

Tetras Asynchronous Multiple Peptide Instrument



Charles Li: Advanced ChemTech, 5609 Fern Valley Rd., Louisville KY 40228 USA,

Oliver J. Kreuzer: peptides&elephants GmbH, Am Mühlenberg 11, 14476 Potsdam, Germany

www.peptides.de

Tetras: made by Advanced ChemTech, USA

www.advancedchemtech.com



The development of the solid phase peptide synthesis strategy by R.B. Merrifield allowed the transfer of chemical synthesis from a manual workflow to a machine based, fully automated process. Merrifield himself developed the first Peptide Synthesizer in 1966. Since that time a number of different machines have been used to automate peptide synthesis. Modern machines are following two general set-ups; the so called “single approach” and the “parallel approach”.

In the single approach, the machine is developed to synthesize one or few peptides simultaneously. The user is able to optimize the synthesis conditions on each single peptide and each single coupling step. The maximum product quality regarding purity and yield is the major task of this approach. In the parallel approach, the machine is developed to synthesize a huge number of different peptides in the same single setup and time-frame. The user always has to find a synthesis protocol appropriate for the needs of each peptide to reach the maximum quality, knowing that there will be always a number of failed peptides. As a result you will find both types of peptide synthesizers in laboratories all over the world: The Single Machine, for the complicated peptides, and the Parallel Machine, allowing generation of multiple peptides with standardized protocols for each.

The Tetras is the first instrument combining the advantages of both machine types and allows the user to synthesize up to 106 different peptides in parallel. Each peptide can have its own individual synthesis protocols, separate of all others. The user can combine different synthesis scales, peptide lengths, and activator reagents in one run. Finished peptides can be removed and new peptides can be started while the Tetras is still running. The Tetras allows the user to establish an uninterrupted production shop using one instrument only.

Different Peptides made on the Tetras

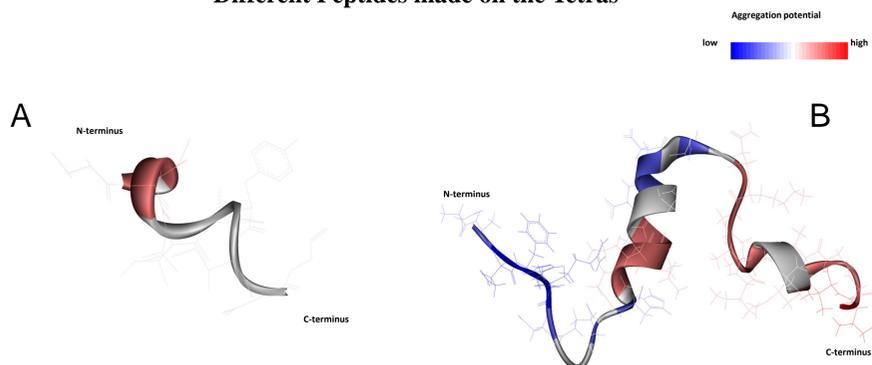


Fig. 1: Structure of the Acyl Carrier Protein ACP amide (65-74) [A] and Human β -Amyloid Peptide (1-42) [B] In colors synthesis difficulties according to the peptides&elephants Prediction Software

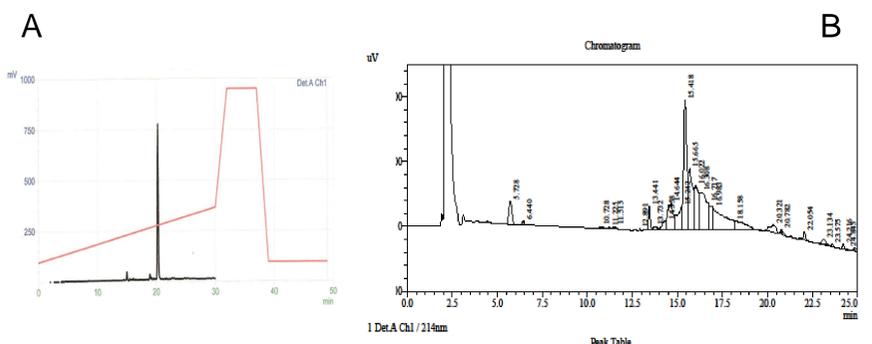


Fig. 2: HPLC for ACP amide (65-74) [A] and Human β -Amyloid Peptide (1-42), C-term Ala Spacer [B]

Purity	ACP amide (65-74)	Human β -Amyloid Peptide (1-42), C-term Ala Spacer
detection 214 nm	> 90%	20% product

Tab. 1: HPLC evaluated purity as % of the total peak areas

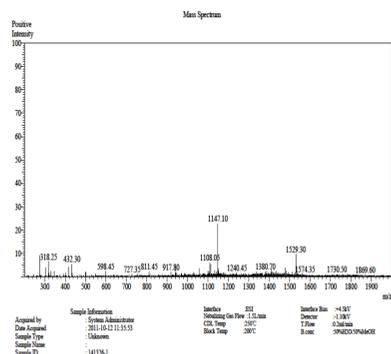


Fig. 3: ESI MS spectra of the Human β -Amyloid Peptide (1-42), C-term Ala Spacer

Human β -Amyloid Peptide (1-42), C-term Ala Spacer	
MW (theory)	MW (found)
4586,4 g/mol	4584,9 g/mol

Tab. 2: confirmation of the product Identity for the Human β -Amyloid Peptide (1-42), C-term Ala Spacer

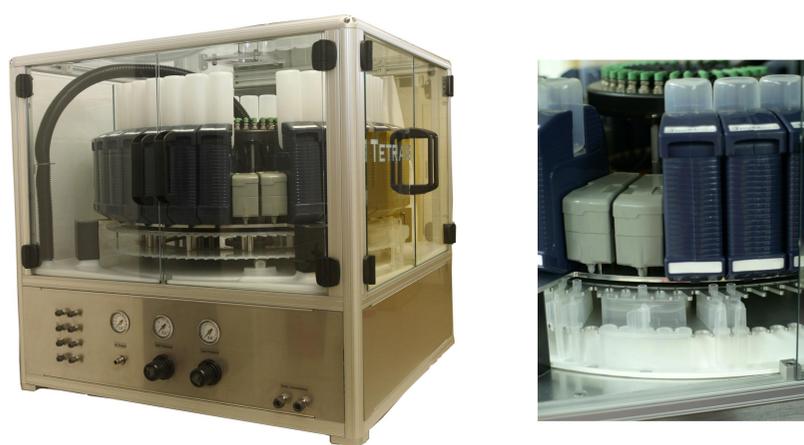


Fig 4: The asynchronous multiple peptide instrument: Tetras

Up to 106 Reactors can be used on the Tetras. The reactors are spaced in a carousel allowing the Tetras to position the reactors under 32 different injection stations delivering solvents and reagents. Standard configuration includes 24 injection stations that are internally supplied by 125 ml supply bottles. There are 8 externally supplied stations that draw material from bulk containers. 4 Purge stations can be used to simultaneously to empty the reaction wells in a “Grouped” configuration.

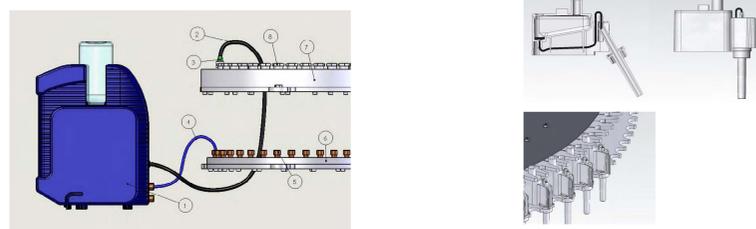


Fig 5: Injection Station with on-board reservoir

Fig 6: Reaction wells and carousel

The geometry of the reaction well allows the resin to swim in the reagent solution. The mixing is performed by automated toggling of the carousel. The reaction wells are emptied by the purge stations using pressurized nitrogen.

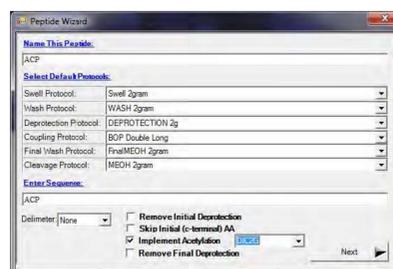


Fig 7 The Peptide Wizard enables to import sequences and to define individual synthesis protocols

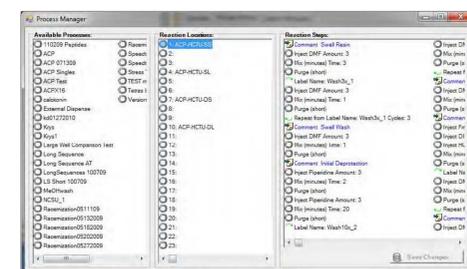


Fig 8: The Process Manager allows to control and to change a synthesis protocol for each peptide.

The GMP applicable Synthesis Software can import and export sequences and Synthesis Processes. Each Peptide can be made by its own fully customizable protocols. Synchronization points allow the user to add or remove peptides within a run and ensure high quality. The intelligent software recognizes and controls the injection stations in a way that reagents can be delivered and reaction vessels can be primed simultaneously. By sending alert E-Mails to the user and service technicians, the Tetras keeps its user updated on the syntheses’ progress as well as alerting technicians to the operational status of the device remotely.