ChemAxon

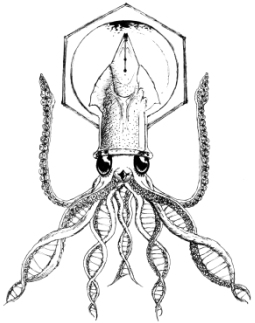
Tim Parrott
Roland Knispel

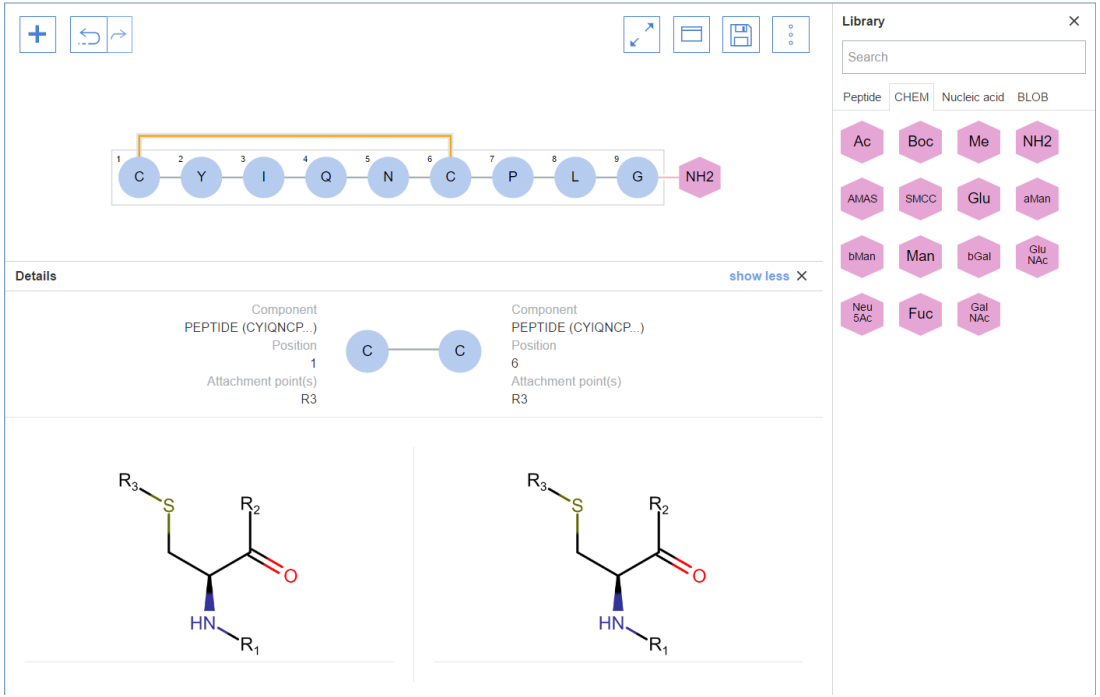
BIOEDDIE AND BIOMOLECULE TOOLKIT

San Diego UGM, March 2019

BioEddie

- JS application for all major browsers
- Easy editing
- No-structure components
- Native support for MOL/HELM/sequence





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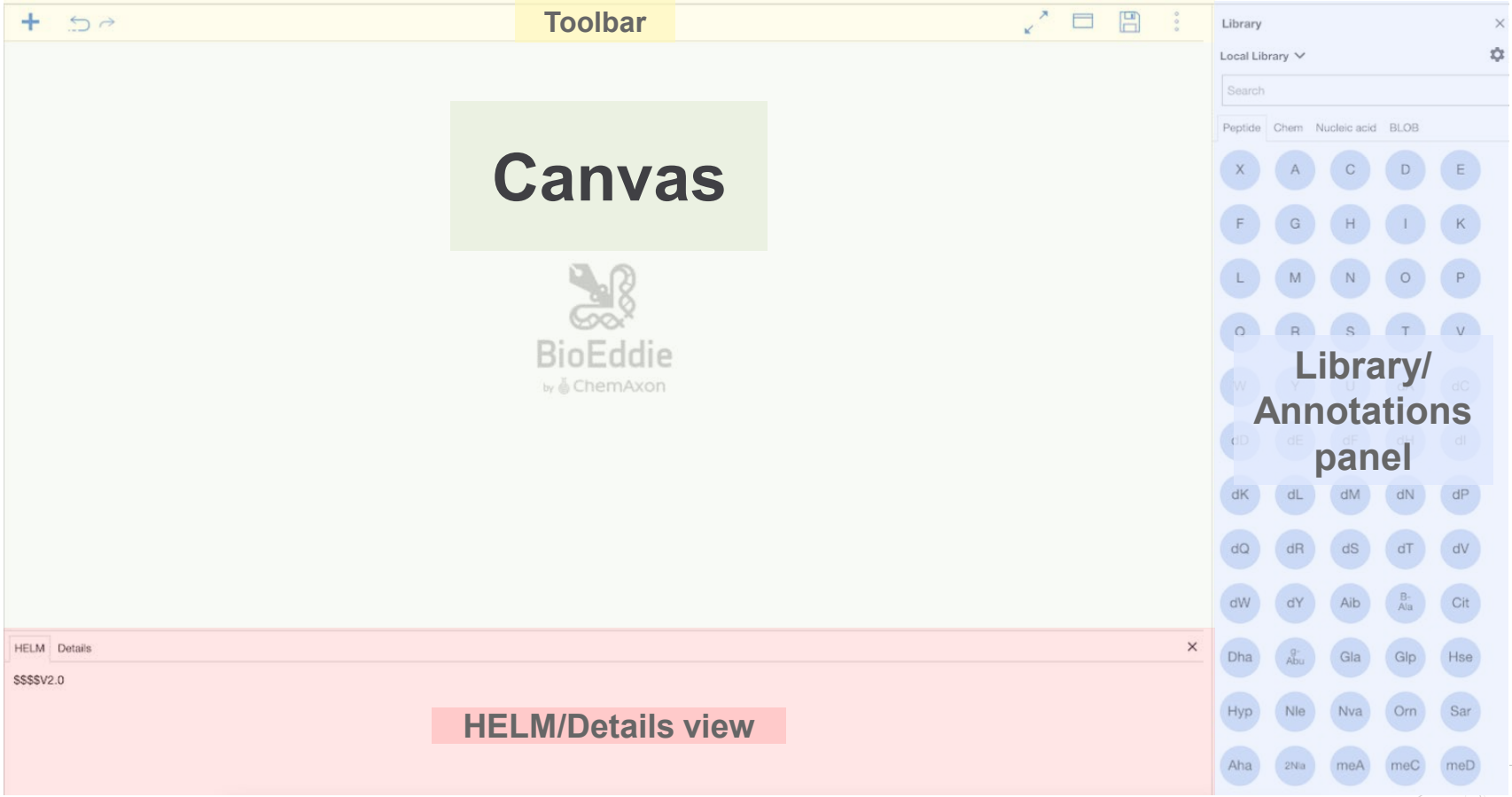
Toolbar
Canvas
BioEddie
by ChemAxon
Library
Local Library
Search
Peptide
Chem
Nucleic acid
BLOB
X A C D E
F G H I K
L M N O P
Q R S T V
dK dL dM dN dP
dQ dR dS dT dV
dW dY Aib β-Ala Cit
Dha γ-Abu Gla Glp Hse
Hyp Nle Nva Orn Sar
Aha 2Nia meA meC meD
Library/ Annotations panel
HELM
Details
$$$$V2.0
HELM/Details view

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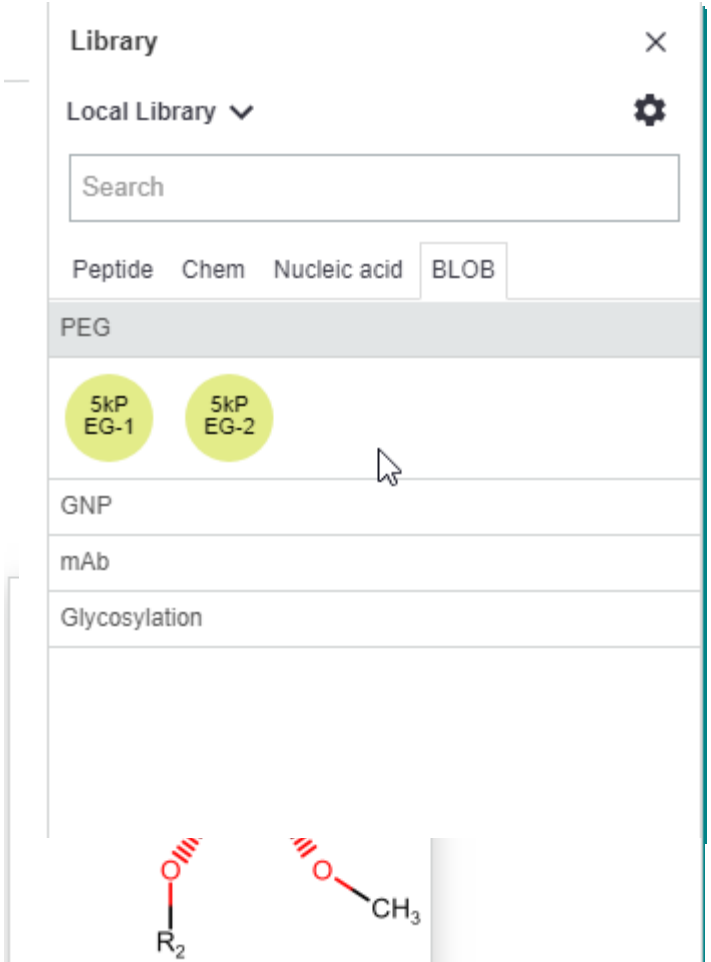
Library Components



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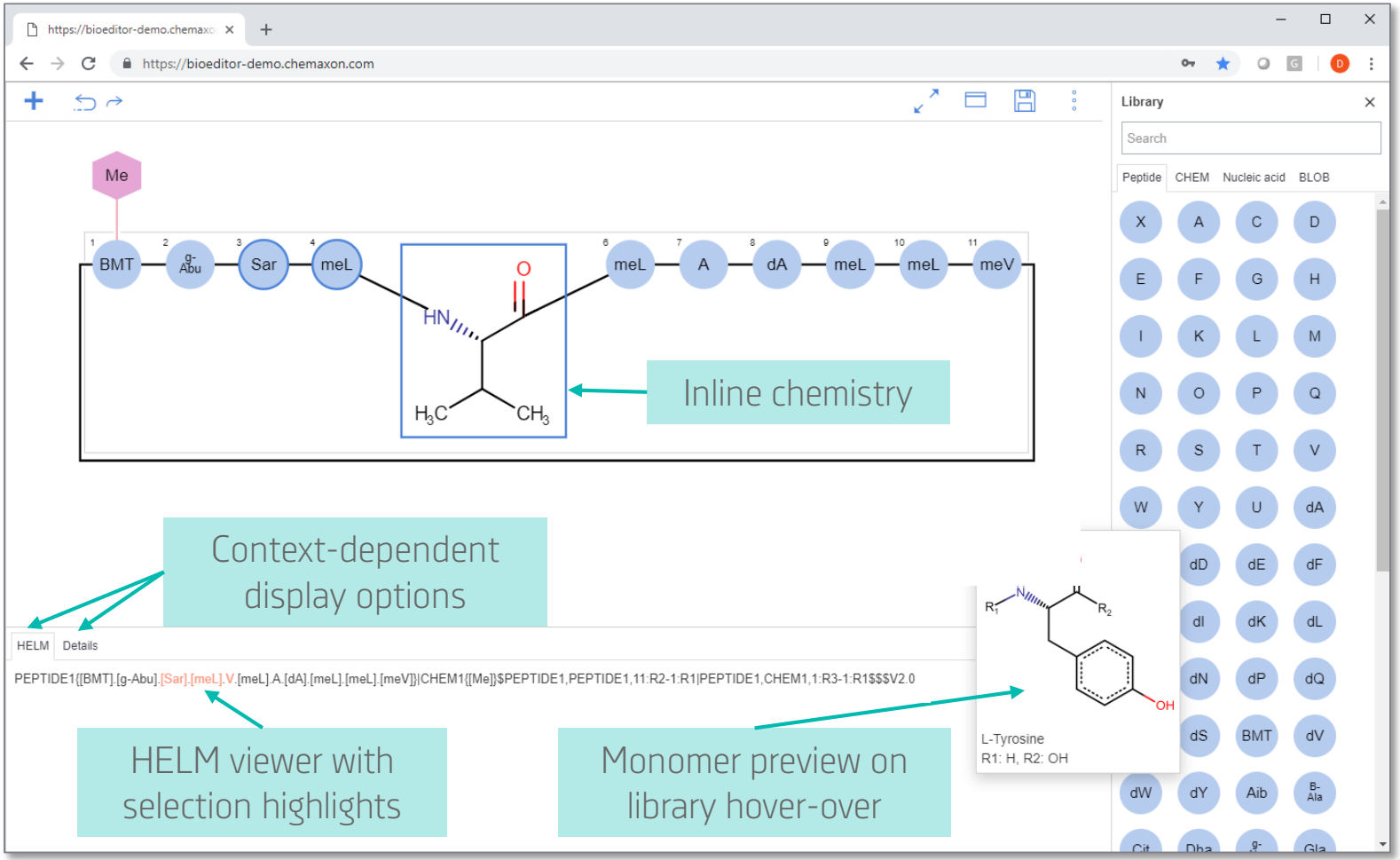
https://bioeditor-demo.chemaxon.com
Me
BMT
g-Abu
Sar
meL
meL
A
dA
meL
meL
meV
HN
O
H3C
CH3
Inline chemistry
Library
Search
Peptide
CHEM
Nucleic acid
BLOB
X
A
C
D
E
F
G
H
I
K
L
M
N
O
P
Q
R
S
T
V
W
Y
U
dA
dD
dE
dF
dI
dK
dL
dN
dP
dQ
dS
BMT
dV
dW
dY
Aib
b-Ala
Cit
Dha
g-Glu
Gla
Context-dependent display options
HELM
Details
PEPTIDE1{[BMT].[g-Abu].[Sar].[meL].V.[meL].A.[dA].[meL].[meL].[meV]}|CHEM1{[Me]}$PEPTIDE1,PEPTIDE1,11:R2-1:R1|PEPTIDE1,CHEM1,1:R3-1:R1$$$V2.0
HELM viewer with selection highlights
R1
R2
OH
L-Tyrosine
R1: H, R2: OH
Monomer preview on library hover-over

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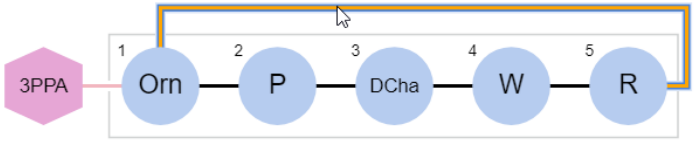
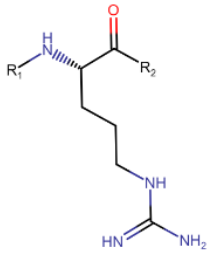
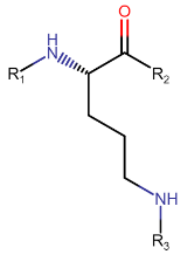
Linkage Details



LM | Details

Component PEPTIDE (OrnPDChaWR) Position 5 Attachment point(s) R2		R — Orn		Component PEPTIDE (OrnPDChaWR) Position 1 Attachment point(s) R3





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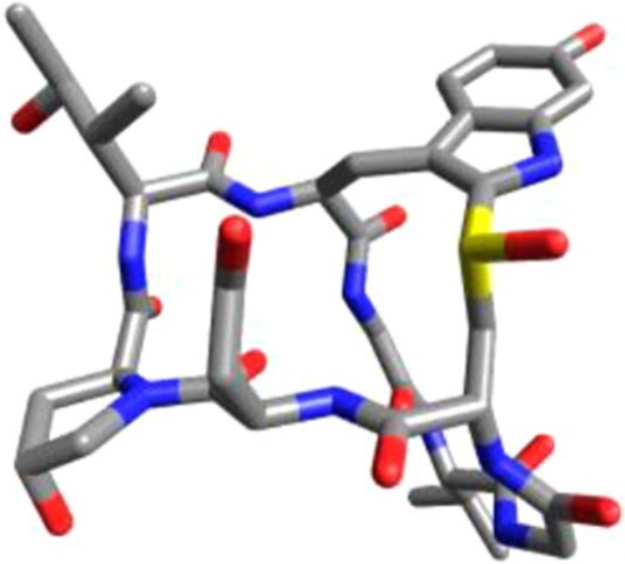
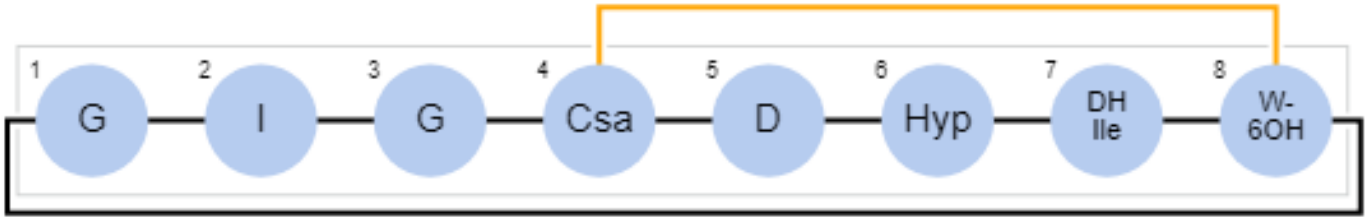
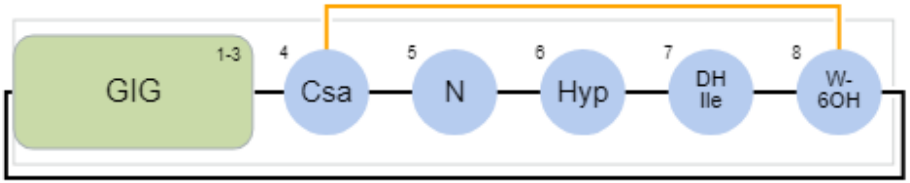
Bicyclic peptides



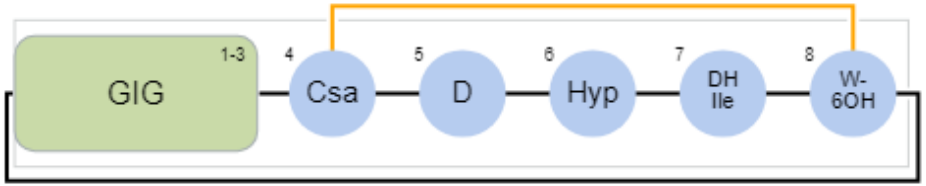


β-Amanitin

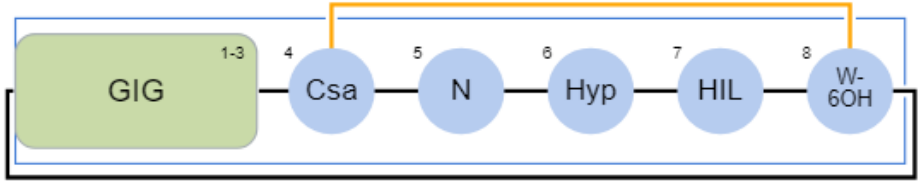
Sequence Comparisons



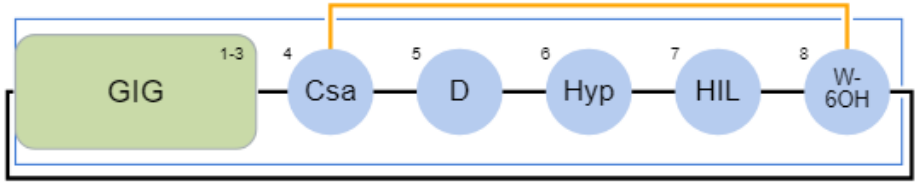
α-Amanitin



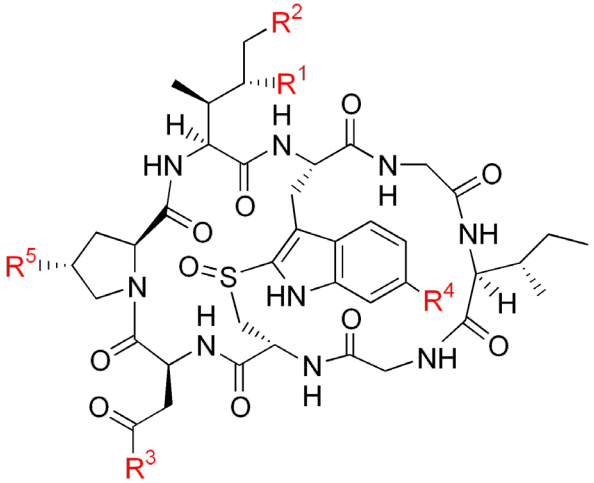
β-Amanitin



γ-Amanitin



ε-Amanitin



Name	R^1	R^2	R^3	R^4	R^5
α-Amanitin	OH	OH	NH_2	OH	OH
β-Amanitin	OH	OH	OH	OH	OH
γ-Amanitin	OH	H	NH_2	OH	OH
ε-Amanitin	OH	H	OH	OH	OH

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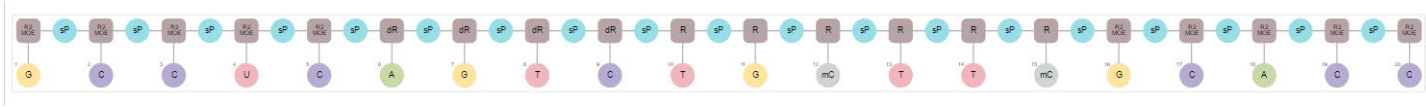
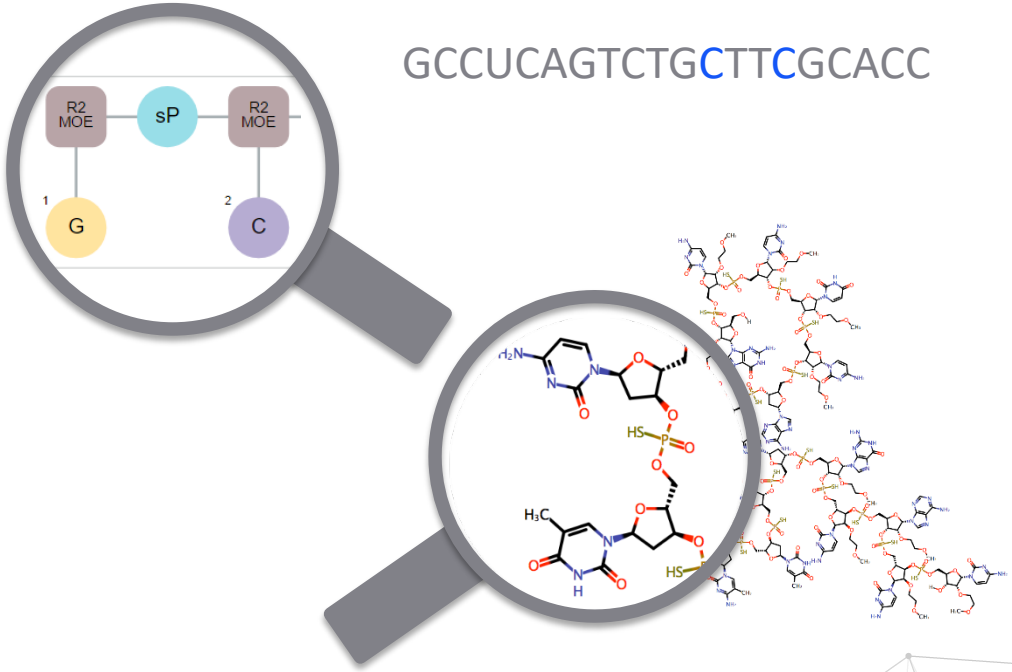
Oligonucleotides



- Natural or modified bases
- Natural or modified sugars
- backbone chain chemistries



Mipomersen (Kynamro)

FDA approved to treat homozygous familiar hypercholesterolemia

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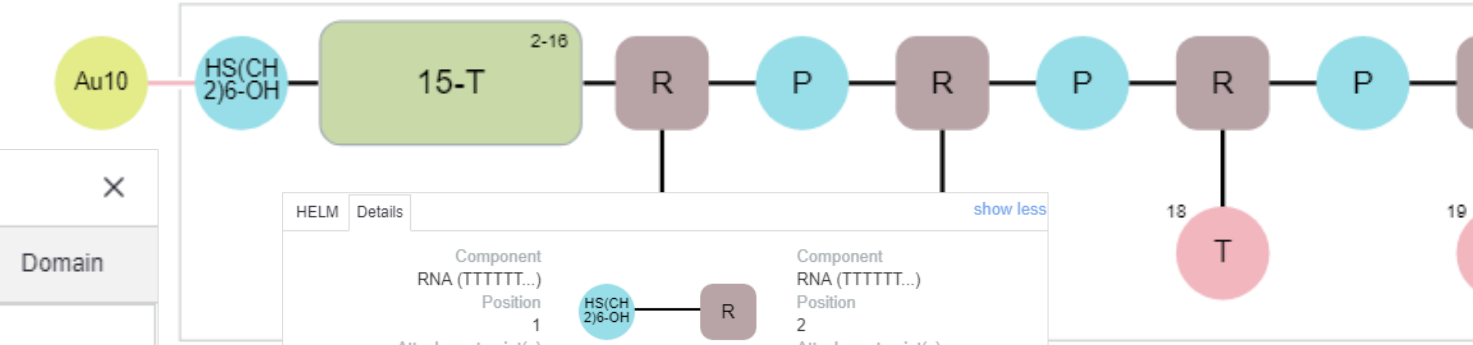
Gold Nanoparticles



Annotations

Macromolecule	Component	Domain

size (nm)	10
Number of particles /ml (OD=1)	4.8-E12
agent	citric acid
functionalized	no
OD /ml	1

J. Am. Chem. Soc., 2004, *126* (38), pp 11768–11769
DOI: 10.1021/ja046970u

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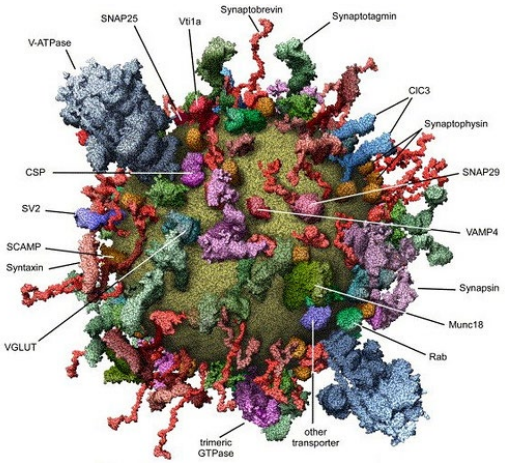
Biomolecule Toolkit



API (Java and REST-ful) for

- Native HELM support (HELM, HELM2, xHELM)
- Standardization
- Centralized DB storage
- Registration of entities and batches with custom business logic
- Search by sequence/chemical structure/metadata
- Conversion to/from Mol/FASTA/HELM
- Property calculations

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New: Similarity-based searching

- Distance-based

TGRWLQAKGV	TG-WIQAKGVW	3
Query sequence	Target sequence	Edit distance

- BLAST (P,N)
  - Using NCBI BLAST binaries
  - Experimenting with BLAST DB updates for large datasets

New: Sequence enumeration

- Ala-Scan

- Exhaustive enumeration of residue replacements

MTGCRLCYWEC

Position	Substitutions
3	V,A,Dha,Hse
6	I,V

MT V CRLCYWEC
MT A CRLCYWEC
MT[Dha]CRLCYWEC
MT[Hse]CRLCYWEC
MT V CRICYWEC
MT A CRICYWEC
…

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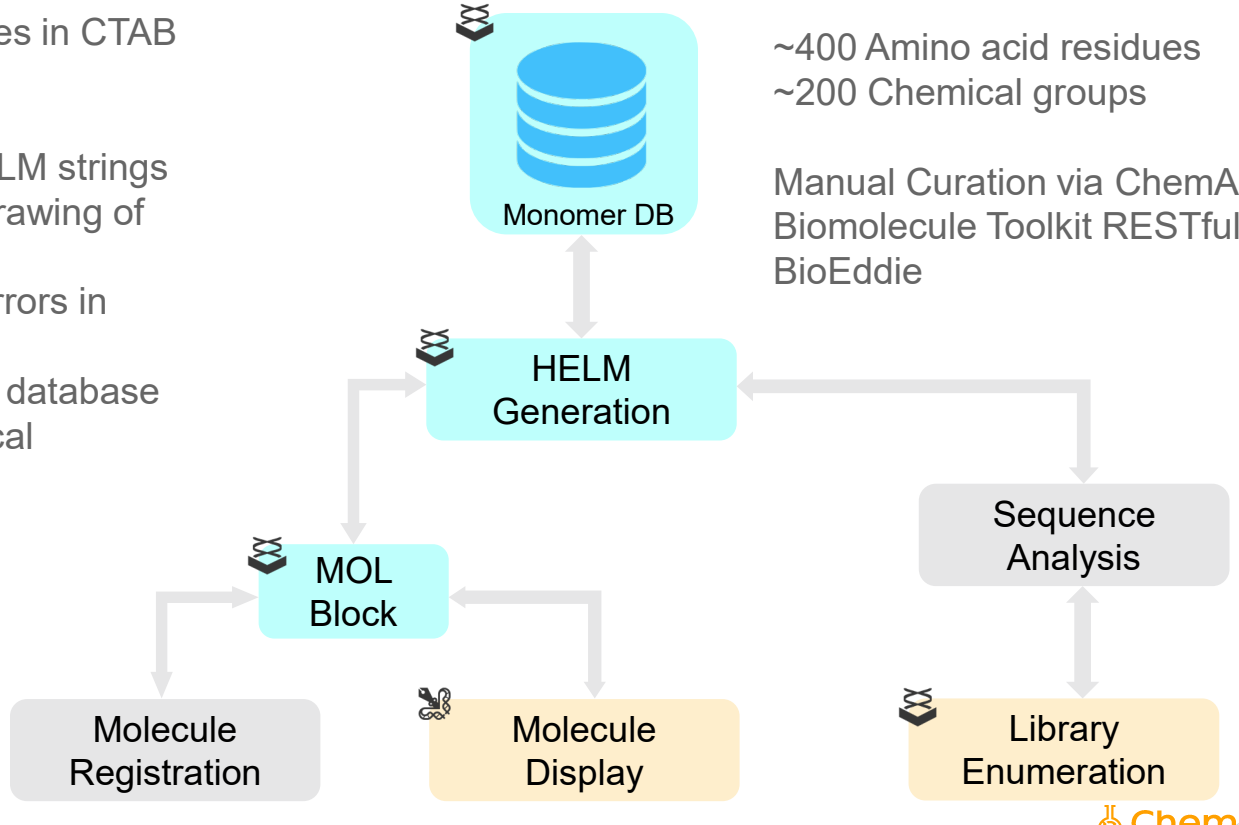
USE CASES

Biomolecule Toolkit Integration at Heptares*

- Registration of peptides in CTAB format
- CTAB generated via interconversion of HELM strings
- Error-prone manual drawing of peptides by users
- Drastic reduction of errors in database registration
- At the core of curated database of peptide and chemical monomers



*See Conor Scully, Heptares, UGM presentation, 2018, Budapest

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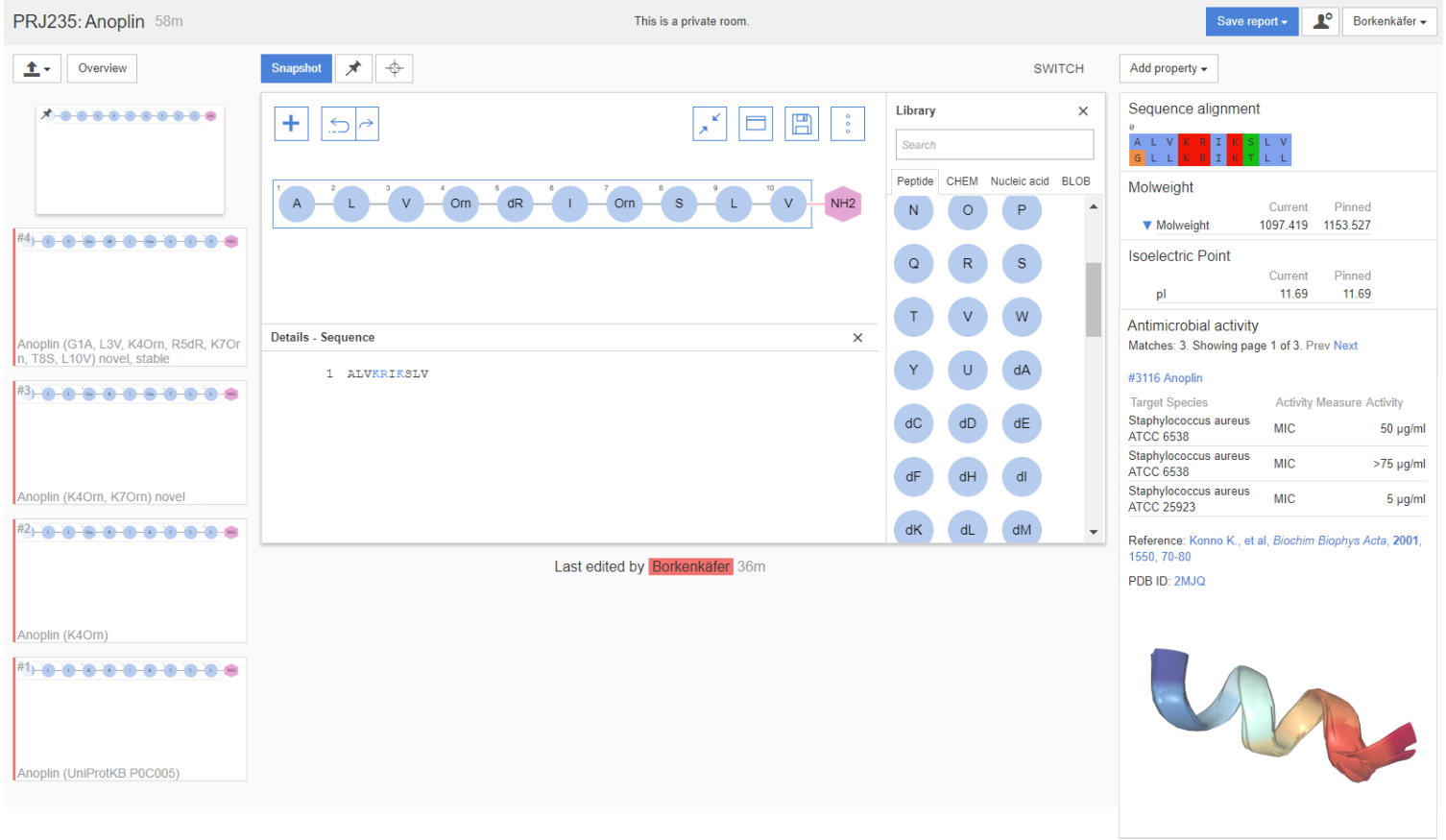

From designing small molecules towards designing peptides

Prototype for enhancing Marvin Live with peptide-specific data plugins featured by public data sources and Biomolecule Toolkit capabilities

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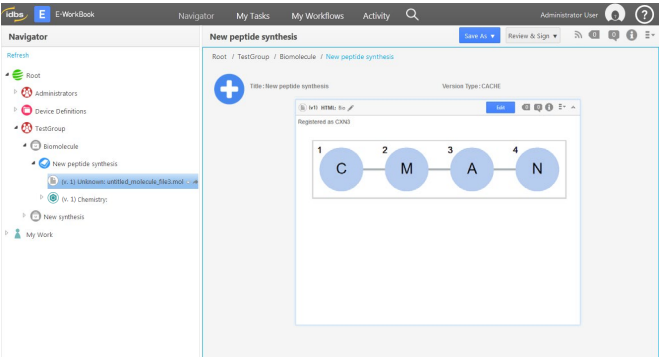
Integration with IDBS EWB



- Registration directly from ELN (in production for 3 US customers)
- Biomolecule Toolkit integrated through REST API
- BioEddie default sketcher for chemically modified sequences

Next steps

- ELN-wide search for sequences
- Add support for bio-synthesis reactions
- Add Support for high-availability cloud deployments (e.g. clustering, distributed transactions)

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Biomolecule Toolkit Roadmap

- Role-based authorization
- ✓Docker image
- ✓BLAST integration
- Genealogy capture
- Distributed deployment in cloud environments

- Focus on agnostic registration and dependent requirements

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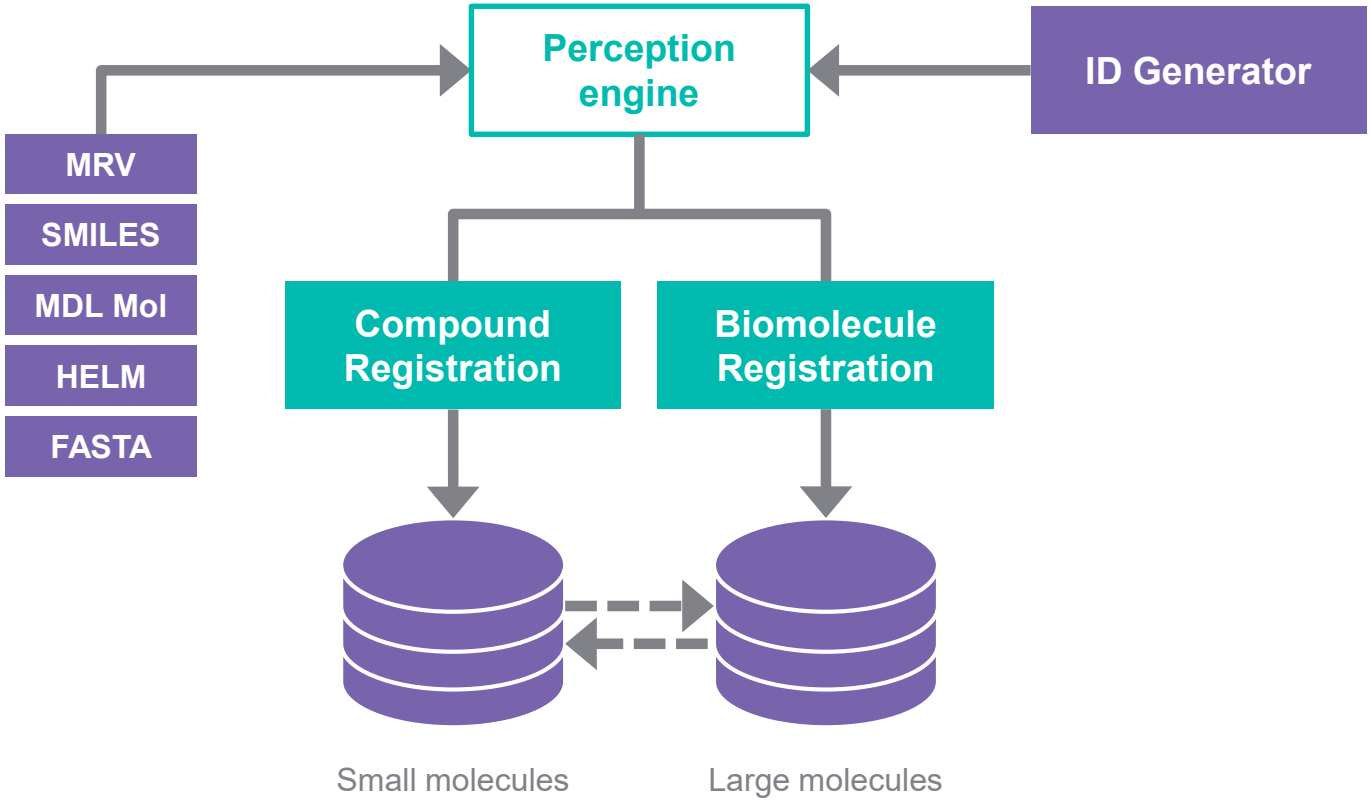
Longterm plans – Agnostic registration



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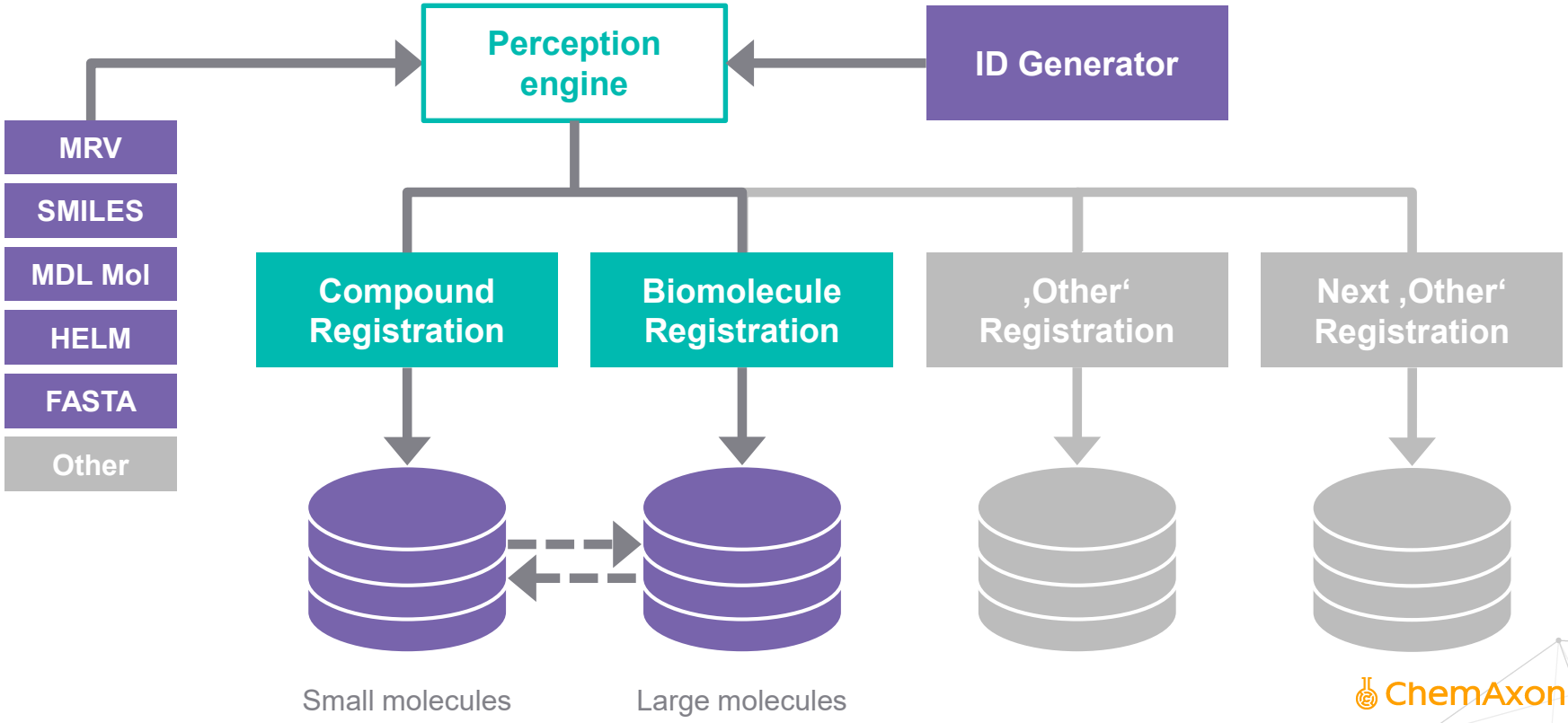
Longterm plans – Agnostic registration



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GET IN TOUCH

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