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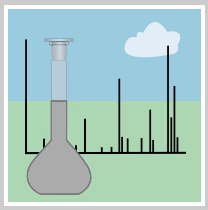

# Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences
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## OMA & OPA – A Software Tool for Mass Spectrometric Sequencing of Nucleic Acids

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Oligonucleotides comprising unnatural building blocks, which interfere with the translation machinery, have gained increased attention for the treatment of gene-related diseases (*e.g.* antisense, RNAi). Due to structural modifications, synthetic oligonucleotides exhibit increased biostability and bioavailability upon administration. Consequently, classical enzyme-based sequencing methods are not applicable to their sequence elucidation and verification. Tandem mass spectrometry is the method of choice for performing such tasks, since gas-phase dissociation is not restricted to natural nucleic acids. However, tandem mass spectrometric analysis can generate product ion spectra of tremendous complexity, as the number of possible fragments grows rapidly with increasing sequence length. The fact that structural modifications affect the dissociation pathways greatly increases the variety of analytically valuable fragment ions. The gas-phase dissociation of oligonucleotides is characterized by the cleavage of one of the four bonds along the phosphodiester chain, by the accompanying loss of nucleobases, and by the generation of internal fragments due to secondary backbone cleavage. For example, an 18-mer oligonucleotide yields a total number of 272'920 theoretical fragment ions.

In contrast to the processing of peptide product ion spectra, which nowadays is highly automated, there is a lack of tools assisting the interpretation of oligonucleotide data. The existing web-based and stand-alone software applications are primarily designed for the sequence analysis of natural nucleic acids, but do not account for chemical modifications and adducts.

Consequently, we developed a software to support the interpretation of mass spectrometric data of natural and modified nucleic acids and their adducts with chemotherapeutic agents. The software package consists of two parts: (i) The Oligonucleotide Mass Assembler (OMA) and (ii) the Oligonucleotide Peak Analyzer (OPA). The OMA represents a tool for calculating all possible fragment ions of a given nucleic acid sequence. The OPA subsequently matches the m/z of the theoretical dissociation products with the experimental data. The library of oligonucleotide building blocks can be expanded by the user in order to address any structural modification.

**The OMA & OPA software is programmed in the platform-independent language Java and it therefore runs on all major operating systems. It can be downloaded for free from: *http://schuerch.dcb.unibe.ch/omaopa/*.**

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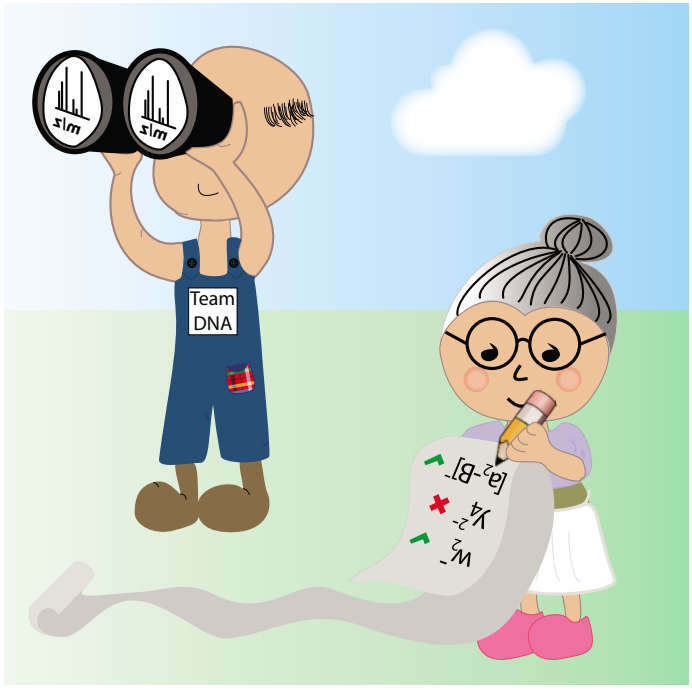
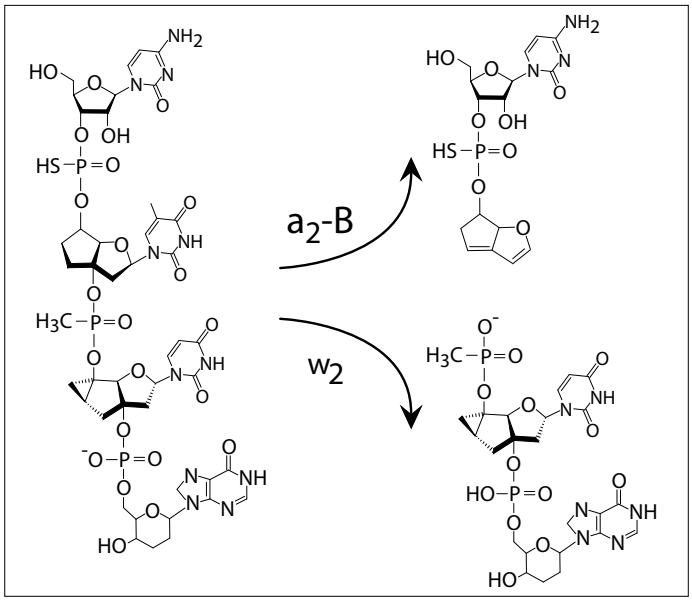
**Reference**

A. Nyakas, L. C. Blum, S. R. Stucki, J. L. Reymond, S. Schürch, *J. Am. Soc. Mass Spectrom.* **2013**, *24*, 249.




A successful team: The Oligonucleotide Mass Assembler (OMA) and the Oligonucleotide Peak Analyzer (OPA) calculate and match the fragment ions of nucleic acids, respectively.




The functionality of the software package is independent of the customized introduction of chemical modifications.

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