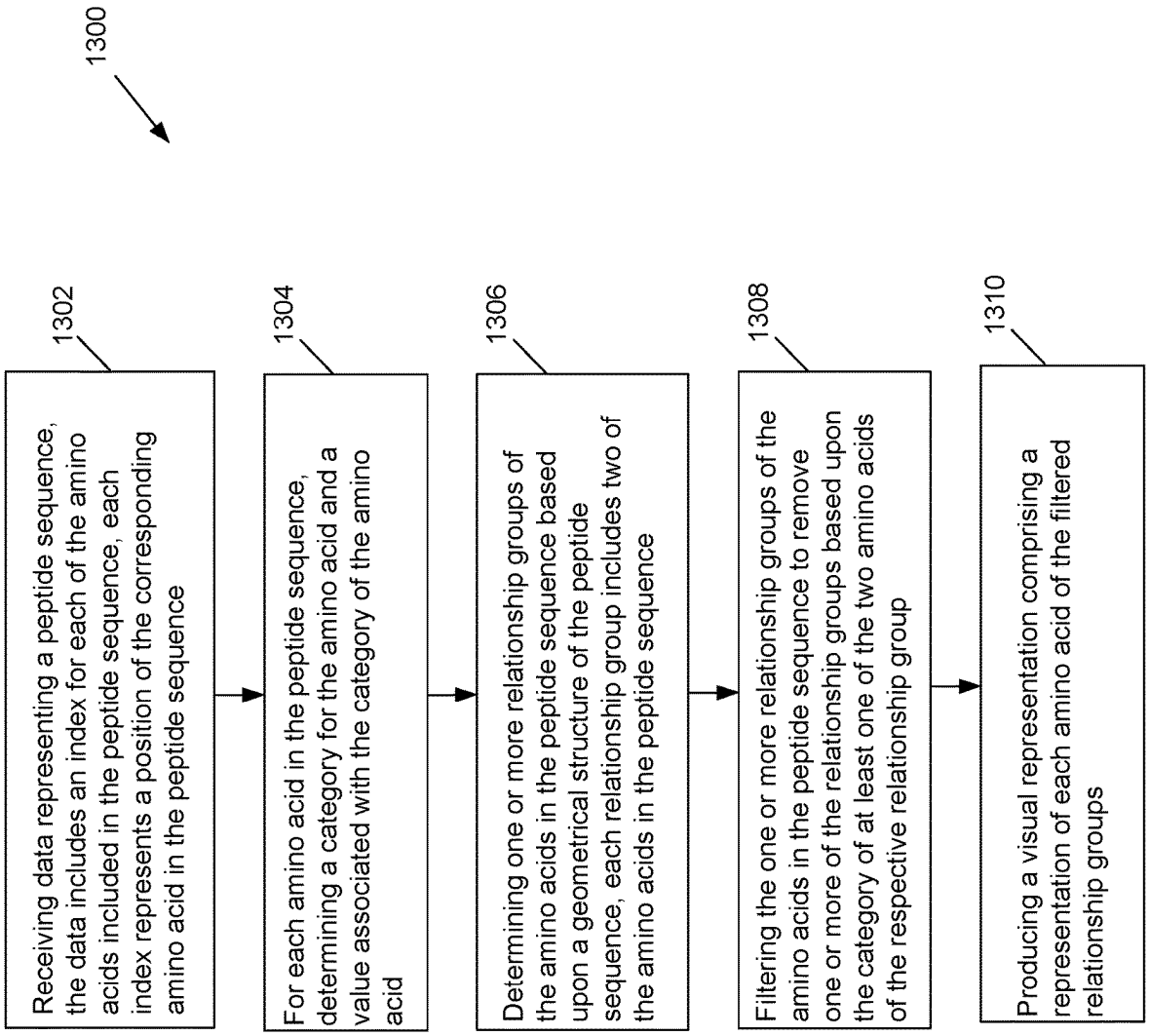
1300
1302
Receiving data representing a peptide sequence, the data includes an index for each of the amino acids included in the peptide sequence, each index represents a position of the corresponding amino acid in the peptide sequence
1304
For each amino acid in the peptide sequence, determining a category for the amino acid and a value associated with the category of the amino acid
1306
Determining one or more relationship groups of the amino acids in the peptide sequence based upon a geometrical structure of the peptide sequence, each relationship group includes two of the amino acids in the peptide sequence
1308
Filtering the one or more relationship groups of the amino acids in the peptide sequence to remove one or more of the relationship groups based upon the category of at least one of the two amino acids of the respective relationship group
1310
Producing a visual representation comprising a representation of each amino acid of the filtered relationship groups

FIG. 13

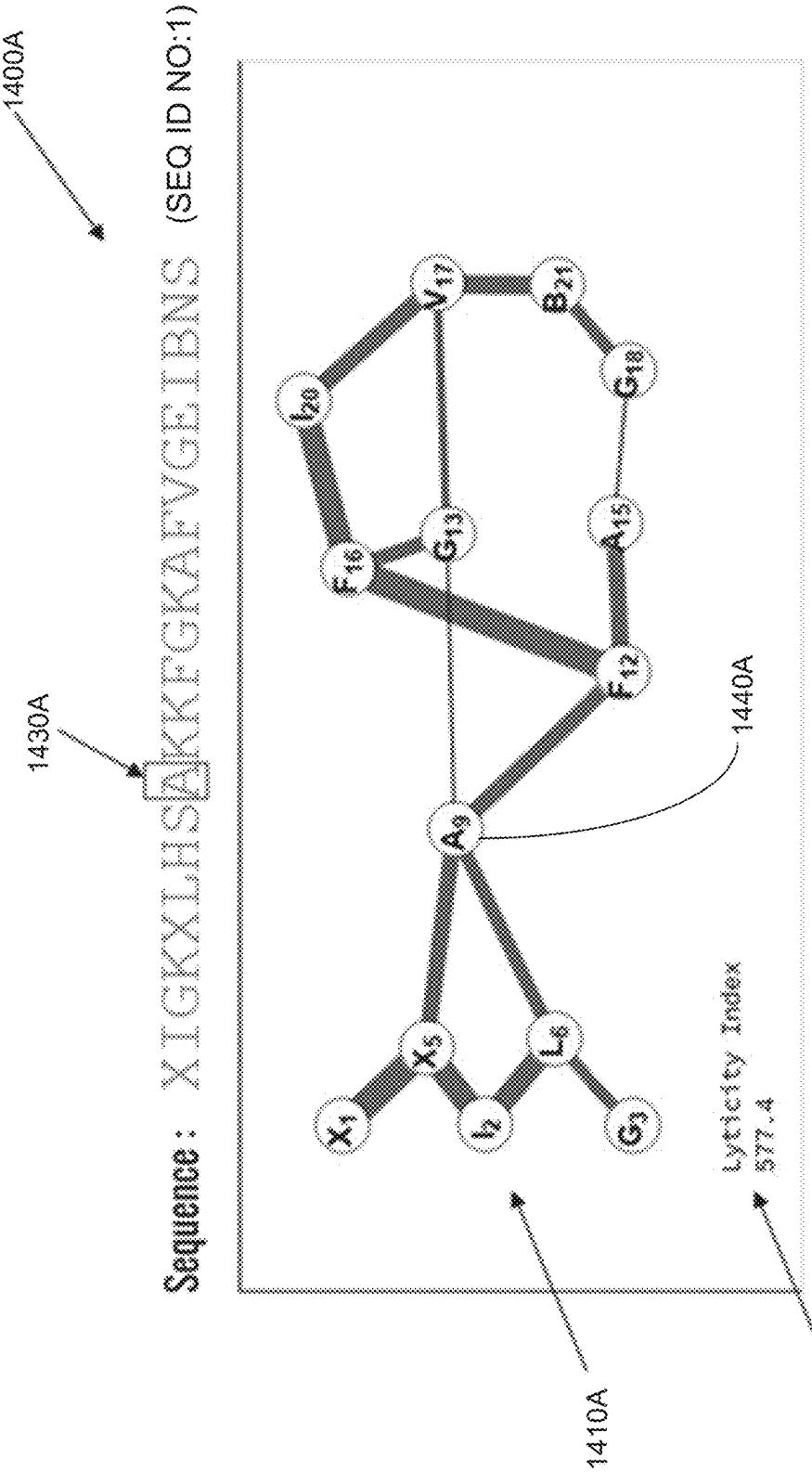
1400A
Sequence: XIGKXLHSAKKFGKAFVGEIBNS (SEQ ID NO:1)
1430A
1440A
1410A
1420A
Lytictty Index
577.4

FIG. 14A

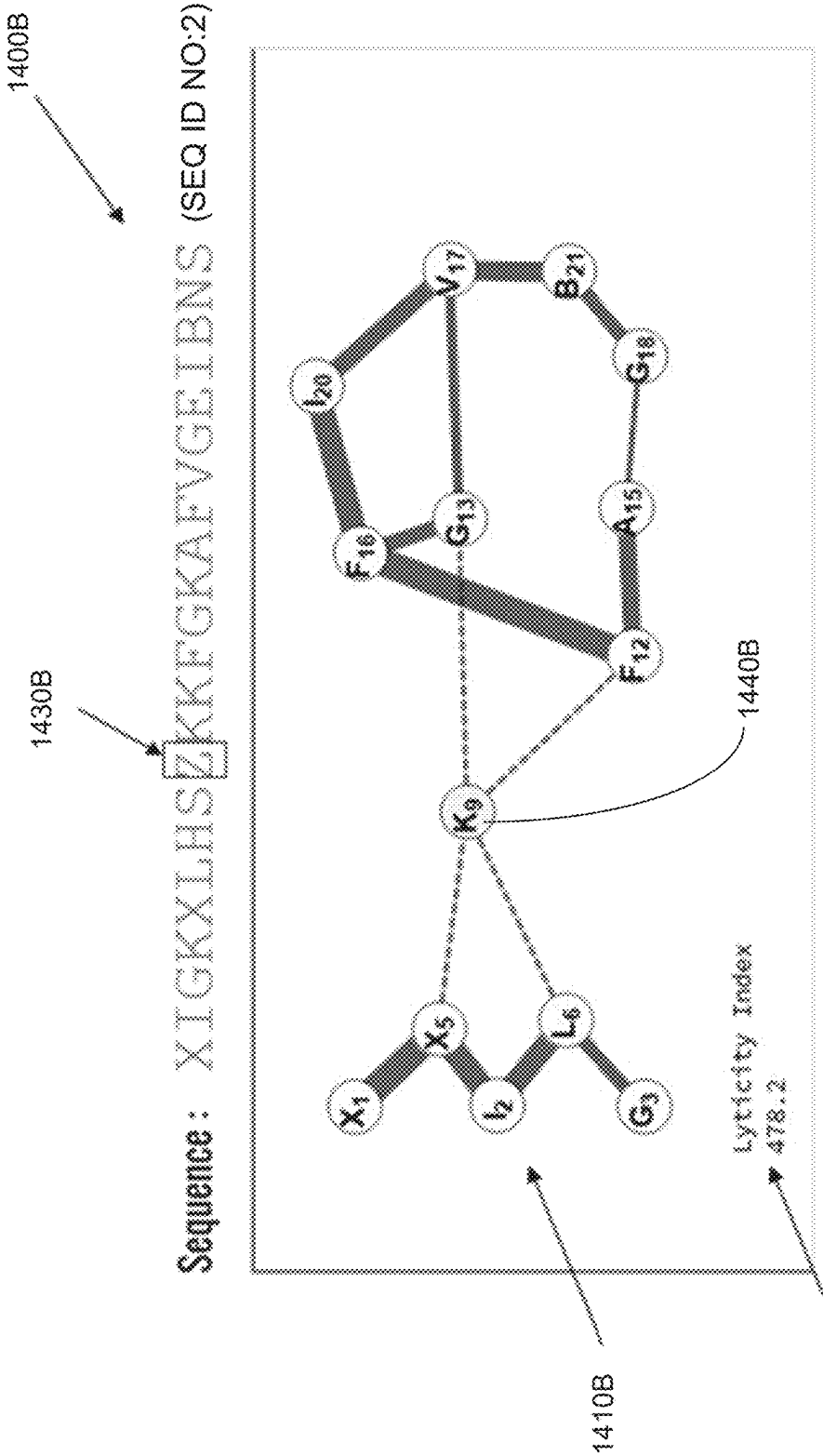
1400B
Sequence : XIGKXLHSXKFGKAFVGEIBNS (SEQ ID NO:2)
1430B
1440B
1410B
1420B
Lyticity Index
478.2

FIG. 14B

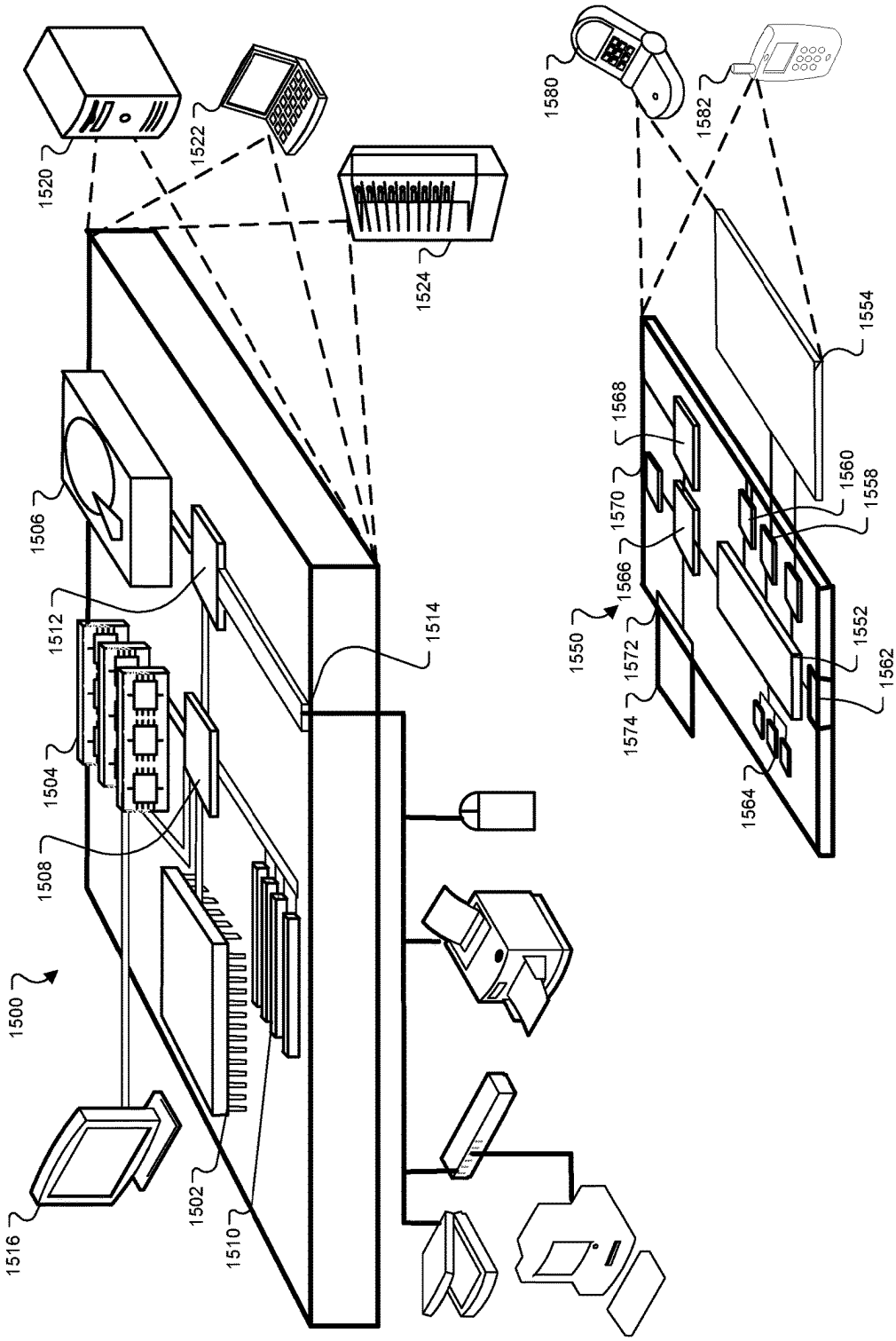
1500
1502
1504
1506
1508
1510
1512
1514
1516
1520
1522
1524
1550
1552
1554
1558
1560
1562
1564
1566
1568
1570
1572
1574
1580
1582

FIG. 15

VISUAL REPRESENTATIONS OF PEPTIDE SEQUENCES

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a National Phase entry of International Patent Application No. PCT/US2019/047884, filed on Aug. 23, 2019, which claims priority to Application No. U.S. 62/722,715, filed on Aug. 24, 2018, the disclosures of which are hereby incorporated by reference in their entireties.

SEQUENCE LISTING

This application contains a Sequence Listing that has been submitted electronically as an ASCII text file named 00530-0350US1_ST25.txt. The ASCII text file, created on Nov. 25, 2024, is 1,254 bytes in size. The material in the ASCII text file is hereby incorporated by reference in its entirety.

BACKGROUND

This description relates to visually representing peptide sequences. Having a graphical representation of the peptide sequences is especially helpful in drug development where therapeutic peptide drug design has become increasingly widespread.

Peptides are complex biomolecules with unique properties, which are afforded by the side chains of the amino acids within their sequences. Due to their ability to interact with a wide variety of biological targets with specificity and potency, peptides are recognized as having large growth potential in therapeutics. Modifying the peptides' sequences is often used to imbue various properties, such as increased stability, and lower toxicity, depending on the desired application of the peptides. Graphically representing peptide sequences can help with understanding various characteristics of the peptide sequences.

SUMMARY

The systems and techniques described can aid individuals such as researchers, drug developers, etc. with therapeutic peptide drug design. Visual representation of peptide sequences in a network format can emphasize relationships between amino acids that are close together in three-dimensional (3D) space. The visual representation allows researchers to quickly recognize the structure of the peptide and identify characteristics of connections between amino acids in the peptide sequence. This can improve efficiency of peptide design by allowing researchers to understand interactions between the amino acids and the overall structure of the peptide sequence.

A graphical map of the peptide's amino acid relationships, where nodes represent amino acids and edges represent connections with amino acid neighbors, can improve efficiency of peptide design by allowing users to quickly recognize the structure of the peptides, understand interactions between peptides, etc. In certain implementations, the peptide's hydrophobic amino acid relationships can be highlighted and used in calculating a lyticity index, which is a predictor of undesirable lytic behavior. This tool can help users with the design effort by assisting in the selection of amino acid substitutions, insertions, deletions, etc. for reducing toxicity. Combining this technique with other metrics besides hydrophobicity and lyticity index (e.g. cationic charge density) can create networks that provide different useful information (e.g. antimicrobial properties). Having a graphical representation of peptide sequences that highlights interactions between amino acids and characterizes properties of peptides, can substantially reduce the amount of time, resources, etc. needed when studying protein folding, designing pharmaceuticals, understanding biochemical pathways, etc.

In one aspect, a computing device implemented method includes receiving data representing a peptide sequence. The data includes an index for each amino acid included in the peptide sequence, and each index represents a position of the corresponding amino acid in the peptide sequence. The method further includes, for each amino acid in the peptide sequence, determining a category for the amino acid and a value associated with the category for the amino acid; and determining one or more relationship groups of the amino acids in the peptide sequence based upon a geometrical structure of the peptide sequence, in which each relationship group includes two of the amino acids in the peptide sequence. The method further includes filtering the one or more relationship groups of the amino acids in the peptide sequence to remove one or more of the relationship groups based upon the category of at least one of the two amino acids of the respective relationship group; and producing a visual representation that includes a representation of each amino acid of the filtered relationship groups.

Implementations may include one or more of the following features. The computing device implemented method can further include determining a peptide index from the values associated with the amino acids of the filtered relationship groups, the peptide index being presented by the visual representation. Determining the peptide index can include summing values associated with amino acids for each filtered relationship group or summing values associated with amino acids for all of the filtered relationship groups. The category for the amino acids can include hydrophobicity or hydrophilicity. The value associated with the category for the amino acid can include a level of hydrophobicity or a level of hydrophilicity. Determining one or more relationship groups of the amino acids in the peptide sequence based upon a geometrical structure of the peptide sequence can include determining two amino acids separated by two or three amino acids. The visual representation can include a graphical representation of a relationship between a pair of amino acids, or a graphical representation of the hydrophobicity of the pair of amino acids.

In another aspect, a system includes a memory configured to store instructions and a processor to execute the instructions to perform operations. The operations include receiving data representing a peptide sequence. The data includes an index for each amino acid included in the peptide sequence, and each index represents a position of the corresponding amino acid in the peptide sequence. The operations further include, for each amino acid in the peptide sequence, determining a category for the amino acid and a value associated with the category for the amino acid; and determining one or more relationship groups of the amino acids in the peptide sequence based upon a geometrical structure of the peptide sequence, in which each relationship group includes two of the amino acids in the peptide sequence. The operations further include filtering the one or more relationship groups of the amino acids in the peptide sequence to remove one or more of the relationship groups based upon the category of at least one of the two amino acids of the respective relationship group; and producing a visual representation that includes a representation of each amino acid of the filtered relationship groups.

Implementations may include one or more of the following features. The operations can further include determining a peptide index from the values associated with the amino acids of the filtered relationship groups, the peptide index being presented by the visual representation. Determining the peptide index can include summing values associated with amino acids for each filtered relationship group or summing values associated with amino acids for all of the filtered relationship groups. The category for the amino acids can include hydrophobicity or hydrophilicity. The value associated with the category for the amino acid can include a level of hydrophobicity or a level of hydrophilicity. Determining one or more relationship groups of the amino acids in the peptide sequence based upon a geometrical structure of the peptide sequence can include determining two amino acids separated by two or three amino acids. The visual representation can include a graphical representation of a relationship between a pair of amino acids, or a graphical representation of the hydrophobicity of the pair of amino acids.

In another aspect, one or more computer-readable media store instructions that are executable by a processing device. Upon such execution, the instructions cause the processing device to perform operations that include receiving data representing a peptide sequence. The data includes an index for each amino acid included in the peptide sequence, and each index represents a position of the corresponding amino acid in the peptide sequence. The operations further include, for each amino acid in the peptide sequence, determining a category for the amino acid and a value associated with the category for the amino acid; and determining one or more relationship groups of the amino acids in the peptide sequence based upon a geometrical structure of the peptide sequence, in which each relationship group includes two of the amino acids in the peptide sequence. The operations further include filtering the one or more relationship groups of the amino acids in the peptide sequence to remove one or more of the relationship groups based upon the category of at least one of the two amino acids of the respective relationship group; and producing a visual representation that includes a representation of each amino acid of the filtered relationship groups.

Implementations may include one or more of the following features. The operations can further include determining a peptide index from the values associated with the amino acids of the filtered relationship groups, the peptide index being presented by the visual representation. Determining the peptide index can include summing values associated with amino acids for each filtered relationship group or summing values associated with amino acids for all of the filtered relationship groups. The category for the amino acids can include hydrophobicity or hydrophilicity. The value associated with the category for the amino acid can include a level of hydrophobicity or a level of hydrophilicity. Determining one or more relationship groups of the amino acids in the peptide sequence based upon a geometrical structure of the peptide sequence can include determining two amino acids separated by two or three amino acids. The visual representation can include a graphical representation of a relationship between a pair of amino acids, or a graphical representation of the hydrophobicity of the pair of amino acids.

These and other aspects, features, and various combinations may be expressed as methods, apparatus, systems, means for performing functions, program products, etc.

Other features and advantages will be apparent from the description and the claims.

DESCRIPTION OF DRAWINGS

FIG. **1** is a 3D structural representation of portions of a peptide sequence presented by a computing device.

FIG. **2** is a network map representation of a complete peptide sequence and a metric presented by a computing device.

FIG. **3** is a user prompt, presented by a computing device, for visually representing a peptide sequence.

FIG. **4** illustrates a vector of amino acids of a peptide sequence, a vector of hydrophobic data, and instructions for retrieving data.

FIG. **5** illustrates determining relationship groups of the amino acids of the peptide sequence.

FIG. **6** illustrates an exemplary data structure for storing relationship groups of amino acids of the peptide sequence.

FIG. **7** illustrates filtering the data structure to remove relationship groups including hydrophilic amino acids.

FIG. **8** illustrates a filtered data structure that includes relationship groups having hydrophobic amino acids.

FIG. **9** illustrates producing a metric for characterizing relationship groups and corresponding executable instructions.

FIG. **10** is a network map representation of a peptide sequence.

FIG. **11** is a listing of instructions for producing a network map representation of a peptide sequence.

FIG. **12** is a function call to initiate operations of a peptide manager to present the user prompt shown in FIG. **3**.

FIG. **13** is an example flow chart of operations of a peptide manager.

FIG. **14**A is an example peptide sequence (SEQ ID NO:1) and its corresponding network map representation.

FIG. **14**B is a modified peptide sequence (SEQ ID NO:2) and its corresponding network map representation.

FIG. **15** illustrates an example of a computing device and a mobile computing device that can be used to implement the techniques described here.

DETAILED DESCRIPTION

Referring to FIG. **1**, a computing device (e.g., a computer system **100**) conveys information about chemical bonds such as information about peptide sequences. In general, a peptide can be considered as including any sequence of amino acids connected to one another by peptide bonds. A peptide sequence can be considered as including a listing of amino acids from the N-terminus to the C-terminus of the peptide, such that the peptide sequence is representative of the primary structure of the peptide. Representing peptide sequences can assist designers in various applications including predicting protein folding configurations, designing pharmaceuticals, and understanding biochemical pathways. In particular, understanding the interactions between the amino acids of a peptide when the peptide is folded in three-dimensional space can assist in these applications. These interactions arise due to the secondary, tertiary, and quaternary structures of peptides. Visual representations of peptides can assist with providing an understanding of the overall structure of the peptide along with the interactions of amino acids that are in close proximity in three-dimensional space. Additionally, such visual representations can assist with understanding other characteristics of the peptide sequence such as toxicity. Such visual representations can take one or more forms; for example, peptides and interactions of associated amino acids can be graphically represented in three-dimensional (3D) space by using a network

representation in which nodes represent amino acids and edges of the network represent interactions between amino acids located in close proximity in three-dimensional space. Various types of implementations can be utilized for generating such graphical representations; for example, such representations can be implemented in executable instructions provided by software-based processes, hardware implementations, combinations of software and hardware, etc.

As illustrated in the figure, the computer system **100** includes a display **102** that presents a representation **104** in 3D of a peptide sequence **106** that includes amino acids **108**, **110**, **112**. Along with providing a general understanding of the structure of the peptide sequence, the representation can provide an understanding of characteristics of the peptide sequence. Such information can be helpful in drug development where therapeutic peptide drug design is becoming more widespread and peptides are recognized for their large growth potential in therapeutics due to their specificity and potency. Further, the representation **104** can graphically represent interactions between the amino acids included in the peptide sequence. Representing such amino acid interactions can be used for designing antimicrobial peptides (AMPs) that are generally minimally toxic to human tissues while retaining antimicrobial potency. Many antimicrobial peptides (AMPs), similarly to cationic antibiotics such as colistin, polymyxin b, and gentamicin, cause nephrotoxicity over the course of treatment. Thus, one approach for designing AMPs is to first minimize toxicity, and then select AMPs with suitable antimicrobial potency.

In some experimental testing (e.g., testing of StAMP51), a stapled antimicrobial peptide and re-engineered variants show that disrupting hydrophobic patches of a peptide in its three-dimensional configuration (e.g., by replacing norleucine residues with alanine) can reduce lytic (i.e. toxic) activity, but also reduces antimicrobial potency. However, by increasing cationic properties on the hydrophilic face of a peptide in its three-dimensional configuration, similar potency to unaltered StAMP51 can be achieved with markedly reduced lytic activity toward human kidney tissue cells (pRPTECs). These results suggest that a design goal for engineering AMPs is to disrupt hydrophobic patches on the three-dimensional peptide structure and increase cationic residues on the hydrophilic face.

In order to disrupt hydrophobic patches and reduce (e.g., minimize) the lyticity of a peptide such as StAMP51, one can refer to a network representation of hydrophobic interactions between amino acids of the peptide that are located in close proximity in three-dimensional space.

As illustrated in the figure, the representation **104** depicts the 3D structure representation of the peptide **106**. This representation **104** shows the alpha-helical structure of the peptide **106** and some sidechains of the amino acid residues. The 3D structure representation of the peptide **106** further shows that given the alpha-helical structure of the peptide, an amino acid of index i in the peptide sequence is most closely located to amino acids of i+3 (highlighted with arrowed line **114**) and i+4 (highlighted by arrowed line **116**) in three-dimensional space. However, due to the peptide's three-dimensional geometry, the representation **104** is unable to show all of the amino acids comprising the peptide sequence simultaneously on the two-dimensional display **102**. In addition, the 3D representation **104** of the peptide **106** does not provide information about the interactions between each amino acid and the amino acids most proximal to it in three-dimensional space. Thus, the 3D structure in representation **104** of the peptide **106** is unable to accurately identify hydrophobic patches of the peptide **106** in order to disrupt the hydrophobic patches and minimize lyticity of the peptide **106**.

Referring to FIG. **2**, to convey a complete information set for a peptide and associated amino acids, a peptide manager **200** is executed by a computing device (e.g., computer system **202**) to present (on a display **204**) a graphical representation **206** of the information. In this example, the visual representation **206** includes a hydrophobicity network map **208**, in which each node (e.g., nodes **210**, **212**, **214**) of the hydrophobicity network map **208** represents an amino acid of the peptide (e.g., peptide **106** shown in FIG. **1**). For this example, amino acids that do not contribute to a hydrophobic patch of the peptide are not presented. An amino acid is considered to not contribute to the hydrophobic patch of the peptide if its side chain is hydrophilic and/or charged. Such visual representations can represent various categories of the peptide sequences; for example, as mentioned above a hydrophobic amino acid category may be used to represent peptides. Other categories associated with hydrophilic amino acids, cationic charge density, anionic charge density, etc. may be used to represent peptides. In some cases, the graphical representation **206** may simultaneously use multiple categories to represent peptides (e.g., by using different colors, different line types, etc.). For example, hydrophobic interactions could be shown with red edges connecting the corresponding nodes while hydrogen bonding interactions can be simultaneously shown with green edges in a single graphical representation **206**.

In general, the hydrophobicity network map **208** represents relationships between each amino acid and the amino acids most proximal to it in three-dimensional space by representing these relationships with a graphical edge connecting the corresponding nodes. In this example, due to the alpha-helical nature of the peptide structure, an edge connects each amino acid with other amino acids located **3** and **4** indices apart from it in the peptide sequence (e.g., i+3 and i+4), as long as they contribute to the hydrophobic patch of the peptide. For example, as illustrated in the figure, the node **210** represents an amino acid and an edge **216** connects to the node **212** that represents another amino acid. Similarly, an edge **218** connects the amino acid represented by node **212** to the amino acid represented by node **214**.

Unlike two-dimensional projections of 3D structure representation **104**, the hydrophobicity network map **208** is a two-dimensional visual representation that is able to present all the amino acids that contribute to the hydrophobic patch of the peptide **106** simultaneously on the two-dimensional on-screen display **104**. Moreover, the hydrophobicity network map **208** has the advantage of being able to provide information about the interactions between each amino acid and the amino acids most proximal to it in three-dimensional space. In the example shown in FIG. **2** each edge thickness corresponds to a sum of the hydrophobicity values of the amino acids represented by the connected nodes, thus representing information about the hydrophobic interactions between them. The information about the hydrophobic interactions across the peptide is further characterized by a quantitative metric called the lyticity index **220** (e.g., having a value of 579.2 as shown in the figure), which is displayed alongside the hydrophobicity network map **208** and is described in further detail below.

Referring to FIG. **3**, to generate a visual representation of a peptide such as the hydrophobicity network map **208** (shown in FIG. **2**), one or more techniques may be employed. For example, one or more software processes may be executed by a computing device to perform opera-

tions to produce such graphical representations. Such operations may include guiding a user through one or more interfaces to collect information, allow preferences selections, and presenting graphics such as network maps. In the example shown in the figure, the peptide manager **200** (executed on the computer system **202** having the display **204**) causes an interface **300** to be presented that prompts a user for information. Through this interface **300**, a peptide can be selected through user interactions; for example, a numerical value can be entered into a field **302** included in the interface **300**. Other user interaction techniques may also be used; for example, one or more menus may be presented for the user to select a peptide for presentation. For instances in which the data representing a peptide of interest is not stored, the interface **300** could direct the user to one or more other software processes for peptide development (e.g., a peptide modeling application) to create a representation of a peptide and storing representative data (e.g., in a storage device **304**).

For the examples described herein, the user selects a peptide in the interface **300** by entering a string of characters into the field **302**. The string of characters can represent a peptide in FASTA format (e.g., using standard IUB/IUPAC amino acid codes). However, modifications and additions can be made to the standard IUB/IUPAC amino acid codes to allow for "stapling" amino acids. Namely, in the examples given below, the character "X" is used to represent the stapling amino acid (S)-2-(4-pentenyl)alanine and the character "8" is used to represent (R)-2-(7-octenyl)alanine. In some implementations, the peptide manager **200** can enforce one or more rules for the input entered in the field **302**. For example, in order to reflect the stapling mechanism of (S)-2-(4-pentenyl)alanine, the peptide manager **200** can require that the character "X" must always be spaced 4 characters away from another "X" or 7 characters away from an "8". In some implementations, if an unrecognized character or invalid string is entered into the field **302**, the peptide manager **200** can cause an error message to be displayed to the user.

Once a valid peptide has been identified, data representing the peptide of interest can be retrieved, for example, from one or more local sources (e.g., the storage device **304**), one or more remote sources (e.g., via a network, the Internet, etc.), etc. Provided the data, a network map of the peptide can be produced by the peptide manager **200** and presented on the display **204**. The map may also be stored in the storage device **304** for later retrieval by the peptide manager **200**.

To produce hydrophobicity network maps, calculate lyticity indices, etc. the peptide manager **200** can employ various types of operations, functions, etc. Referring to FIGS. **4-10**, an example peptide sequence is used to illustrate the operations of the peptide manager **200** to determine and provide this information. Referring to FIG. **4**, a data importation operation of the peptide manager **200** can be implemented using example data importation instructions **400**. Executed, the instructions **400** extract data (e.g., from an MS-Excel spreadsheet called "Data Set.xls" stored on the storage device **304**) and enters the data (e.g., into vector format). In this example, the instructions **400** produce two vectors; a first vector **402** includes data that represents the peptide sequence of interest, where each character (e.g., a letter of the alphabet) represents an individual amino acid and the characters are placed in sequential order according to the primary structure of the peptide. A second vector **404** is a vector containing the hydrophobicity values of the amino acids in the first vector **402**, where the sequential order is maintained. As such, read from left to right, the first character of the first vector **402** (e.g., the letter "X") has a corresponding hydrophobicity value (e.g., 29.5) provided by the first element of the second vector **404**. Similarly, the second character of the first vector **402** (e.g., the letter "I") has a hydrophobicity value (e.g., 22.4) that is provided by the second element of the second vector **404**. This correspondence continues for the remaining elements of the first vector **402** and the second vector **404**; however, other type of protocols, data structures, etc. may be employed. For example, in some cases, a single vector (e.g., a concatenation of the two vectors described above) may be used to represent both the amino acid codes and the hydrophobicity values of the peptide sequence. In general, the data related to the peptide sequence of interest can be stored in any suitable data structure including lists, 2D arrays, multidimensional matrices, dictionaries, and hashtables, among others. One or more sources may be used for values such as hydrophobicity values, for example; values can be utilized from "Determination of Intrinsic Hydrophilicity/Hydrophobicity of Amino Acid Side Chains in Peptides in the Absence of Nearest Neighbor or Conformation Effects," Biopolymers 84(3): 283-97, January 2006, which is incorporated in its entirety by reference herein. In some cases, the hydrophobicity value for (S)-2-(4-pentenyl)alanine can be estimated by combining (e.g. summing) the hydrophobicity values for alanine and norleucine. In some cases, the hydrophobicity value for (R)-2-(7-octenyl)alanine can be estimated by combining the hydrophobicity values for one alanine and two leucine residues.

In some arrangements, the peptide manager **200** may use the information provided by the first vector **402**, the second vector **404**, etc. to determine one or more categories of an amino acid. For example, the values provided in second vector **402** (e.g., hydrophobicity values) may be used to identify a corresponding amino acid (in the first vector **402**) as being hydrophobic or hydrophilic. The information contained in the first vector **402** may also be used to determine the category of each amino acid. For example, based upon the character used to represent the amino acid in the first vector **402**, the peptide manager **200** may be able to determine if the corresponding amino acid is a member of a hydrophobic category or a hydrophilic category. Other types of categories may be determined and used to identify different characteristics of the amino acids; for example, one or more categories may be determined from cationic charge densities by the peptide manager **200**.

Referring to FIG. **5**, with the first and second vectors **402**, **404** produced, the peptide manager **200** executes relationship grouping operations **500**. Due to the alpha-helical structure of the peptide, in three-dimensional space each amino acid in a peptide is generally located most closely to the amino acids located **3** and **4** indices apart from it in the peptide sequence. As such, a relationship group is created between each amino acid of index i and the amino acids of index i+3 and i+4. In other examples, larger or smaller separations between the amino acids may be employed (e.g., for protein structures such as beta sheets, disulfide bridges, etc.). In the illustrated example, relationship groupings are shown for the first amino acid represented (by the letter "X") in the first vector **402** that represents the peptide sequence. This first amino acid "X" is located at the first sequence position, or index, in the first vector **402** (as highlighted by dashed arrow **504** with respect to a vector **506** of position values). The first amino acid "X" also has a hydrophobicity of 29.5, as provided by the value of the first sequence

position in the second vector **404** (as highlighted by dashed arrow **508** with respect to the vector **506**).

To form an i+3 relationship group (illustrated by bracket **500**), the amino acid identity (letter "X"), hydrophobicity value, and sequence position of the amino acid are stored with the amino acid identity, hydrophobicity value, and sequence position of the amino acid located **3** indices after "X". Since "X" is located at the first sequence position, the i+3 relationship group is formed between "X" and the amino acid at the fourth (i+3) index, which, in the example shown, is amino acid "K". In the figure, data associated this i+3 relationship group is shown with graphical representation **510**.

To form an i+4 relationship group (illustrated by bracket **502**), the amino acid identity, hydrophobicity value, and sequence position of "X" is stored with the amino acid identity, hydrophobicity value, and sequence position of the amino acid located **4** indices after "X". Since "X" is located at the first sequence position, a relationship group is formed between "X" and the amino acid at the fourth (i+4) index, which, in the example shown, is also amino acid "X". In the figure, the i+4 relationship group is shown with graphical representation **512**.)

This process is repeated for every amino acid in the first vector **402** until the i+3 or i+4 index exceeds the length of the first vector **402**. In general, if the first vector **402** that represents the peptide sequence is of length n, the number of relationship groups formed is equal to 2n−7, with n−3 relationship groups between the amino acids of index i and i+3, and n−4 relationship groups between the amino acids of index i and i+4.

Referring to FIG. **6**, using the first and second vectors **402**, **404** (representing the peptide sequence and the hydrophobicity), the peptide manager **200** can produce one or more data structures that contain the relationship groups. As illustrated, a data structure **600** includes each of the relationship groups for amino acids with indices i and i+4, as graphically highlighted with dashed box **602**. The data structure **600** also includes the relationship groups for amino acids with indices i and i+3, as graphically highlighted with dashed box **604**. While various formats may be used for each of the relationship groups (i.e., the i+4 groups, and the i+3 groups), the following format is employed in this example:

(Amino acid identity 1, Index 1, Hydrophobicity value 1)→(Amino acid identity 2, Index 2, Hydrophobicity value 2).

Referring to FIG. **7**, upon determining the relationship groups (e.g., the i+3 and i+4 relationship groups), the peptide manager **200** is capable of processing the data of these groups. For example, if a researcher is interested in identifying the hydrophobic regions of a peptide, the researcher may only be interested in relationship groups in which both amino acids are hydrophobic. For relationship groups that do not solely include hydrophobic amino acids, they may be filtered out by the peptide manager **200**. Filtering the groups can result in non-hydrophobic amino acids being removed. For example, a vector **700** of hydrophilic amino acids may be provided to the peptide manager **200** (e.g., retrieved from storage device **304**) for removing relationship groups (from the relationship groups of the data structure **600**) that have at least one hydrophilic amino acid. In this example, the vector of all hydrophilic amino acids **700** is entitled "wamino" and is provided to the peptide manager **200**. To remove the hydrophilic amino acids from the relationship groups of data structure **600**, the peptide manager **200** executes instructions **702** that use the vector **700** of hydrophilic amino acids; however other types of instructions, functions, etc. may be used. Through the processing, the peptide manager **704** produces another data structure **704**, within which graphical bars are used to represent which relationship groups have been filtered out (i.e., groups that contain at least one of the hydrophilic amino acids **700** are removed). Referring to FIG. **8**, based upon the removal of relationship groups containing one or more hydrophilic amino acids, a filtered data structure **800** is produced, which includes only relationship groups where both amino acids are hydrophobic.

Referring to FIG. **9**, upon producing the filtered data structure **800**, the peptide manager **200** can execute operations; for example, one or more metrics may be determined for assisting the researcher in attaining a better understanding of the peptide sequence. Such metrics could be reviewed alone or in combination with one or more graphical representations of the peptide sequence. In this example, hydrophobicity values of the amino acids in each remaining relationship group are summed to attain a lyticity index. For example, the hydrophobicity values of the two amino acids of the first relationship group (highlighted with bracket **900**) are summed (29.5+29.5=59) and stored in a first element of a vector **902** (labeled "Edgethicklist2"). Similarly the hydrophobicity values of the two amino acids in the second relationship group (highlighted with bracket **904**) are summed (22.4+24.2=46.6) and are stored in a second element of the Edgethicklist2 vector **902**. The peptide manager **200** continues to sum the hydrophobicity values of the relationship groups and store the values in elements of the vector **902**. In this case, the vector **902** includes seventeen elements, one for each of the seventeen relationship groups.

To calculate the metric, e.g., a lyticity index **906**, the peptide manager **200** computes the sum of the elements of the vector **902**. In this example, the lyticity index **906** has a value of 577.4. In general, hydrophobic patches in peptides with alpha-helical structure correspond to increased lytic activity. As such, the lyticity index **906**, which is representative of the amount and degree of hydrophobic amino acid interactions in the peptide, is a metric that increases with lytic activity. The lyticity index **906** has the advantage of giving researchers a single quantitative value for a peptide that serves as an indicator of a peptide's toxicity. To perform these operations, various types of executable instructions may be employed; for example, instructions **908** may be used by the peptide manager **200** to determine the lyticity index from the hydrophobicity values of the relationship groups.

Referring to FIG. **10**, along with determining one or metrics such as the lyticity index (shown in FIG. **9**), the peptide manager **200** produces a visual representation of the peptide sequence using the information from the filtered data structure **800** (shown in FIG. **8**). As illustrated in this example, a network map representation **1000** (similar to the representation of FIG. **2**) includes nodes that represent each hydrophobic amino acid included in the peptide sequence. To assist the viewer, each node includes information associated with the respective amino acid; for example, an identifier of amino acid (e.g., "X", "I", "G", "K", etc.) along with the hydrophobic amino acid's position in the peptide sequence (e.g., "1", "2", "3", "5", . . . , "21") is presented in each node. In this example, each distinct amino acid (from the filtered data structure **800**) is represented once as a single node. If the amino acid is part of multiple relationship groups, the node representing the amino acid has multiple edges that connect to nodes representing other amino acids to form the corresponding relationship groups (e.g., i+3 and i+4 relationship groups). For example, relationship groups

that include node **1002** (that represents amino acid "A" in the ninth position of the peptide sequence) are illustrated by connections with node **1004** (that represents amino acid "X" in the fifth position of the peptide sequence), node **1006** (that represents amino acid "L" in the sixth position of the peptide sequence), node **1008** (that represents amino acid "F" in the twelfth position of the peptide sequence), and node **1010** (that represents amino acid "G" in the thirteenth position of the peptide sequence). Each relationship group is represented by a graphical edge that connects the two nodes of the group. Additionally, each edge is represented as having a graphical characteristic (e.g., thickness) that is proportional to the sum of the hydrophobicity values of the amino acids being represented by the connected nodes. For example, an edge **1012** connecting nodes **1002** and **1004** is relatively thick to represent a large sum of hydrophobicity values (e.g., 33.4) while an edge **1014** is thinner to represent a comparatively smaller sum hydrophobicity values (e.g., 3.9).

In some implementations, the positioning of the nodes in the network map representation **1000** can be determined based on one or more criteria. For example, in some cases, the nodes may be placed to minimize the total length of the edges between nodes. In some cases, the nodes may be placed to minimize the number of intersections between edges. In some cases, the nodes may be placed such that they are always farther than a threshold distance from the nearest node. In some cases, a combination of these criteria, and/or additional criteria can be used to determining the positioning of each node.

In some implementations, the network map representation **1000** may be interactive, enabling a user to control the positioning of nodes. For example, in some cases, the user may be able to click-and-drag a node to a new location, while the network map representation **1000** maintains the edges between nodes. This may provide the advantage of allowing a user to customize the shape of the network map representation **1000** by creating a configuration more conducive to their exploration of the interactions between amino acids in the peptide sequence of interest.

By such a presentation, the network map representation **1000** is able to clearly display all of the amino acids and hydrophobic interactions of a peptide sequence in a two-dimensional representation, including interactions between closely proximal amino acids. Furthermore, the edge thicknesses give a clear visual representation of the relative hydrophobicity of each interaction. The network map representation **1000** also provides researchers with a sense of the amino acids with the most hydrophobic interactions, such as amino acid A_9 (represented by the node **1002**), which may serve as useful targets of interest for disrupting large hydrophobic patches of the peptide **106**. Additionally, to further assist the researcher, the lyticity index **906** (e.g., value 577.4) can be presented with the network map representation **1000** to provide an indication of the peptide's toxicity (as presented in FIG. **2**).

While the network map representation **1000** is described as a two-dimensional representation, in some cases, it can be presented as a three-dimensional representation. In such cases, the nodes may be positioned in a three-dimensional environment according to one or more of the criteria described above. The three-dimensional environment may be interactive, allowing the user to rotate, zoom, and pan in order to view the peptide from different perspectives. Furthermore, as described above, the network map representation **1000** may itself be interactive, enabling a user to manually control the positioning of the nodes within the three-dimensional environment.

The peptide manager **200** may employ one or more techniques to prepare a visual representation such as the network map representation **1000**. Referring to FIG. **11**, a listing **1100** of exemplary executable instructions is shown that can be used by the peptide manager **200** to produce the network map representation. Along with instructions for producing such visual representations, the peptide manager **200** can provide other functionality to assist the researcher; for example, referring to FIG. **12**, a function call **1200** may be employed to generate a user prompt (e.g., the interface **300** shown in FIG. **3**), which prompts a user to input a peptide of interest. In this particular example, a single function initiates execution of the operations that leads to the selection of a peptide, presentation of the visual representation (e.g., a network map representation of the peptide, the lyticity index of the peptide,), etc. Additional functionality can also be initiated by such a function; for example, storing, cataloging, retrieval, etc., of peptide information, representations, etc. may be initiated by one or more function calls.

Referring to FIG. **13**, a flowchart **1300** represents operations of a peptide manager (e.g., the peptide manager **200** shown in FIG. **2**). Operations of the peptide manager are typically executed by a single computing device (e.g., the computer system **202**); however, operations of the peptide manager may be executed by multiple computing devices. For example, the peptide manager may be an application program that is executed for use by one computing device. In some arrangements, the peptide manager may be accessible by multiple computing devices (e.g., via a cloud service) and executed by one computing device (e.g., a server at the cloud service) or multiple computing devices. Along with being executed at a single site (e.g., a peptide research facility, a cloud service site, etc.), the peptide manager may be executed in a distributed manner among two or more locations.

Operations of the peptide manager may include receiving **1302** data representing a peptide sequence, the data includes an index for each amino acid included in the peptide sequence. Each index represents a position of the corresponding amino acid in the peptide sequence. For example, based upon a peptide being select by a user (e.g., using the interface **300** shown in FIG. **3**), data can be retrieved that represents a vector of amino acids included in a peptide sequence. The position of the amino acid in the vector can correspond to the position of the amino acid in the peptide sequence. Retrieved data may also include other information such as values representing the hydrophobicity of the amino acids (as provided by the instructions shown in FIG. **4**). Operations of the peptide manager may also include, for each amino acid in the peptide sequence, determining **1304** a category for the amino acid and a value associated with the category for the amino acid. For example, from retrieved hydrophobicity values the peptide manager can determine if each amino acid is a member of a hydrophobic category or a hydrophilic category. Operations of the peptide manager may also include, determining **1306** one or more relationship groups of the amino acids in the peptide sequence based upon a geometrical structure of the peptide sequence. Each relationship group includes two of the amino acids in the peptide sequence. For example, relationship groups can be determined based upon the separation of the amino acids in the peptide sequence. In one arrangement, amino acids separated by two amino acids (e.g., i+3 relationship groups) and amino acids separated by three amino acids (e.g., i+4 relationship groups) of the peptide sequence may be identified. Operations of the peptide manager may also include filtering **1308** the one or more relationship groups of the

amino acids in the peptide sequence to remove one or more of the relationship groups based upon the category of at least one of the two amino acids of the respective relationship group. For example, the i+3 and i+4 relationship groups may be filtered for removing any relationship group that includes a hydrophilic amino acid. Operations of the peptide manager may also include producing **1310** a visual representation comprising a representation of each amino acid of the filtered relationship groups. For example, as illustrated in FIG. **10**, a network map representation may be produced that presents a representation of all the amino acids in hydrophobic relationship groups included in the peptide sequence. In some instances, additional information may be included in the visual representation; for example, one or more metrics such as a lyticity index may be presented to provide the viewer with a measure of the toxicity of the presented peptide along with the overall structure and interactions of the hydrophobic amino acids.

In some implementations, peptide manager **200** can be configured not only to create a visual representation of a peptide sequence, but also to create a visual representation of the effects of mutating the peptide sequence. For example, referring to FIG. **14**A, the network map representation **1410**A for an example peptide sequence (SEQ ID NO:1) **1400**A is shown along with the calculated lyticity index **1420**A, which has a value of 577.4. In this case, the example peptide sequence **1400**A is "XIGKXLHSAKKFGKAFVGEIBNS", which, for the purposes of demonstration, is the same peptide sequence used for the description of FIGS. **4-10** above.

In some cases, a user may be interested in visualizing the changes to a hydrophobicity network map in the case of a mutation. For example, a user may desire to visualize the effect of replacing a hydrophobic amino acid such as "A" in the 9th index of peptide sequence **1400**A with a hydrophilic residue. Referring to FIG. **14**B, in order to observe this effect, the user can modify the input peptide sequence to "XIGKXLHSZKKFGKAFVGEIBNS" (**1400**B), replacing the "A" at the 9th index (**1430**A) with a "Z" (**1430**B). In this case, the character "Z" serves as an indicator that the user would like to substitute a hydrophilic amino acid (e.g., lysine) at this index of the peptide sequence. In other implementations, the peptide manager **200** can be configured to recognize other codes or indicators.

Referring still to FIG. **14**B, in response to receiving the modified peptide sequence (SEQ ID NO:2) **1400**B, the peptide manager **200** generates the updated network map representation **1410**B. As shown, the A_9 node (**1440**A) has been replaced with a K_9 node (**1440**B), representing a lysine residue at the 9th index of the peptide sequence. In some cases, other hydrophilic amino acids may be used. Furthermore, referring to both FIG. **14**A and FIG. **14**B, the edges connecting the A_9 node to other nodes in the network map representation **1410**A have been replaced with dotted lines in the updated network map representation **1410**B. In this case, the dotted lines provide a visual representation of the disruption to the hydrophobic interactions that result from replacing the A_9 node with a K_9 node. The user is also presented with an updated lyticity index value (**1420**B) of 478.2, which is lower than the original lyticity index value (**1420**A) of 577.4. In this case, the lyticity index value is reduced because the edges connecting to the A_9 node in network map representation **1410**A have been replaced with edges that do not contribute to the lyticity index. This visual comparison of the original peptide sequence **1400**A with the mutated, or modified, peptide sequence **1400**B can assist the user in understanding the effects of various modification to a peptide's hydrophobic network.

Along with producing visual representations of the peptide sequences and calculating metrics, the peptide manager **200** may process the peptide information for other functionality. For example, through evaluation, characterization, etc. particular peptides, amino acids, relationship groups, etc. may be identified that could be helpful in peptide development. The peptide manager **200** can provide such functionality by using peptide information with machine learning techniques to recommend amino acid substitutions, deletions, insertions, etc. Machine learning techniques can be used to identify peptides (or other information such as amino acids, relationship groups, etc.) for development efforts, a recommendation service, etc. For example, through the use of these techniques libraries may be created and used to detect particular aspects of peptides and provide suggestions. Along with information associated with peptides (e.g., identified amino acids, hydrophobicity data, etc.), processed data may be used in the machine learning techniques (e.g., to train a machine learning system). For example, processed data such as one or more calculated metrics (e.g., lyticity indices) may be employed for system training. Experimental data can also be used for training a machine learning system. Various data sources can provide this information: local storage (e.g., storage device **304**) and/or remote storage locations (e.g., accessible by one or more networks such as the Internet).

By training the machine learning system, the peptide manager **200** is capable of contributing to a number of functions. For example, characteristics, capabilities, etc. of peptides may be determined in advance by the peptide manager **200** for future use. For example, as new peptides are developed, the peptide manager **200** may categorize the new peptides and determine similarities with these peptides and previously analyzed peptides. Such preparation work could improve efficiency in peptide development. The peptide manager **200** can also manage data that represents similarities (or dissimilarities) among the peptide sequences, characteristics of the peptides, amino acids present in the peptides, etc. As such, similar peptide sequences may be quickly identified and provided to a requesting researcher's computing device. In one arrangement, a database (e.g., stored on storage device **304**) includes records that represent the similarities (or dissimilarities) among peptides and is accessible by the peptide manager **200**. In some instances, the similarity (or dissimilarity) information may be monitored, tracked, etc. by the peptide manager **200**. For example, records may be stored that reflect particular peptides that have been requested, identified by the machine learning system, etc.

One or more forms of artificial intelligence, such as machine learning, can be employed such that a computing process or device may learn to determine peptide similarities (or dissimilarities) from training data, without being explicitly programmed for the task. Using this training data, machine learning may employ techniques such as regression to estimate peptide similarities. To produce such estimates, one or more quantities may be defined as a measure of peptide similarity. For example, amino acids, group relationships, hydrophobicity, lyticity index values, etc. may be used to define differences between two peptides. One or more conventions may be utilized; for example, a pair of peptides that have relatively close lyticity index values can be considered similar. Alternatively a large difference in lyticity index values can be indicative of peptides being considered different. As such, upon being trained, a learning

machine may be capable of outputting a numerical value that represents the difference in lyticity index values of two peptides.

To implement such an environment, one or more machine learning techniques may be employed. For example, supervised learning techniques may be implemented in which training is based on a desired output that is known for an input. Supervised learning can be considered an attempt to map inputs to outputs and then estimate outputs for previously unused inputs. Unsupervised learning techniques may also be used in which training is provided from known inputs but unknown outputs. Reinforcement learning techniques may also be employed in which the system can be considered as learning from consequences of actions taken (e.g., inputs values are known and feedback provides a performance measure). In some arrangements, the implemented technique may employ two or more of these methodologies. For example, the learning applied can be considered as not exactly supervised learning since the level of difference between two peptides can be considered unknown prior to executing computations. While the difference level is unknown, the implemented techniques can check the computed peptide differences in concert with comparing lyticity index values. By using both information sources regarding peptide similarity, a reinforcement learning technique can be considered as being implemented.

In some arrangements, neural network techniques may be implemented using the peptide information (e.g., vectors of numerical values that represent features of the peptides) to invoke training algorithms for automatically learning the peptides and related information. Such neural networks typically employ a number of layers. Once the layers and number of units for each layer is defined, weights and thresholds of the neural network are typically set to minimize the prediction error through training of the network. Such techniques for minimizing error can be considered as fitting a model (represented by the network) to the training data. By using the peptide information (e.g., peptide features), a function may be defined that quantifies error (e.g., a squared error function used in regression techniques). By minimizing error, a neural network may be developed that is capable of estimating amino acid recommendations (e.g., for substitution, deletion, insertion, etc.), peptide similarity, etc. Other factors may also be accounted for during neutral network development. For example, a model may too closely attempt to fit data (e.g., fitting a curve to the extent that the modeling of an overall function is degraded). Such overfitting of a neural network may occur during the model training and one or more techniques may be implements to reduce its effects.

A variety of peptide features may be used for training and using a machine learning system. For example, tens of features may be calculated for each peptide. Features may include, for example, the amino acids found in peptide, most common amino acids found in peptides, amino acid categories (e.g., hydrophobic, hydrophilic, etc.), amino acid relationship groups, hydrophobicity of amino acids, hydrophobicity of relationship groups, etc. In some arrangements, peptide features may be processed prior to being used for machine training (or for use by a trained machine to determine amino acid recommendations). For example, a vector that represents a collection of peptide features may be normalized so that training data used can be considered as being placed on an equal basis (and one or more particular peptide features are not overly emphasized). Such normalizing operations may take many forms. For example, an estimated value (e.g., average) and standard deviation (or variance) may be calculated for each feature. Once these quantities are calculated (e.g., the average and standard deviation), each feature is normalized using the data.

Once trained, the peptide manager **200** may be used to recommend amino acids (e.g., for substitution, deletion, insertion). The peptide manager **200** can calculate and compare, for example, features such as lyticity index values to determine amino acid recommendations. Along with determining amino acid recommendations, the peptide manager **200** may provide other functionality. For example, the peptide manager **200** may also initiate the storage of data that represents peptides, amino acid recommendations, preferences of researchers using the peptide manager **300**, etc. Storing such data generally allows the information to be quickly retrieved rather than being recalculated. For example, for peptide (represented in data stored in the storage device **304**), a list of recommended amino acids may be produced and stored for quick retrieval. As new peptides appear (e.g., are developed, identified, etc.) operations may be executed to quickly present recommended amino acids, update a peptide database, etc. Techniques such as batch processing may be implemented for determining amino acid recommendations relatively large numbers of peptides. In some situations multiple new peptides may be introduced together and techniques may be employed to efficiently recommend amino acids from the machine learning system. For example, trained on previously known peptides and associated amino acids and operations executed to recommend amino acids for each of the new peptides. By implementing batch processing or other similar techniques, updating of databases (to reflect new peptides) may be executed during less busy time periods (e.g., overnight).

FIG. **15** shows an example of example computer device **1500** and example mobile computer device **1550**, which can be used to implement the techniques described herein. For example, a portion or all of the operations of the peptide manager **200** (shown in FIG. **2**) may be executed by the computer device **1500** and/or the mobile computer device **1550**. Computing device **1500** is intended to represent various forms of digital computers, including, e.g., laptops, desktops, workstations, personal digital assistants, servers, blade servers, mainframes, and other appropriate computers. Computing device **1550** is intended to represent various forms of mobile devices, including, e.g., personal digital assistants, tablet computing devices, cellular telephones, smartphones, and other similar computing devices. The components shown here, their connections and relationships, and their functions, are meant to be examples only, and are not meant to limit implementations of the techniques described and/or claimed in this document.

Computing device **1500** includes processor **1502**, memory **1504**, storage device **1506**, high-speed interface **1508** connecting to memory **1504** and high-speed expansion ports **1510**, and low-speed interface **1512** connecting to low-speed bus **1514** and storage device **1506**. Each of components **1502**, **1504**, **1506**, **1508**, **1510**, and **1512**, are interconnected using various busses, and can be mounted on a common motherboard or in other manners as appropriate. Processor **1502** can process instructions for execution within computing device **1500**, including instructions stored in memory **1504** or on storage device **1506** to display graphical data for a GUI on an external input/output device, including, e.g., display **1516** coupled to high-speed interface **1508**. In other implementations, multiple processors and/or multiple busses can be used, as appropriate, along with multiple memories and types of memory. Also, multiple computing devices **1500** can be connected, with each device providing

portions of the necessary operations (e.g., as a server bank, a group of blade servers, or a multi-processor system).

Memory **1504** stores data within computing device **1500**. In one implementation, memory **1504** is a volatile memory unit or units. In another implementation, memory **1504** is a non-volatile memory unit or units. Memory **1504** also can be another form of computer-readable medium (e.g., a magnetic or optical disk. Memory **1504** may be non-transitory.).

Storage device **1506** is capable of providing mass storage for computing device **1500**. In one implementation, storage device **1506** can be or contain a computer-readable medium (e.g., a floppy disk device, a hard disk device, an optical disk device, or a tape device, a flash memory or other similar solid state memory device, or an array of devices, such as devices in a storage area network or other configurations.) A computer program product can be tangibly embodied in a data carrier. The computer program product also can contain instructions that, when executed, perform one or more methods (e.g., those described above.) The data carrier is a computer- or machine-readable medium, (e.g., memory **1504**, storage device **1506**, memory on processor **1502**, and the like.)

High-speed controller **1508** manages bandwidth-intensive operations for computing device **1500**, while low-speed controller **1512** manages lower bandwidth-intensive operations. Such allocation of functions is an example only. In one implementation, high-speed controller **1508** is coupled to memory **1504**, display **1516** (e.g., through a graphics processor or accelerator), and to high-speed expansion ports **1510**, which can accept various expansion cards (not shown). In the implementation, low-speed controller **1512** is coupled to storage device **1506** and low-speed expansion port **1514**. The low-speed expansion port, which can include various communication ports (e.g., USB, Bluetooth®, Ethernet, wireless Ethernet), can be coupled to one or more input/output devices, (e.g., a keyboard, a pointing device, a scanner, or a networking device including a switch or router, e.g., through a network adapter.).

Computing device **1500** can be implemented in a number of different forms, as shown in the figure. For example, it can be implemented as standard server **1520**, or multiple times in a group of such servers. It also can be implemented as part of rack server system **1524**. In addition or as an alternative, it can be implemented in a personal computer (e.g., laptop computer **1522**.) In some examples, components from computing device **1500** can be combined with other components in a mobile device (not shown), e.g., device **1550**. Each of such devices can contain one or more of computing device **1500**, **1550**, and an entire system can be made up of multiple computing devices **1500**, **1550** communicating with each other.

Computing device **1550** includes processor **1552**, memory **1564**, an input/output device (e.g., display **1554**, communication interface **1566**, and transceiver **1568**) among other components. Device **1550** also can be provided with a storage device, (e.g., a microdrive or other device) to provide additional storage. Each of components **1550**, **1552**, **1564**, **1554**, **1566**, and **1568**, are interconnected using various buses, and several of the components can be mounted on a common motherboard or in other manners as appropriate.

Processor **1552** can execute instructions within computing device **1550**, including instructions stored in memory **1564**. The processor can be implemented as a chipset of chips that include separate and multiple analog and digital processors. The processor can provide, for example, for coordination of the other components of device **1550**, e.g., control of user interfaces, applications run by device **1550**, and wireless communication by device **1550**.

Processor **1552** can communicate with a user through control interface **1558** and display interface **1556** coupled to display **1554**. Display **1554** can be, for example, a TFT LCD (Thin-Film-Transistor Liquid Crystal Display) or an OLED (Organic Light Emitting Diode) display, or other appropriate display technology. Display interface **1556** can comprise appropriate circuitry for driving display **1554** to present graphical and other data to a user. Control interface **1558** can receive commands from a user and convert them for submission to processor **1552**. In addition, external interface **1562** can communicate with processor **1542**, so as to enable near area communication of device **1550** with other devices. External interface **1562** can provide, for example, for wired communication in some implementations, or for wireless communication in other implementations, and multiple interfaces also can be used.

Memory **1564** stores data within computing device **1550**. Memory **1564** can be implemented as one or more of a computer-readable medium or media, a volatile memory unit or units, or a non-volatile memory unit or units. Expansion memory **1574** also can be provided and connected to device **1550** through expansion interface **1572**, which can include, for example, a SIMM (Single In Line Memory Module) card interface. Such expansion memory **1574** can provide extra storage space for device **1550**, or also can store applications or other data for device **1550**. Specifically, expansion memory **1574** can include instructions to carry out or supplement the processes described above, and can include secure data also. Thus, for example, expansion memory **1574** can be provided as a security module for device **1550**, and can be programmed with instructions that permit secure use of device **1550**. In addition, secure applications can be provided through the SIMM cards, along with additional data, (e.g., placing identifying data on the SIMM card in a non-hackable manner.).

The memory can include, for example, flash memory and/or NVRAM memory, as discussed below. In one implementation, a computer program product is tangibly embodied in a data carrier. The computer program product contains instructions that, when executed, perform one or more methods, e.g., those described above. The data carrier is a computer- or machine-readable medium (e.g., memory **1564**, expansion memory **1574**, and/or memory on processor **1552**), which can be received, for example, over transceiver **1568** or external interface **1562**.

Device **1550** can communicate wirelessly through communication interface **1566**, which can include digital signal processing circuitry where necessary. Communication interface **1566** can provide for communications under various modes or protocols (e.g., GSM voice calls, SMS, EMS, or MMS messaging, CDMA, TDMA, PDC, WCDMA, CDMA2000, or GPRS, among others.) Such communication can occur, for example, through radio-frequency transceiver **1568**. In addition, short-range communication can occur, e.g., using a Bluetooth®, WiFi, or other such transceiver (not shown). In addition, GPS (Global Positioning System) receiver module **1570** can provide additional navigation- and location-related wireless data to device **1550**, which can be used as appropriate by applications running on device **1550**. Sensors and modules such as cameras, microphones, compasses, accelerators (for orientation sensing), etc. may be included in the device.

Device **1550** also can communicate audibly using audio codec **1560**, which can receive spoken data from a user and convert it to usable digital data. Audio codec **1560** can

likewise generate audible sound for a user, (e.g., through a speaker in a handset of device **1550**.) Such sound can include sound from voice telephone calls, can include recorded sound (e.g., voice messages, music files, and the like) and also can include sound generated by applications operating on device **1550**.

Computing device **1550** can be implemented in a number of different forms, as shown in the figure. For example, it can be implemented as cellular telephone **1580**. It also can be implemented as part of smartphone **1582**, personal digital assistant, or other similar mobile device.

Various implementations of the systems and techniques described here can be realized in digital electronic circuitry, integrated circuitry, specially designed ASICs (application specific integrated circuits), computer hardware, firmware, software, and/or combinations thereof. These various implementations can include implementation in one or more computer programs that are executable and/or interpretable on a programmable system including at least one programmable processor. The programmable processor can be special or general purpose, coupled to receive data and instructions from, and to transmit data and instructions to, a storage system, at least one input device, and at least one output device.

These computer programs (also known as programs, software, software applications or code) include machine instructions for a programmable processor, and can be implemented in a high-level procedural and/or object-oriented programming language, and/or in assembly/machine language. As used herein, the terms machine-readable medium and computer-readable medium refer to a computer program product, apparatus and/or device (e.g., magnetic discs, optical disks, memory, Programmable Logic Devices (PLDs)) used to provide machine instructions and/or data to a programmable processor, including a machine-readable medium that receives machine instructions.

To provide for interaction with a user, the systems and techniques described here can be implemented on a computer having a device for displaying data to the user (e.g., a CRT (cathode ray tube) or LCD (liquid crystal display) monitor), and a keyboard and a pointing device (e.g., a mouse or a trackball) by which the user can provide input to the computer. Other kinds of devices can be used to provide for interaction with a user as well; for example, feedback provided to the user can be a form of sensory feedback (e.g., visual feedback, auditory feedback, or tactile feedback); and input from the user can be received in a form, including acoustic, speech, or tactile input.

The systems and techniques described here can be implemented in a computing system that includes a backend component (e.g., as a data server), or that includes a middleware component (e.g., an application server), or that includes a frontend component (e.g., a client computer having a user interface or a Web browser through which a user can interact with an implementation of the systems and techniques described here), or a combination of such back end, middleware, or frontend components. The components of the system can be interconnected by a form or medium of digital data communication (e.g., a communication network). Examples of communication networks include a local area network (LAN), a wide area network (WAN), and the Internet.

The computing system can include clients and servers. A client and server are generally remote from each other and typically interact through a communication network. The relationship of client and server arises by virtue of computer programs running on the respective computers and having a client-server relationship to each other. For example, in some implementations, the functionality of the peptide manager **200** executed by computer system **202** (e.g., a server) can be provided as a web application. For example, an external computer system (e.g., a client) may, over the Web, request computer system **202** to execute at least a portion of the functionality of the peptide manager **200**. In response, the computer system **202** can execute the peptide manager **200** and send data corresponding to a resulting network map representation to the client for presentation at the external computer system.

In some implementations, the engines described herein can be separated, combined or incorporated into a single or combined engine. The engines depicted in the figures are not intended to limit the systems described here to the software architectures shown in the figures.

A number of embodiments have been described. Nevertheless, it will be understood that various modifications can be made without departing from the spirit and scope of the processes and techniques described herein. In addition, the logic flows depicted in the figures do not require the particular order shown, or sequential order, to achieve desirable results. In addition, other steps can be provided, or steps can be eliminated, from the described flows, and other components can be added to, or removed from, the described systems. Accordingly, other embodiments are within the scope of the following claims.

SEQUENCE LISTING

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<223> OTHER INFORMATION: (S)-2-(4-pentenyl)alanine

<400> SEQUENCE: 1

-continued

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1               5                   10                  15

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            20


<210> SEQ ID NO 2
<211> LENGTH: 23
<212> TYPE: PRT
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<220> FEATURE:
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<223> OTHER INFORMATION: (S)-2-(4-pentenyl)alanine

<400> SEQUENCE: 2

Xaa Ile Gly Lys Xaa Leu His Ser Glx Lys Lys Phe Gly Lys Ala Phe
1               5                   10                  15

Val Gly Glu Ile Asx Asn Ser
            20
```

What is claimed is:

1. A method comprising:

receiving data representing a first antimicrobial peptide sequence;

receiving data representing a second antimicrobial peptide sequence that comprises one or more modifications of the first antimicrobial peptide sequence, wherein the data includes an index for each amino acid included in the second antimicrobial peptide sequence, and wherein each index represents a position of the corresponding amino acid in the second antimicrobial peptide sequence;

for each amino acid in the second antimicrobial peptide sequence, determining a category for the amino acid and a value associated with the category for the amino acid;

determining one or more relationship groups of the amino acids in the second antimicrobial peptide sequence based upon a geometrical structure of the second antimicrobial peptide sequence, wherein each relationship group includes two of the amino acids in the second antimicrobial peptide sequence;

filtering the one or more relationship groups of the amino acids in the second antimicrobial peptide sequence to remove one or more of the relationship groups if at least one of the two amino acids of the respective relationship group is hydrophilic;

producing a visual representation of hydrophobic interactions of the second antimicrobial peptide sequence, the visual representation comprising a network map with nodes and edges, wherein each node represents an individual amino acid of the filtered relationship groups, and wherein the edges represent the filtered relationship groups;

computing a lyticity metric for the second antimicrobial peptide sequence corresponding to the visual representation of hydrophobic interactions of the second antimicrobial peptide sequence;

comparing the lyticity metric for the second antimicrobial peptide sequence with a lyticity metric for the first antimicrobial peptide sequence;

determining that the lyticity metric for the second antimicrobial peptide sequence is less than the lyticity metric for the first antimicrobial peptide sequence; and

in response to determining that the lyticity metric for the second antimicrobial peptide sequence is less than the lyticity metric for the first antimicrobial peptide sequence, synthesizing a peptide in accordance with the second antimicrobial peptide sequence, wherein the synthesized peptide has a lower toxicity than another peptide corresponding to the first antimicrobial peptide sequence.

2. The method of claim **1**, further comprising:

determining a peptide index from the values associated with the amino acids of the filtered relationship groups,

wherein the visual representation represents the peptide index.

3. The method of claim **2**, wherein determining the peptide index comprises summing values associated with amino acids for each filtered relationship group.

4. The method of claim **2**, wherein determining the peptide index comprises summing values associated with amino acids for all of the filtered relationship groups.

5. The method of claim **1**, wherein the category for the amino acid includes one of hydrophobicity and hydrophilicity.

6. The method of claim **1**, wherein the value associated with the category for the amino acid includes one of a level of hydrophobicity and a level of hydrophilicity.

7. The method of claim **1**, wherein determining one or more relationship groups of the amino acids in the second antimicrobial peptide sequence based upon a geometrical structure of the second antimicrobial peptide sequence comprises determining two amino acids separated by two amino acids.

8. The method of claim 1, wherein determining one or more relationship groups of the amino acids in the second antimicrobial peptide sequence based upon a geometrical structure of the second antimicrobial peptide sequence comprises determining two amino acids separated by three amino acids.

9. The method of claim 1, further comprising experimentally testing at least one of a lytic activity or an antimicrobial potency of the synthesized peptide.

10. The method of claim 1, comprising:

obtaining experimental data about one or more peptide features of a plurality of additional peptides;

training a machine learning model, using the experimental data, to recommend amino acid substitutions, deletions, or insertions to the plurality of additional peptides to achieve target peptide features;

utilizing the machine learning model to recommend a modification to the second antimicrobial peptide sequence; and

producing a modified visual representation corresponding to the recommended modification to the second antimicrobial peptide sequence.

11. The method of claim 1, wherein a visual characteristic of the edges represents a hydrophobicity of the filtered relationship groups.

12. The method of claim 11, wherein the visual characteristic is an edge thickness.

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