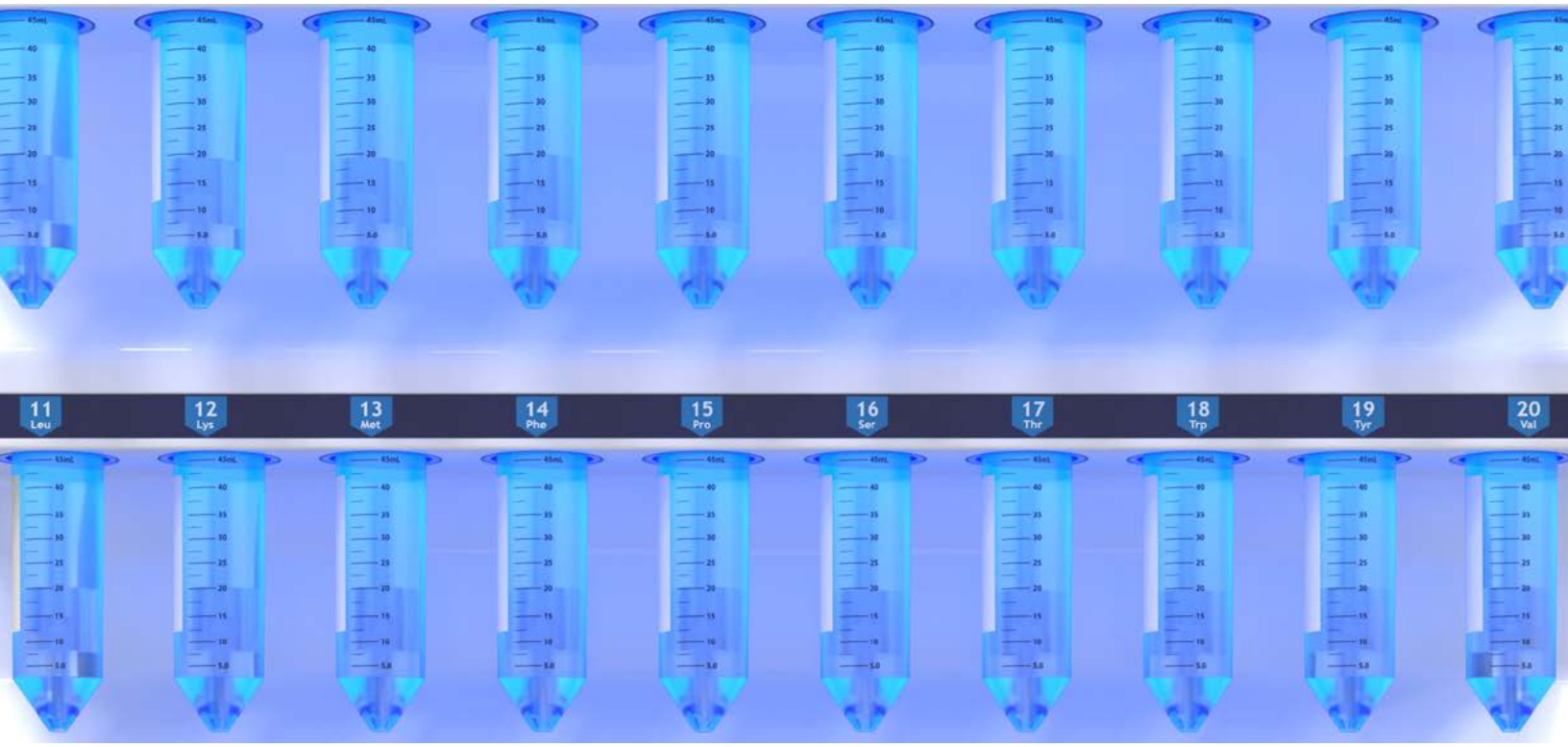
Unparalleled

Peptide Synthesis



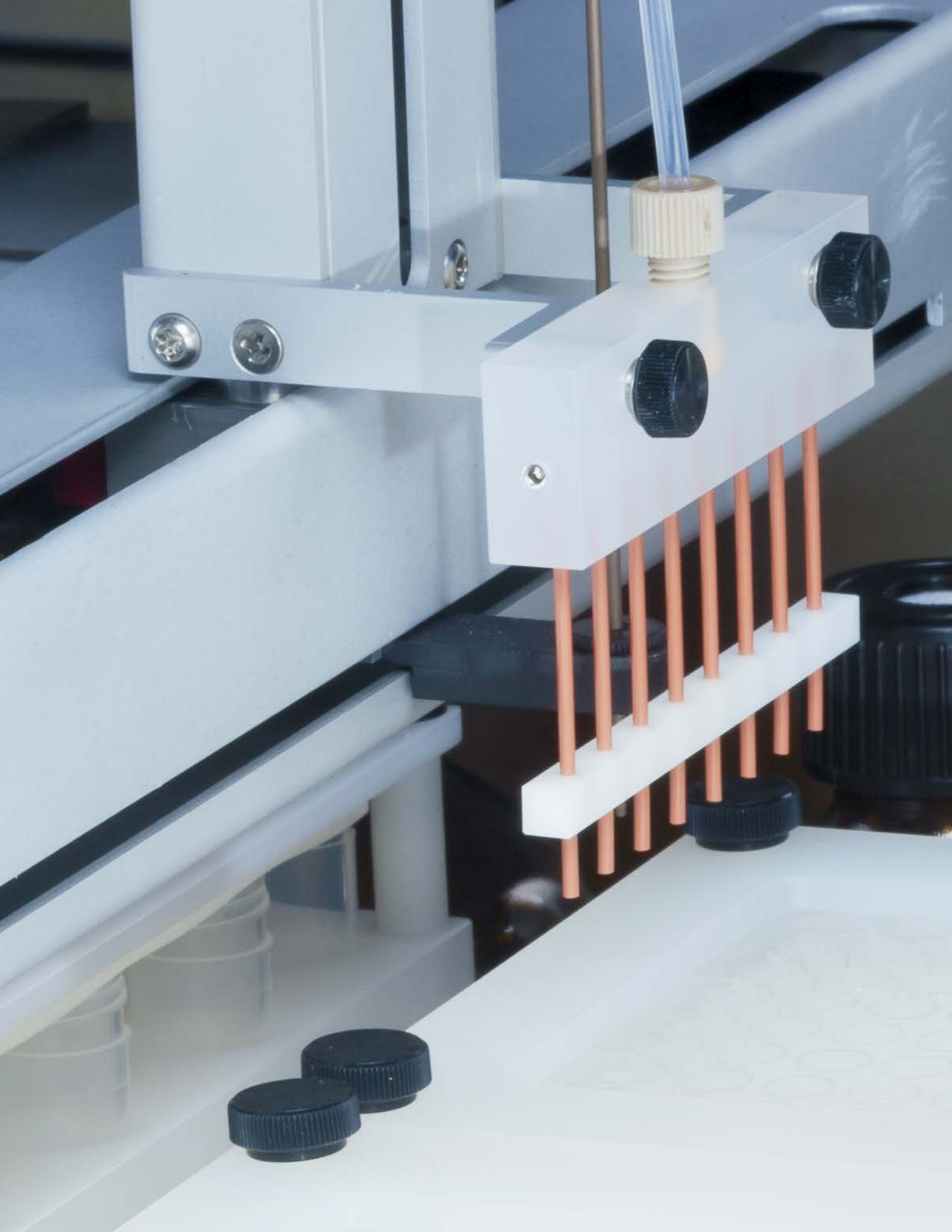
Chemistry Technologies

Peptide Synthesizers

Peptide Cleavage

SPPS Reagents

We Simplify Science



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CEM Overview

Innovations in Microwave Peptide Synthesis

1978 CEM Corporation founded as a new company, based on microwave laboratory instrumentation

2001 CEM launches a single mode microwave system for chemical synthesis

2003 CEM develops the world's first automated microwave peptide synthesizer[1]

2007 CEM publishes research for optimized methods for aspartimide formation and epimerization under microwave SPPS[2]

2013 Liberty Blue™ peptide synthesizer developed based on High Efficiency Solid Phase Peptide Synthesis (*HE*-SPPS)

2014 *HE*-SPPS methodology published[3]

2016 CEM launches new universal load resins eliminating the need for pre-loaded resins historically used

2016 CEM offers the world's first large-scale microwave peptide synthesis, with capabilities of up to 500 grams of a purified peptide, in a single batch

2016 CEM develops improved carbodiimide coupling methods for peptide synthesis at elevated temperature (CarboMAX™)

2017 CEM develops a novel one-pot coupling/ deprotection process reducing SPPS cycle time and waste usage (Liberty PRIME™)

2019 CEM acquires the Intavis line of peptide synthesizers used for small scale high throughput screening including the SPOT and CelluSPOTs technology

Founding Fathers (circa 1980)

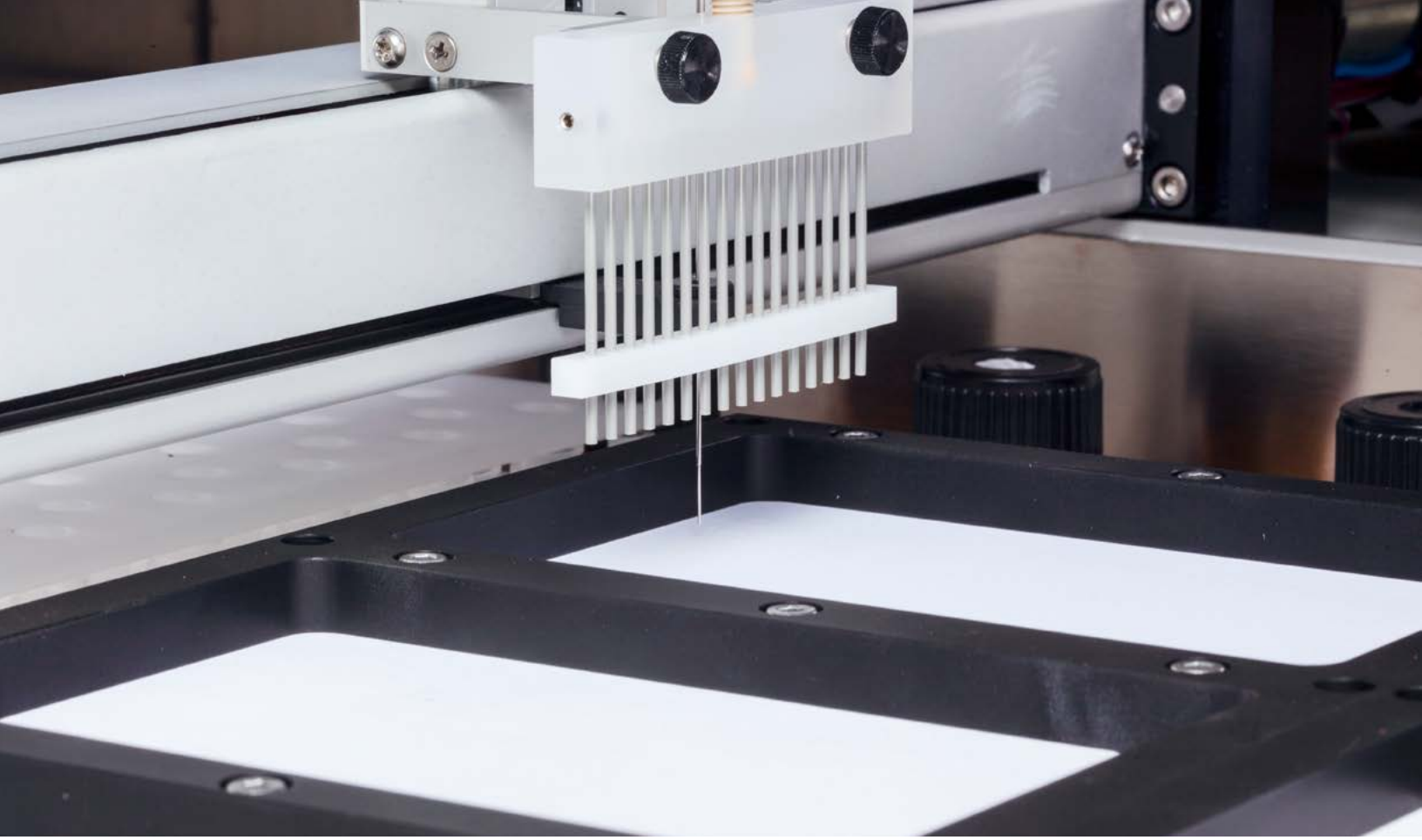
Chemist: Dr. Michael J. Collins (Middle)
Electrical Engineer: Ron Goetchius (Left)
Mechanical Engineer: Bill Cruse Jr. (Right)

[1] Collins J.M., Collins M.J., Steorts R.C. Biopolymers 71, 361 2003
[2] Palasek S., Cox Z., Collins J. J. Pept. Sci. 13, 143-148 2007
[3] Collins, J., Porter K., Singh S., Vanier G. Org. Lett. 16, 940-943 2014

Corporate Legacy

Founded in 1978 by our current CEO, Dr. Michael J. Collins, CEM has pioneered the field of microwave chemistry. For nearly 40 years we have designed and developed laboratory instrumentation and scientific methods (both microwave-based and non-microwave technologies) that are used by major companies, prestigious research institutes, and universities around the world. The company's major products provide unique solutions for compositional analysis of food and chemical samples, acid digestion for elemental analysis, and chemical synthesis of peptides and small molecules.

CEM is a private company with global headquarters outside Charlotte, North Carolina, along with offices in England, Germany, Japan, France, Italy, Singapore, and Ireland. The company's annual revenue is > 100M USD (2018) with more than 300 employees worldwide. Since 2003, CEM has pioneered the area of microwave peptide synthesis. The company sells an elite line of microwave-based peptide synthesizers, based on unique high efficiency solid phase peptide synthesis (*HE*-SPPS) which provides unmatched purity, ultra-fast cycle times, and up to a 90% reduction in total waste, compared to traditional technologies. More than 600 peptide synthesizers from CEM have been installed throughout the world.



96/384 Well Plates and Cellulose Membranes

The Leaders in Peptide Arrays

Screening of peptides for potential activity is a fundamental technique for research toward drug development. It requires the synthesis of large numbers of peptides in various formats that investigate peptide interactions with targets of interest. This includes epitope mapping, profiling antibodies, determining active substrates of enzymes, and ligand to receptor interactions. CEM's MultiPep 1 and 2 peptide synthesizers provide the most advanced formats for generating peptide arrays.

Peptide Arrays

Synthesize peptide arrays using up to 4 x 96 well plates or 72 columns (2, 5, 10 mL sizes) in parallel with the MultiPep 2 peptide synthesizer. Optional heating blocks are available for both plate and columns options to generate arrays in higher crude purity.

Peptide Microarrays

Even larger numbers of peptides can be produced using the SPOT synthesis. This technique available on the MultiPep 1 and 2 systems allows for the parallel synthesis of up to 2400 peptides at a time by repeated deposition of activated amino acids as spots on a specially derivatized filter sheet. The SPOT methodology has been demonstrated in > 400 scientific articles for analysis of protein-protein interactions and allows the synthesis of multiple peptides at a fraction of synthesis on resin[1]. The synthesized peptides can then be cleaved or remain bound to the cellulose membrane for direct screening.

[1] Winkler, D. et al *Peptide Microarrays – Chapter 5*, Meth. Mol. Biol. 570, **2009**

Identical Copies of Peptide Microarrays — CelluSpots™

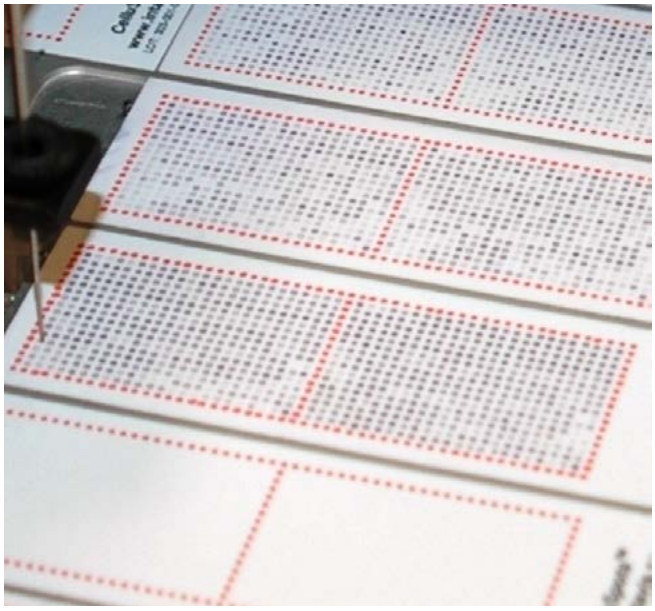
Reuse of SPOT membrane is limited (some assays can only be used once) and production of duplicate SPOT arrays with identical quality is time consuming. Additionally, membranes are large compared to microarrays on glass slides and require large sample volumes.

CelluSpots overcomes these limitations while maintaining the advantages of traditional SPOT membranes. With the CelluSpots methodology, peptides are synthesized on a modified cellulose support which can be uniquely dissolved after synthesis. The solutions of individual peptides covalently linked to a macromolecular cellulose can then be spotted many times onto multiple copies a surface of choice generating many copies of a peptide array on glass slides. After evaporation of the solvent a three-dimensional layer is formed which is not dissolved in aqueous reagents used for standard assays. The three-dimensional structure holds up to 1000 times more peptides per area as compared to conventional monolayer deposition. This shifts the binding equilibrium in a favorable direction for low affinity protein-protein interactions.

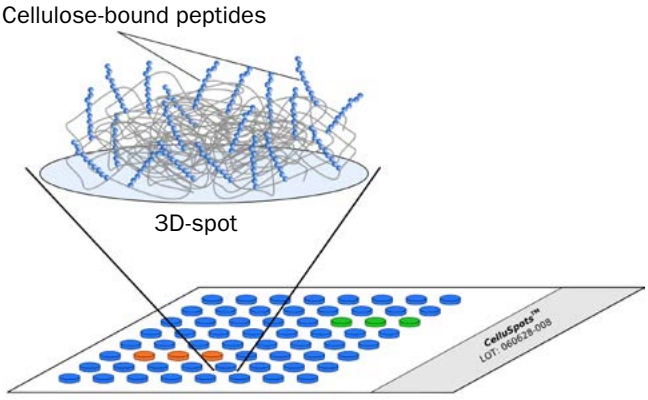
Benefits of CelluSpots

- Easily create many copies of a peptide array
- Higher peptide density allows for detection of low affinity interactions and only limited sample volume
- Detection by chemiluminescence, autoradiography or enzymatic color development
- Compatible with standard equipment for microarray (ex. hybridization chambers and scanners)
- Low non-specific protein binding of cellulose

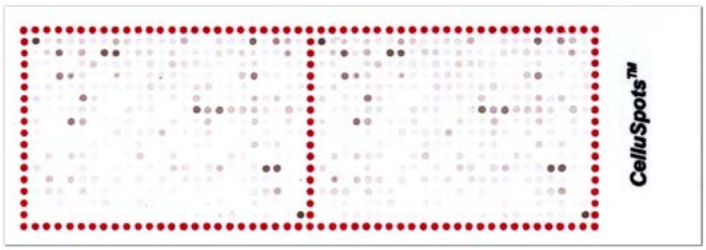
Dissolved peptide-cellulose conjugates in 384 well being spotted onto CelluSpots slides.



Spotting of peptide-cellulose conjugates on many identical slides using the Slide Spotting Robot.



CelluSpots – Peptide Array



HE-SPPS

High Efficiency Solid Phase Peptide Synthesis (*HE*-SPPS)

HE-SPPS is a significant advancement for solid phase peptide synthesis. It originates from our pioneering work in developing microwave assisted SPPS, introduced at the 2003 American Peptide Symposium.[1] At this time, we introduced a new process for making peptides, based on the use of microwave energy for both the deprotection and coupling steps in SPPS. This technology has demonstrated improvements for thousands of peptides with CEM's peptide synthesis instrumentation.[2] To support microwave SPPS, we have also utilized in-situ fiber optic temperature monitoring to provide true internal solution temperature control. This is essential for fast reaction heating with temperature control, as it is well known that the outside of a reaction vessel can be at a significantly different temperature than the inside.[3]

In 2013, we developed an improved methodology for microwave SPPS, based on the use of higher temperature carbodiimide based coupling at 90 °C, along with the elimination of all washing after each coupling step.[4] These insights led to significant time and solvent savings, while providing peptides of incredibly high purity. The more acidic coupling environment with carbodiimide chemistry overcomes coupling issues for cysteine (epimerization) and arginine (γ-lactam formation), which were previously an issue under more basic coupling conditions (ex. HCTU/DIEA). The instrumentation design used on CEM's Liberty Blue™ peptide synthesizer is also a critical component of *HE*-SPPS to eliminate inefficient internal fluidic and reagent path cleaning that increases waste generated. *HE*-SPPS used on the Liberty Blue is now used in hundreds of laboratories worldwide and provides very fast, high purity peptides with incredibly low waste generated.

[1] Collins, J.M., Collins, M.J., and Steorts, R.C., "A Novel Method for Solid Phase Peptide Synthesis Using Microwave Energy" Biopolymers, 71, 361 2003.

[2] US7393920; US7582728; US8058393; JP4773695

[3] M. Herrero, J. Kremsner and C.O. Kappe, "Nonthermal Microwave Effects Revisited: On the Importance of Internal Temperature Monitoring and Agitation in Microwave Chemistry," J. Org. Chem., vol. 73, pp. 36 – 47, 2008.

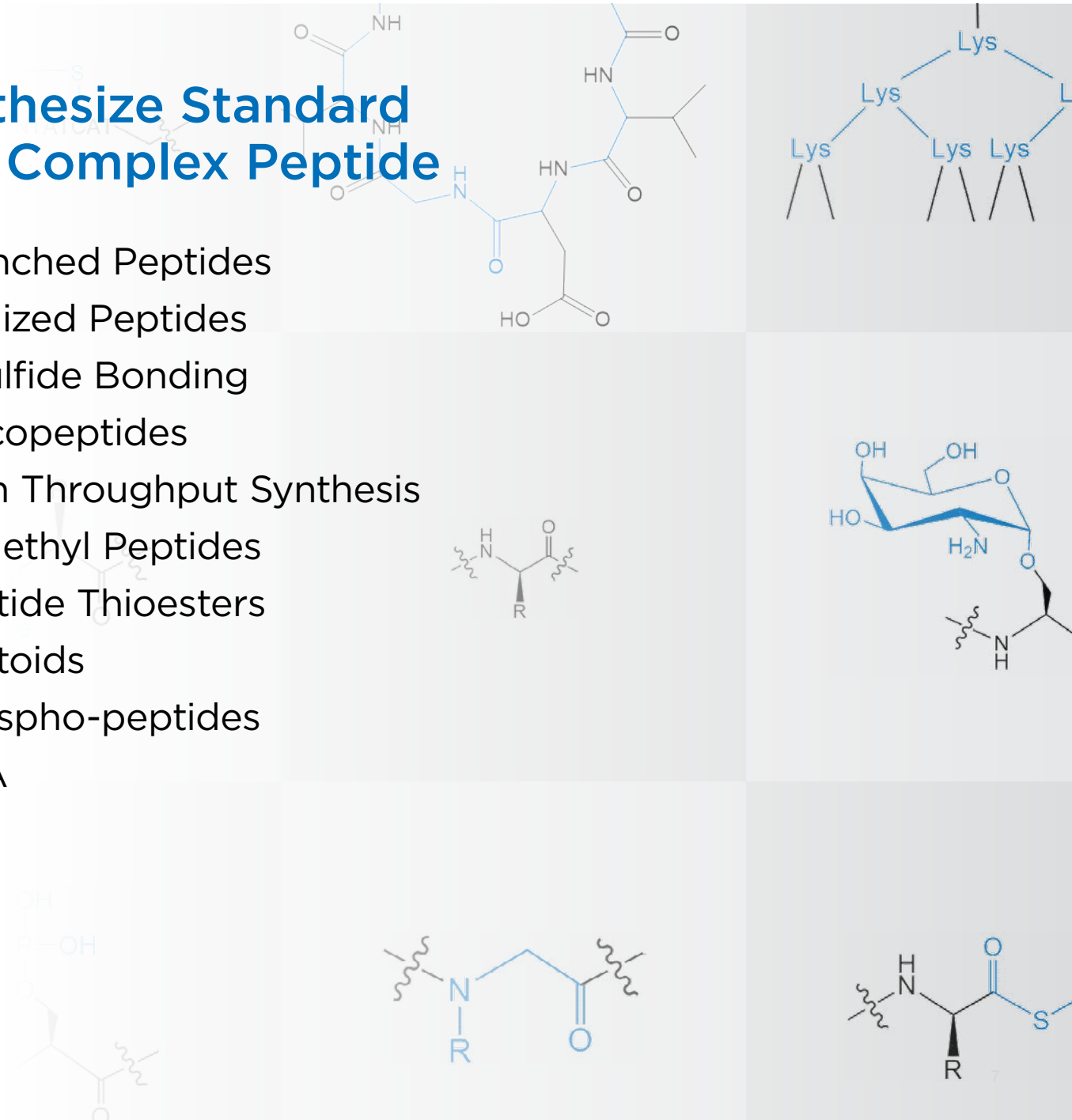
[4] J. Collins, K. Porter, S. Singh and G. Vanier, "High-Efficiency Solid Phase Peptide Synthesis (*HE*-SPPS)," Org. Lett., vol. 16, pp. 940-943, 2014.

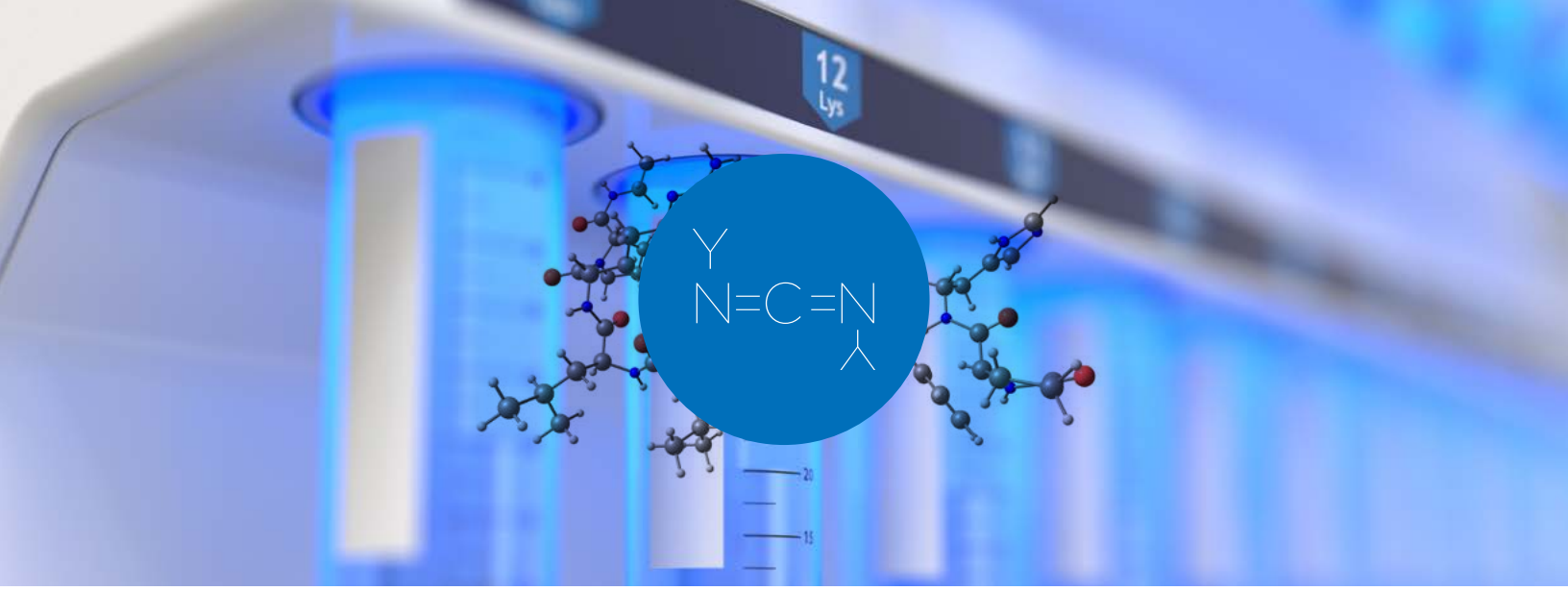
Selected Peptides Synthesized with *HE*-SPPS

Peptide	Sequence	UPLC Purity	Synthesis Time	Total Waste (mL)
$^{65-74}$ACP	VQAAIDYING	93%	44 m	154 mL
JR-10mer	WFTTLISTIM-NH_2	67%	49 m	170 mL
ABRF 1992	GVRGDKGNPGWPGAPY	82%	1 h 37 m	272 mL
ABC-20mer	VYWTSPFMKLIHEQCNRADG-NH_2	73%	2 h 7 m	340 mL
Thymosin	SDAAVDTSSEITTKDLKEKKEVVEEAEN-NH_2	61%	2 h 11 m	468 mL
$^{1-42}$β-amyloid	DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA-NH_2	72%	3 h 49 m	1019 mL

Synthesize Standard and Complex Peptide

- Branched Peptides
- Cyclized Peptides
- Disulfide Bonding
- Glycopeptides
- High Throughput Synthesis
- N-Methyl Peptides
- Peptide Thioesters
- Peptoids
- Phospho-peptides
- PNA



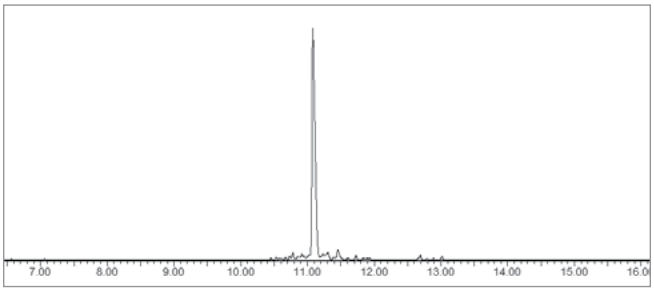


CarboMAX™ (Enhanced Carbodiimide Chemistry)

Faster Coupling: Improved Purity with Less Epimerization

Coupling with carbodiimide chemistry has significant benefits over aminium/phosphonium salts (ex. HATU, HCTU, PyBOP) at elevated temperature. This includes major reductions of epimerization for cysteine and γ-lactam formation of arginine. However, activation by carbodiimides is relatively slow. We developed an improved coupling process which allows for faster formation of the key O-acylisourea intermediate by increasing the amount of carbodiimide to 2 equivalents relative to the amino acid.[1]

By forming more activated amino acid faster than standard carbodiimide chemistry the subsequent coupling will happen quicker. This provides not only a faster coupling time, but also less epimerization from less time as a sensitive activated amino acid. This methodology termed CarboMAX is patent pending and exclusively licensed for use on CEM's peptide synthesizers.



UPLC-MS Analysis of crude Liraglutide (CarboMAX)

Reduced Epimerization (ex. Liraglutide)

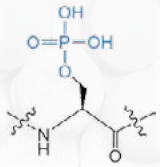
Epimer	DIC/Oxyma (%)	CarboMAX (%)
D-Asp	0.23	0.31
D-Ala	0.33	0.25
D-Arg	0.29	0.2
D-Glu	0.39	0.3
D-His	N/A	N/A
D-Ile	< 0.10	< 0.10
L-allo Ile	< 0.10	< 0.10
D-allo Ile	< 0.10	< 0.10
D-Leu	0.17	0.13
D-Lys	< 0.10	0.1
D-Phe	0.2	0.16
D-Ser	0.16	0.12
D-Thr	< 0.10 < 0.10 < 0.10	< 0.10
D-Trp	0.24	< 0.10
D-Tyr	0.12	0.11
D-Val	< 0.10	< 0.10

[1] Patent Pending: US15686719; EP17188963.7

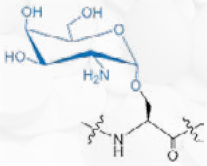
Improved Purity

Peptide	Sequence	% Crude Purity DIC/Oxyma	% Crude Purity CarboMAX
Thymosin	SDAAVDTSSEITTKDLKEKKEVVEEAEN	63	75
GRP	VPLPAGGGTVLTKMYPRGNHWAVGHLM	62	74
Bivalirudin	fPRPGGGGNGDFEEIPEEYL	80	82
$^{1\text{-}34}$PTH	SVSEIQLMHNLGKHLNSMERVEWLRKKLQDVHNF	67	85
$^{35\text{-}55}$MOG	MEVGWYRSPFSRVVHLYRNGK	77	91
Magainin 1	GIGKFLHSAGKFGKAFVGEIMKS	71	79
Dynorphin A	YGGFLRRIRPKLKWDNQ	74	82
Liraglutide	HAEGTFTSDVSSYLEGQAAK(γ-Glu-palmitoyl) EFIAWLVRGRG	74	88

Stabilizing Acid-sensitive Linkages



Phosphopeptides



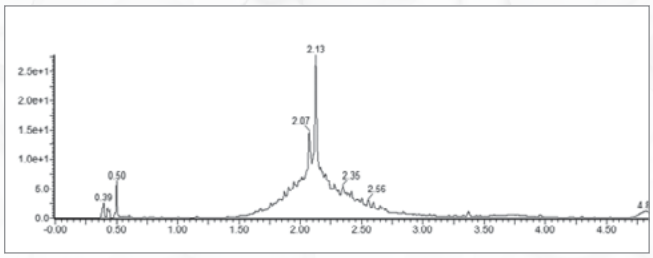
Glycopeptides

Many important side chain modifications are sensitive to acidic activators, such as Oxyma Pure and HOBt used under elevated temperature. With traditional carbodiimide chemistry, this can lead to undesirable cleavage of sensitive groups, such as phospho and O-linked carbohydrates.

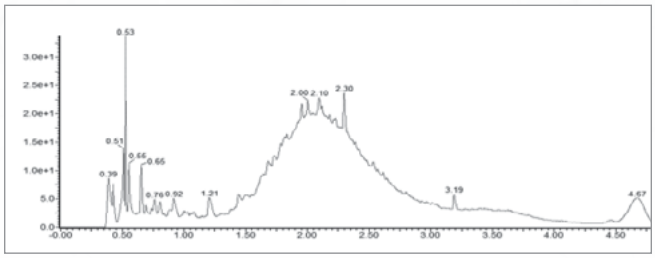
We developed a patented process of incorporation of < 1 equivalent base to stabilize these linkages while using carbodiimide chemistry at elevated temperature. This method which is part of CarboMAX chemistry is only available on CEM's peptide synthesizers and allows access to the synthesis of these peptides at high temperatures with unmatched speed and purity.

[3] Patent Pending: US20160176918; EP3037430; JP2016138090; CN105713066; AU2017204172

Multi-phosphorylated peptide - TpTGNGKPVECpSQPESSFKMpSFKR



CarboMAX Synthesis
(Fmoc-AA/DIC/Oxyma Pure/DIEA) – 1/1/1/0.4



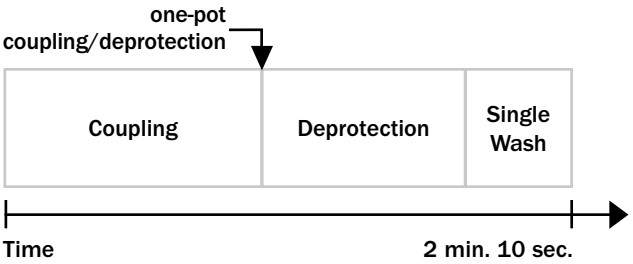
Standard Synthesis
(Fmoc-AA/DIC/Oxyma Pure) – 1/1/1

One-Pot Coupling/Deprotection

Unparalleled Speed and Efficiency

Traditional solid phase peptide synthesis involves the use of iterative and separate deprotection and coupling steps with washing in-between. This is based on the assumption that undesirable amino acid insertions can occur without complete draining and washing between each step. In 2013, it was demonstrated that washing after the coupling step can be eliminated without effect on peptide purity.[1]

The Liberty PRIME™ takes this further by using a new one-pot coupling and deprotection process.[2] This technique involves addition of the deprotection reagent (base) directly to the undrained post-coupling mixture. The ability to do this is based on the insight that faster reaction kinetics in the solution phase promote rapid hydrolysis or self-condensation of the active ester, thereby avoiding potential side reactions at the resin bound amino functionality. The Fmoc removal then proceeds uninterrupted at elevated temperature. An optimized use of reagents results in an essentially neutral reaction mixture towards the end of deprotection step. This new procedure offers several advantages such as (a) approximately 90% reduction in solvent requirement for the deprotection step, (b) 75% reduction in solvent requirement for post-deprotection washings, (c) faster deprotection step since the microwave ramp time is not needed, and (d) shorter cycle time due to absence of the post-coupling drain step.



Utilization of the one-pot coupling/deprotection methodology requires the ability to consistently add precise small volumes of concentrated base. To achieve this, the Liberty PRIME incorporates a new dedicated pumping module with the ability to rapidly add the deprotection reagent precisely at the end of the coupling step in volumes as low as 0.25 mL. The pre-calibrated pump module does not require on-going calibration thereby avoiding drifting delivery amounts. Additionally, the main solvent and the activator (Oxyma Pure) are also delivered through similar individual pumps within the module for improved performance.

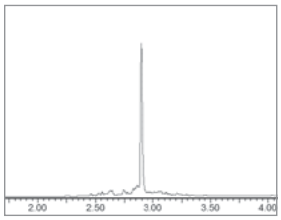
[1] J. Collins, K. Porter, S. Singh and G. Vanier, "High-Efficiency Solid Phase Peptide Synthesis (HE-SPPS)," Org. Lett., vol. 16, pp. 940-943, 2014.

[2] Patent Pending: US20170226152; WO2017070512

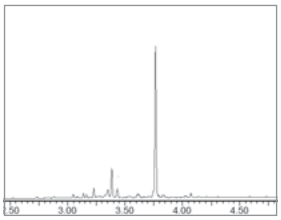
Integrated pumping module utilized on the Liberty PRIME

Peptide Synthesis on the Liberty PRIME[3]

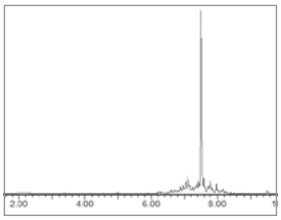
Peptide	Sequence	Crude Purity (UPLC-MS)	Total Synthesis Time	Total Chemical Waste
$^{65-74}$ACP	VQAAIDYING-NH_2	94%	25 m	92 mL
ABC-20 mer	VYWTSPFMKLIHEQCNRADG-NH_2	83%	48 m	172 mL
JR-10 mer	WFTTLISTIM-NH_2	70%	25 m	92 mL
Exenatide	HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPS-NH_2	57%	1 h 36 m	273 mL
$^{7-37}$GLP1	HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG	47%	1 h 14 m	217 mL
PnIA(A10L)	GCCSLPPCALNNPDYC-NH_2	77%	43 m	112 mL
Circulin A	GIPCGESCVWIPCISAALGCSCKNKVCYRN	79%	1 h 10 m	252 mL
Parigidin-br-1	GGSVPCGESCVFIPCITSLAGCSCKNKVCYYD	74%	1 h 14 m	264 mL



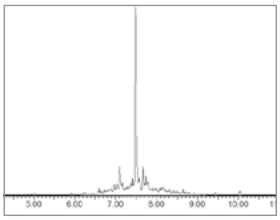
ABC-20 mer



JR-10 mer



Exenatide



$^{7-37}$GLP1

[3] Refer to CEM Application Note, "Liberty PRIME – Ultrafast Peptide Synthesis at Elevated Temperature"

Minimal Epimerization

The potential for epimerization was then investigated on the elevated temperature coupling methods used on the Liberty PRIME. In particular, cysteine and histidine are known to be sensitive to epimerization during coupling. The epimerization level was therefore investigated through a well-known standard method involving hydrolysis, subsequent derivatization, and gas chromatography analysis (C.A.T. GmbH). Epimerization levels observed with HBTU/DIEA activation at room temperature were found to be higher than those from 90 °C standard or CarboMAX couplings, as well as from 105 °C CarboMAX coupling on the Liberty PRIME. Use of Fmoc-His(Boc)-OH instead of Fmoc-His(Trt)-OH allowed coupling temperatures of 90 °C or 105 °C without any increase in epimerization levels. These results further demonstrate that standard *HE*-SPPS or CarboMAX coupling methods are particularly well-suited for peptide synthesis at elevated temperature.

Epimerization Levels of Cysteine and Histidine in ABC 20mer

Epimer	Conventional RT - HBTU/DIEA	Liberty Blue 90 °C CarboMAX	Liberty PRIME 105 °C CarboMAX
D-His	1.79%[1,a]	1.12%[b]	1.05%[b]
D-Cys[c]	1.38%[1]	0.64%	0.68%

[a]Fmoc-His(Trt)-OH; [b]Fmoc-His(Boc)-OH; [c]Fmoc-Cys(Trt)-OH

Synthesizer Comparison

Pick the Synthesizer That's Best for You

MultiPep Series

	MultiPep 1	MultiPep 2
		
Scale Range	0.001 – 0.3 mmol	0.001 – 0.5 mmol
Synthesis Formats:		
Well Plates	1 x 96 well plates	4 x 96 well plates
Mini-columns	24/48 mini columns (250, 500 µL)	24/48 mini columns (250, 500 µL)
Columns	8 columns (2,5,10 mL)	48 columns (2, 5, 10, 20 mL) 72 columns (2, 5, 10 mL)
Micro Peptide Arrays: **SPOT Synthesis on Cellulose Membranes**	Up to 1200 peptides in parallel on 2 sheets	Up to 2400 peptides in parallel on 4 sheets
Copies of Arrays: **CelluSpots**	Many copies of arrays up to 768 peptides each with our Slide Spotting Robot (See specs below)	Many copies of arrays up to 768 peptides each with our Slide Spotting Robot (See specs below)
Amino Acid Positions	26 standard (up to 48)	31 standard (up to 48)
Other Positions	Up to 15	Up to 20
Fluid Delivery	Digital syringe pump	Digital syringe pump
Dimensions	22.8" W x 20.9" D x 28.3" H (58 cm x 53 cm x 72 cm)	35.0" W x 25.6" D x 31.1" H (89 cm x 65 cm x 79 cm)
Accessories	· CleavagePro · Slide Spotting Robot – CelluSpots	· CleavagePro · Slide Spotting Robot – CelluSpots

Slide Spotting Robot — CelluSpots

Used in conjunction with the MultiPep 1 and 2 systems for making copies of peptide arrays on slides (CelluSpots)

Work Area	2 x Microtiter plates (96 or 384 well)
Slide Area	26 x 75 mm slides with freely defined grids
Total Slides	29 slides for target
Droplet size	As low as 100 nL

Liberty Series

	Liberty Lite	Liberty Blue	Liberty Blue HT12	Liberty PRIME	Liberty PRO
					
Cycle Time	15 minutes	4 minutes	4 minutes	2 minutes	15 – 45 minutes (3 L – 15 L)
Waste/Cycle	40 mL (0.1 mmol)	16 mL (0.1 mmol)	16 mL (0.1 mmol)	8.5 mL (0.1 mmol)	Variable
Scale Range	0.005 – 5 mmol	0.005 – 5 mmol	0.005 – 5 mmol	0.005 – 4 mmol	15 – 1000 mmol (3 L, 8 L, 15 L)
Peptide Positions	1	1	12	24	1
Amino Acid Positions	20	27	27	27	15
Other Positions	4	4	4	4 (upgrade to 5 available)	4
Fluid Delivery	**Flex-Add™:** Amino Acids & Activators **Timed Delivery:** Wash & Deprotection	**Flex-Add:** Amino Acids & Activators **Timed Delivery:** Wash & Deprotection	**Flex-Add:** Amino Acids & Activators **Timed Delivery:** Wash & Deprotection	**Flex-Add:** Amino Acids **Pre-Calibrated Pumps:** Wash, Deprotection & Oxyma Pure	**Positive Displacement Pump, Full Bottle Add:** Amino Acids **Positive Displacement Pump, 0.05 – 10 L:** Wash, Deprotection & Activators (2 positions)
Dimensions	20" W x 18" D x 30" H (51 cm x 46 cm x 76 cm)	20" W x 18" D x 30" H (51 cm x 46 cm x 76 cm)	27" W x 18" D x 30" H (69 cm x 46 cm x 76 cm)	42" W x 18" D x 30" H (107 cm x 46 cm x 76 cm)	65" W x 40" D x 70" H (165 cm x 102 cm x 178 cm)
Upgrades	Upgrade to the Liberty Blue	· HT12 · HT24	· HT24	GMP Documentation	GMP Documentation
Accessories	Razor Cleavage System	· Integrated Camera, · Razor Cleavage System · Flex-Add Large Scale	· Integrated Camera · Razor Cleavage System · Flex-Add Large Scale	· Integrated Camera · Razor Cleavage System	· Vessel head holder · 1L bottle cradles

MultiPep 2™

Automated Parallel Peptide Synthesizer

Overview

The MultiPep 2 is the state of the art automated parallel peptide synthesizer. It features unmatched flexibility for screenings hundreds of peptides in parallel using plates, columns, or cellulose membranes formats.

Features

- Flexible Formats
  - Plates: Up to 384 (4 x 96) peptides at 1 – 10 µmol
  - Columns:
    - 48 mini-columns (0.25, 0.50 mL) — 1– 15 µmol
    - 48 columns (2, 5, 10, 20 mL)
    - 72 columns (2, 5, 10 mL)
  - Peptide Microarrays: SPOT Synthesis — Up to 2400 peptides on four cellulose membranes
- Heating option for elevated temperature synthesis (plates/columns
- Fast synthesis with 8 position parallel washing arm
- Vortex mixing
- Pre-activation or *in-situ* activation

Flexible Parallel Peptide Synthesis

Peptide Libraries — 96 Well Plates and Columns

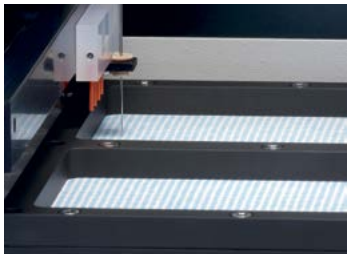
Easily synthesize large libraries of peptides using 96 well plates. With the MultiPep 2 up to 4 x 96 well plates can be utilized allowing for 384 peptides to be synthesized in parallel. Alternatively, up to 72 columns can be run in parallel (2,5, or 10mL sizes).

Parallel Peptide synthesis at Elevated Temperature

Apply elevated temperature synthesis conditions to either 96 well plates or columns run on the MultiPep 2. This is made easy with optional heating block accessories with adjustable temperature control. Elevated temperature is helpful for improving the purity of difficult and longer sequences.

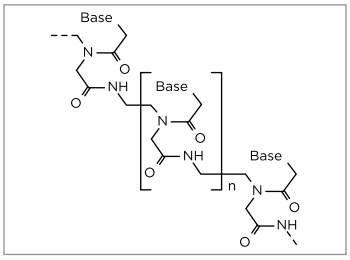
CelluSPOTS — Multiple Copies of Peptide Arrays on Glass Slides

Easily make many copies of a peptide array on glass slides. CelluSpots technology combines the advantages of traditional SPOT synthesis with a unique dissolvable cellulose support for making many identical copies of a peptide arrays. Based on the use of the unique Slide Spotting robot after SPOT synthesis on the dissolvable cellulose support.



Peptide Microarrays — SPOT Synthesis

SPOT synthesis allows for the synthesis of thousands of immobilized cellulose membrane peptides. This is useful for on-support binding studies as well as solution and cell based assays. With the MultiPep 2 the SPOT synthesis option allows for the synthesis up to 2400 peptides in a batch for high-throughput screening applications.



Ideal for PNA Synthesis

The MultiPep 2 is a powerful tool for small scale synthesis requiring expensive monomers such as PNA. Perform PNA synthesis as low as 1µmol with the small fluid delivery capabilities of the MultiPep 2. "Up to 48 smaller columns in parallel (250µL, 500µL sizes) can be used.

MultiPep 1™

Automated Parallel Peptide Synthesizer

Overview

The MultiPep 1 features similar capabilities to the MultiPep 2 in an entry level format. It allows for:

- Plates: Up to 96 peptides at 1 – 10 µmol
- Columns:
  - 48 mini-columns (0.25, 0.50 mL) — 1 – 15 µmol
  - 8 columns (2, 5, 10 mL)
- Peptide Microarrays: SPOT Synthesis — Up to 1200 peptides on two cellulose membranes
- Heating option for elevated temperature synthesis (plates/columns)
- Vortex mixing
- Pre-activation or *in-situ*

Discover Bio™

Manual Microwave Peptide Synthesizer

Overview

The world's best selling microwave peptide synthesizer is also available in a research scale manual system that offers a cost-effective alternative to purchasing peptides. Enhance your laboratory's capabilities with the benefits of microwave-assisted peptide synthesis.

Features

- Integrated module for washing and adding deprotection
- Easy access port for addition of activated amino acids
- True Internal fiber-optic temperature control
- 0.005 - 1 mmol scale range
- Ability to upgrade to Liberty Blue

Chemistry Technology

- CarboMAX

Liberty Lite™

Microwave Peptide Synthesizer

Overview

An entry-level option for the globally recognized Liberty Blue technology. The Liberty Lite provides advantages over existing peptide synthesizers.

Features

- Flex-Add™ critical reagent delivery system (patented)
- True Internal fiber-optic temperature control
- 20 amino acid positions
- 0.005 - 5 mmol scale range
- Ability to upgrade to Liberty Blue

Chemistry Technology

- CarboMAX

Liberty Blue™

Microwave Peptide Synthesizer

Overview

The Liberty Blue Automated Microwave Peptide Synthesizer is the gold standard for peptide synthesis. It features unmatched 4-minute cycle times along with a 90% solvent reduction based on High Efficiency Solid Phase Peptide synthesis (*HE*-SPPS), developed in 2013.

Features

- Flex-Add™ critical reagent delivery system (patented)
- True Internal fiber-optic temperature control
- 27 amino acid positions
- 0.005 - 5 mmol scale range
- Integrated Camera (optional)
- Ability to upgrade to Liberty Blue HT12

Chemistry Technology

- *HE*-SPPS
- CarboMAX

Liberty Blue HT12™

High-Throughput
Microwave Peptide Synthesizer

Overview

The Liberty Blue HT12 features all the advantages of the Liberty Blue with the added capability of the HT12 resin loader. This allows for the automated sequential synthesis of up to 12 different peptides.

Features

- Flex-Add™ critical reagent delivery system (patented)
- True Internal fiber-optic temperature control
- 27 amino acid positions
- 0.005 - 5 mmol scale range
- Integrated Camera (optional)

Chemistry Technology

- *HE*-SPPS
- CarboMAX


CEM
HT12
Liberty PRIME
Microwave Peptide Synthesizer

Liberty PRIME™

High-Throughput Microwave Peptide Synthesizer

Overview

The Liberty PRIME peptide synthesizer is the most advanced platform available for microwave peptide synthesis. It features a revolutionary one-pot deprotection and coupling process, allowing for a remarkable **2-minute cycle time,** with only **8.5 mL waste per cycle** (at 0.1 mmol).

- Individual 20-mers every 45 minutes
- Batches of 24 peptides (20-mers) every 20 hours, with only 4.5 liters total waste produced

Chemistry Technology

- One-Pot Coupling/Deprotection
- CarboMAX

Performance

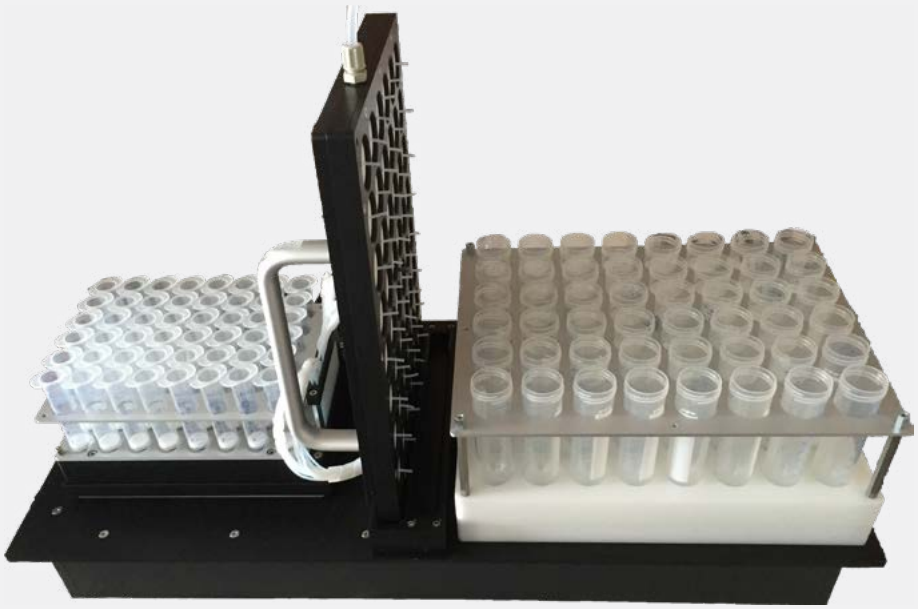
Scale	Cycle Time	AA Equiv.	Waste/Cycle
0.1 mmol	2 m 10 s	5	8.5 mL
0.3 mmol	3 m 40 s	5	20 mL
0.4 mmol	3 m 50 s	4	20 mL

Enhanced Hardware

The Liberty PRIME features enhanced delivery options of the main solvent and Deprotection solutions compared to the Liberty Blue system. These reagents are delivered by a pre-calibrated pumping system, not requiring calibration or affected by restriction changes in the delivery path. This reduces system maintenance and provides an ideal system for GMP environments that is free of calibration.

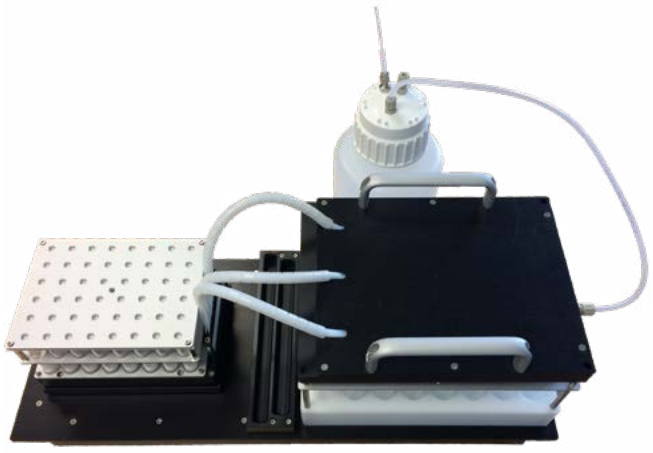
CleavagePro

High Throughput Peptide Cleavage System



Overview

Cleave up to 48 peptides in parallel using the CleavagePro system. This system is ideal for high-throughput cleavage and directly utilizes the 2 mL, 5 mL, or 10 mL synthesis columns from the MultiPep 1 or 2 systems without requiring transfer into a new vessel. The system incorporates orbital shaking during the cleavage process and is compact and easily fits in a fume hood.



- High-throughput peptide cleavage of up to 48 resins in parallel directly using the 2mL, 5mL, or 10mL reaction columns from the MultiPep 1 or 2 systems
- Controlled orbital shaking for mixing
- Vacuum transfer of TFA solution into collection tubes (15mL or 50mL in size)
- Compact and fits in fume hoods

Razor®

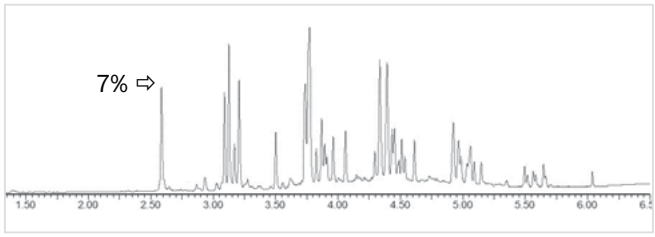
Rapid Peptide Cleavage System

Overview

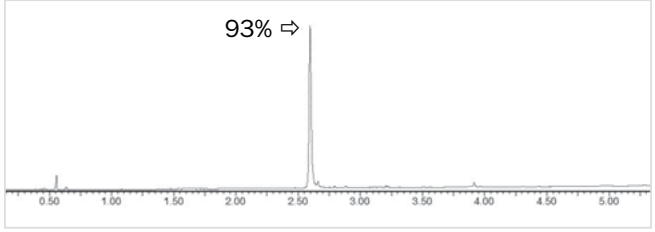
Cleave up to 12 peptides in only 30 minutes. The Razor features a compact design that easily fits in a fume hood and allows for temperature at +/- 1 °C control for up to 12 different vessels. Cleavage is typically complete in 30 minutes for standard peptides and allows for draining into a centrifuge tube for subsequent centrifugation. This system is ideal for both single peptides and large batches.

- Elevated Temperature Cleavage Block With +/- 1 °C Control
- Valve Control For Independently Draining Each Vessel
- Convenient Tray For Holding & Transporting Each Collection Tube
- Compact Design That Easily Fits In Standard Fume Hoods

Peptide: Fmoc-YGRKKRRQRRR
Conditions: TFA/TIS/H2O/DODT (92.5/2.5/2.5/2.5)



30 minutes, room temperature

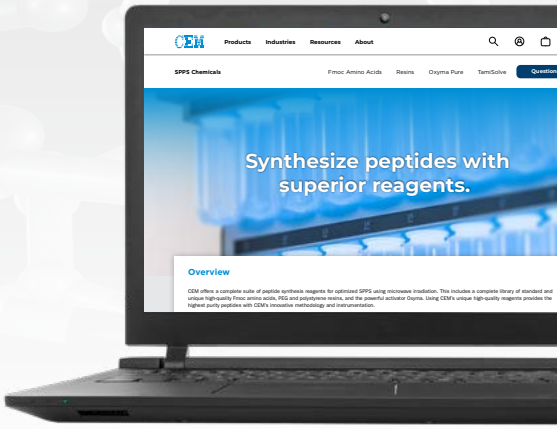


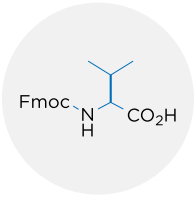
30 minutes, Razor

SPPS Chemicals

High Quality Chemicals, Guaranteed

CEM offers a complete suite of peptide synthesis reagents for optimized SPPS, whether using conventional synthesis or microwave irradiation. This includes a complete library of standard and unique, high-quality Fmoc amino acids, PEG and polystyrene resins, and the powerful Oxyma Pure activator. Using CEM's unique high-quality reagents provides the highest purity peptides, with CEM's innovative methodology and instrumentation.





Fmoc Amino Acids

Extremely High Quality at an Affordable Price

Overview

Using Fmoc amino acids of lower quality can have a significant impact on peptide purity and yield, resulting in hard to separate impurities and even total synthesis failures. CEM's Fmoc amino acids are the highest quality available on the market and provide the best purities and yields possible for peptide synthesis.

Standard Specifications

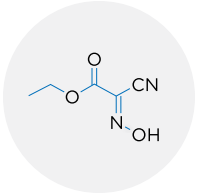
- HPLC purity ≥ 99.0%
  - Enantiomeric purity ≥ 99.8%
  - 100% fully synthetic amino acids
  - Continuously used and tested in CEM's peptide synthesis laboratory

Pre-Weighed

Eliminate your weighing step by using amino acids that have been pre-weighed specifically for your Liberty system.

Full Library

A catalogue of Fmoc amino acids is available for synthesizing standard and modified peptides, for use with any peptide synthesizer.

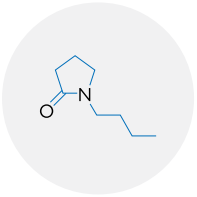


Oxyma Pure

The Perfect Activator for Elevated Temperature

Overview

Oxyma Pure used with DIC produces peptides with increased yield and decreased epimerization, when used as an alternative to HOBt.1 This safe, non-explosive auxiliary nucleophile works with carbodiimide coupling strategies to provide the best results for a peptide synthesis. Additionally, the use of DIC/Oxyma avoids side reactions associated with high levels of base (≥ 1 equiv. DIEA), using onium salt methods such as HBTU/DIEA.



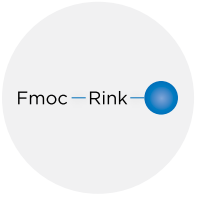
TamiSolve™ NxG

(Also known as NBP, N-butylpyrrolidone, N-butylpyrrolidin-2-one, 1-butylpyrrolidin-2-one)

High-boiling, Dipolar Aprotic Solvent

Overview

TamiSolve is non-teratogenic (does not risk reproductive harm) and less toxic than DMF. The product has good solvency for a wide range of compounds, including peptides, and has high chemical and thermal stability. It is designed as a less toxic replacement for DMF (Dimethylformamide) and NMP (N-methyl-2-pyrrolidone). TamiSolve is ideal for microwave peptide synthesis and is not classified as a developmental toxin. It can be stored in large volumes due to its high flash point.

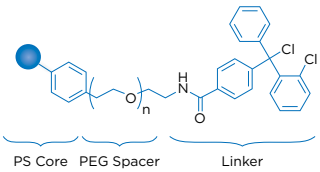


Resins

High Quality Unique Resins for SPPS

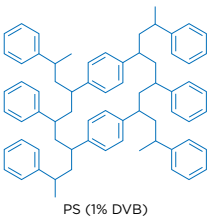
Overview

A full library of PEG and polystyrene resins for SPPS. CEM's SPPS resins are of the highest quality and optimized for the synthesis of standard and difficult peptides, with a variety of linkers.



ProTide™ Resins

Based on a PEG-PS core with optimal swelling, ProTide is recommended for synthesis of very long and difficult peptides.

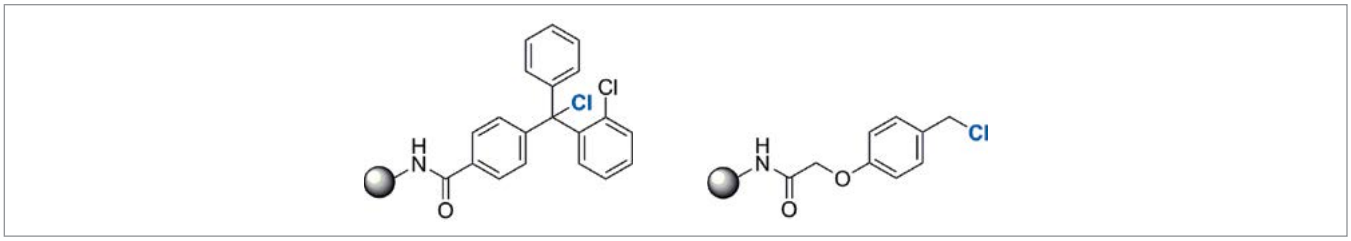


Polystyrene Resins

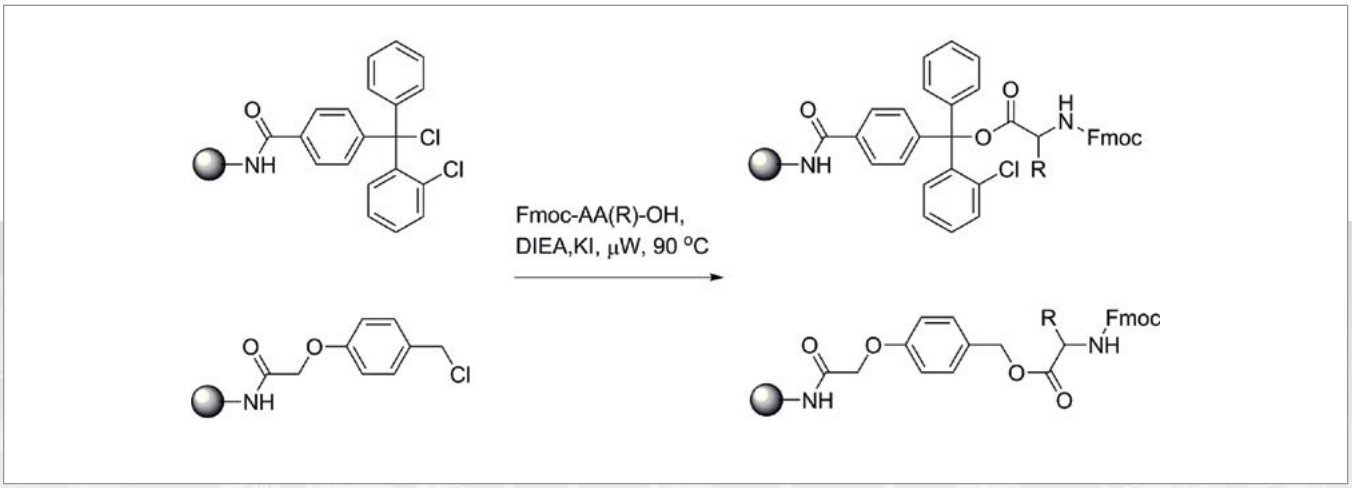
High quality, pre-loaded, polystyrene resins are great for synthesis of standard and difficult peptides.

[1] R. Subirós-Funosas, et al. (2009) Chem. Eur. J., 15, 9394.

Optimized PEG Resin Core with Cl-TCP(Cl) and Cl-MPA Universal Linkers



ProTide resins contain an ideal PEG and polystyrene core, leading to an optimized environment for the synthesis of difficult peptides, with excellent swelling properties. New Cl-TCP(Cl) and Cl-MPA linkers incorporated onto ProTide, eliminate the necessity for purchasing resins with pre-loaded C-terminal amino acids. The C-terminal amino acid reacts with the linker-chloride, in the presence of potassium iodide (KI)1, N,N-diisopropylethylamine (DIEA), and microwave irradiation. The process is automatically carried out on CEM's microwave peptide synthesizers, using pre-programmed methods in the software. The result, any amino acid can be loaded on the resins in 10 minutes.

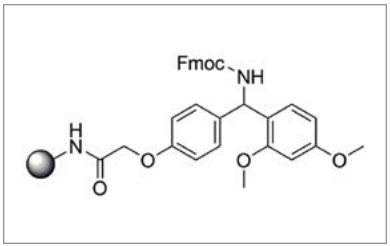


Key Advantages:

- Automated, high-temperature loading procedure complete in 10 min, whereas room temperature takes up to 24 hours
- Avoids coupling reagents; therefore, eliminating epimerization and dipeptide formation that can occur during loading
- No longer need to buy/store > 20 different, pre-loaded acid-linked resins
- Exhibit strong stability towards hydrolysis during storage and handling
- TCP(Cl) is hyperacid sensitive and will produce protected peptides with 1% TFA/DCM and further minimizes diketopiperazine and 3-(1-piperidinyl)alanine formation[2]

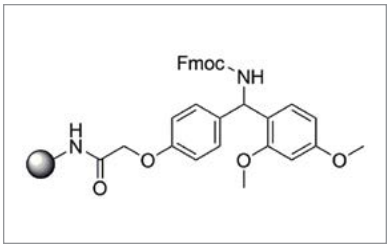
[1] Sandhya K., Ravindranath B. *Tetrahedron Lett.* 49, 2435 **2008**

[2] Heinlein C., Silva D., Tröster A., Schmidt J., Gross A., Unverzagt C. *Angew. Chem.* 50, 6406 **2011**



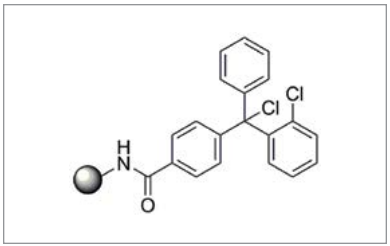
Rink Amide ProTide Resin (LL)

The ultimate resin recommended for longer and more difficult sequences of peptide amides. Based on ideal swelling properties from a TentaGel® core, incorporating PEG PS with a loading of 0.15 – 0.25 mmol/g. This resin is unmatched for the routine synthesis of difficult peptides, even > 75 amino acids.



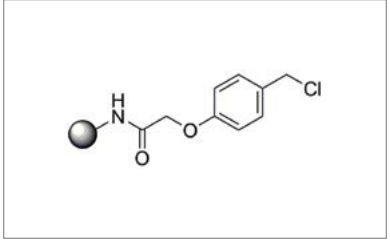
Rink Amide ProTide Resin

A powerful resin recommended for the synthesis of peptides with amide linkages < 30 amino acids. Based on ideal swelling properties from incorporating a PEG PS core with a loading of 0.55 - 0.8 mmol/g.



Cl-TCP(Cl) ProTide Resin

A powerful resin recommended for the synthesis of peptides with acid linkages < 30 amino acids. Based on ideal swelling properties from a TentaGel® core, incorporating PEG PS with a loading of 0.4 – 0.6 mmol/g. This resin features an activated chloride linker, allowing for attachment of the first amino acid in an unactivated form. This resin is recommended for protection of C-terminal cysteine and proline residues, due to its steric protection against diketopiperazine formation and 3-(1-Piperidinyl)alanine formation.

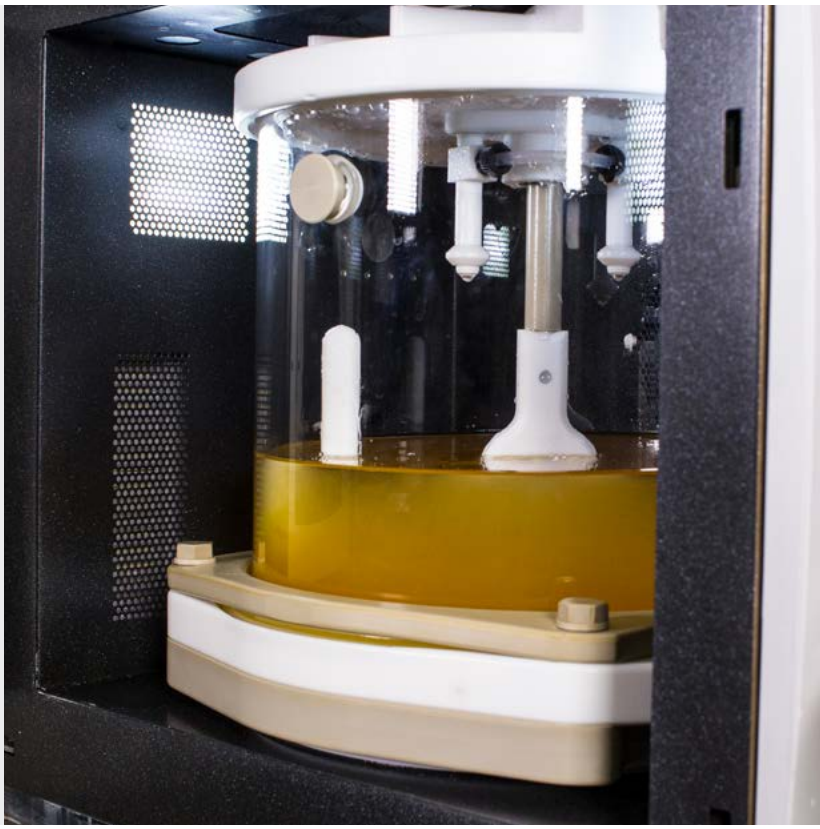


Cl-MPA ProTide Resin (LL)

The ultimate resin recommended for longer and more difficult sequences of peptide acids. Based on ideal swelling properties from a TentaGel® core, incorporating PEG PS with a loading of 0.15 – 0.25 mmol/g. This resin is unmatched for the routine synthesis of difficult peptides even, > 75 amino acids. This resin features an activated chloride linker, allowing for attachment of the first amino acid in an unactivated form.

Liberty PRO™

Automated Production Scale Microwave Peptide Synthesizer



Introducing Liberty PRO

The world's first large-scale microwave peptide synthesizer. Allows for the batch synthesis of peptides up to 500 grams with rapid delivery times.

- Low cost & rapid delivery times
- Improved synthesis efficiency with microwave irradiation
- Batch sizes up to 500 grams of purified peptide (15 L reaction vessel)
- Match synthesis profiles of peptides made on the Liberty Blue

Available Options

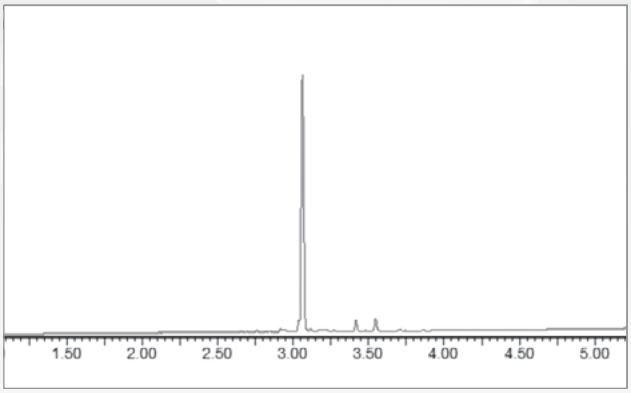
- Instrumentation (Liberty PRO)
- Large-scale custom peptide synthesis services

Contact Us To Get Started

- 800-726-3331
- peptide.support@cem.com

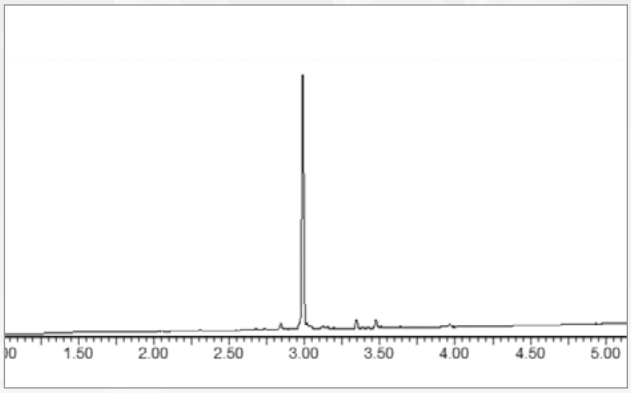
Synthesis Examples

Peptide Sequence: 9 mer
Resin: Rink Amide AM PS (0.75 mmol/g)
Excess Reagents: 2.0 fold



Liberty Blue™

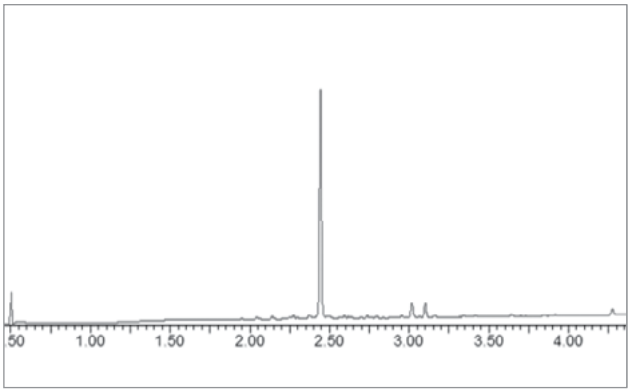
Scale: 0.1 mmol



Liberty PRO™

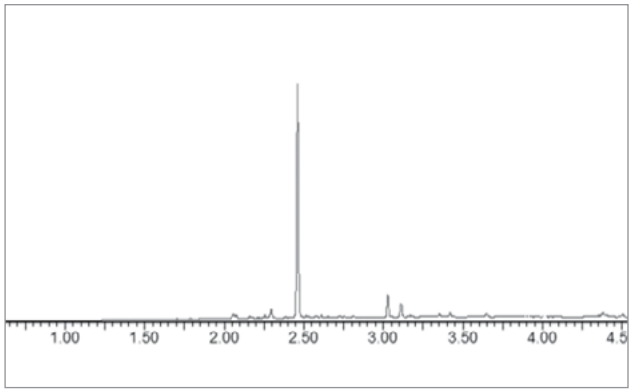
Scale: 700 mmol
Synthesis Time: 9 h

Peptide Sequence: 7 mer
Resin: Rink Amide AM PS (0.97 mmol/g)
Excess Reagents: 2.5 fold



Liberty Blue

Scale: 0.1 mmol



Liberty PRO

Scale: 360 mmol
Synthesis Time: 6 h

"The Liberty Blue is fast, reliable, and makes difficult peptides in high purity. We are very satisfied with the Liberty Blue and would highly recommend it for both protein synthesis and methodological development."

Prof. Fernando Albericio
Group Leader Chemistry & Molecular Pharmacology
Institute for Research in Biomedicine (IRB)
University of Barcelona

"The Liberty Blue system is unquestionably the best peptide synthesizer available today and represents the major workhorse for PeptiDream (12 systems). It is highly recommended to any company looking to synthesize peptides chemically, specifically those containing nonstandard amino acids."

Dr. Patrick C. Reid
President and Director
PeptiDream Inc.

"We are very satisfied with the Liberty Blue system. The system is one of the best peptide synthesizers available today for research and medicinal chemists...*HE*-SPPS using Liberty Blue, features overwhelming speed."

Dr. Hajime Hibino
Research Chemist
Peptide Institute

"The Liberty Blue is the best peptide synthesizer on the market. It's synthesis speed and purity are unmatched. Using the Liberty Blue has also made our subsequent purifications easier, which is a major benefit."

Prof. Anna Maria Papini
Coordinator of Interdepartmental Laboratory
PeptLab

Worldwide Support for Peptide Synthesis

We are where you are.

Many companies say they have great customer service, at CEM, we prove it.

Knowledgeable Sales People

With an average of 15 years with CEM.

Experienced Field Technicians

Close by, to keep you up and running.

Expert Chemists

To help with custom or advanced applications.

We Simplify Science

cem.com

Over 50,000 systems sold worldwide

CEM has been an ISO-certified facility since 1994

All systems serviced & supported by experts with an average of 15 years of experience

CEM invests 12% of annual revenue into R&D, the result... 11 R&D 100 awards

IQ/OQ/PQ Validation by certified CEM Technicians

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