Computer Program for Interpreting Peptide Mass Spectra Utilizing Hydrogen-Deuterium Exchange Information

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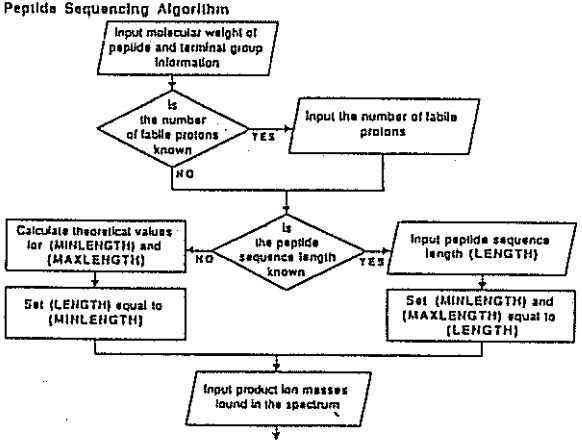
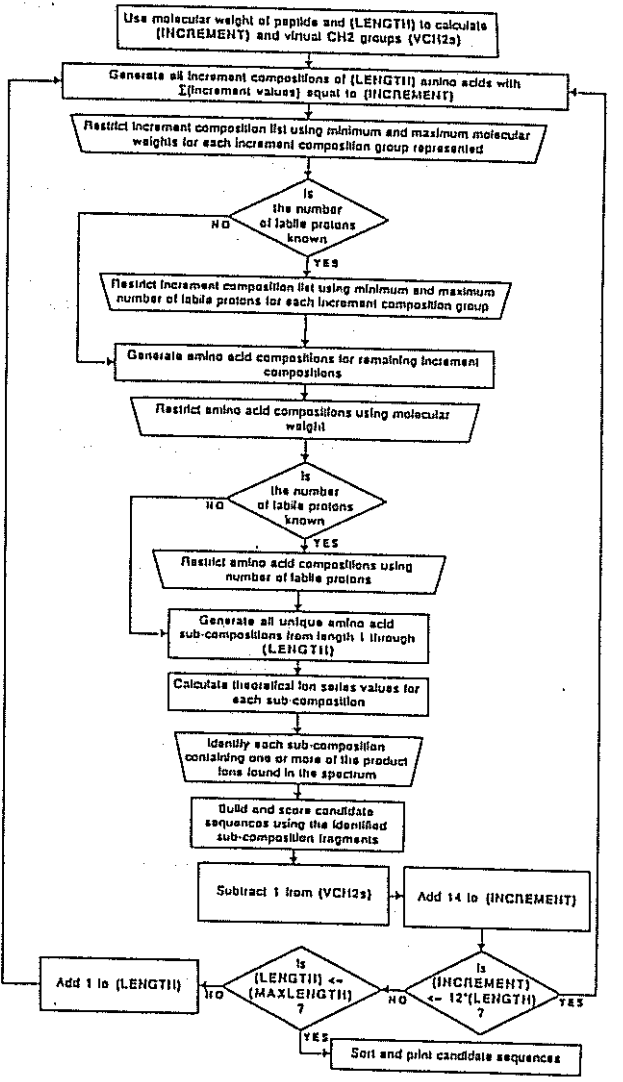
Recently we reported the use of hydrogen/deuterium exchange to facilitate peptide sequence analysis by mass spectrometry [1]. Information about the number of exchangeable hydrogens can be used to filter the list of candidate sequences obtained from computer interpretation programs, thereby significantly decreasing the number of possible sequences to be considered. We have since developed an efficient peptide sequencing algorithm which utilizes the experimentally determined number of exchangeable protons as a key input parameter. The basic approach is to first calculate possible compositions that are consistent with the molecular weight. A novel method reduces the customary list of 20 amino acids to nine groups and dramatically decreases the time needed to do the calculations. By using information about the number of exchangeable hydrogens, the final list of possible compositions is reduced to a manageable size. Possible compositions are then calculated for each significant ion in the mass spectrum. These subcompositions are then combined to yield a final list of possible sequences. The program was written in the C programming language in conformance with the ANSI programming standard to ensure code portability. The code was generated and tested on a Dell 433DE desktop computer using the Microsoft Quick C compiler version 2.5. Future work will optimize the process of building sequences from composition data and to analyze deuterium exchanged fragment ion spectra.

[1] N.F. Sepetov, O.L. Issakova, M. Lebl, K. Swiderek, D.C. Stahl, T.D. Lee, Rapid Commun. Mass Spectrom., 7 (1993) 58-62.




Use molecular weight of peptide and (LENGTH) to calculate (INCREMENT) and virtual CH2 groups (VCH2s)
Generate all increment compositions of (LENGTH) amino acids with Σ(increment values) equal to (INCREMENT)
Restrict increment composition list using minimum and maximum molecular weights for each increment composition group represented
Is the number of labile protons known
NO
YES
Restrict increment composition list using minimum and maximum number of labile protons for each increment composition group
Generate amino acid compositions for remaining increment compositions
Restrict amino acid compositions using molecular weight
Is the number of labile protons known
NO
YES
Restrict amino acid compositions using number of labile protons
Generate all unique amino acid sub-compositions from length 1 through (LENGTH)
Calculate theoretical ion series values for each sub-composition
Identify each sub-composition containing one or more of the product ions found in the spectrum
Build and score candidate sequences using the identified sub-composition fragments
Subtract 1 from (VCH2s)
Add 14 to (INCREMENT)
Is (INCREMENT) <= 12*(LENGTH) ?
NO
YES
Is (LENGTH) <= (MAXLENGTH) ?
NO
YES
Add 1 to (LENGTH)
Sort and print candidate sequences