KR-MED 2006
International Workshop - November 8, 2006 in Baltimore, MD, USA
"Biomedical Ontology in Action"
AMIA

"*Lmo-2 interacts with Elf-2*" On the Meaning of Common Statements in Biomedical Literature

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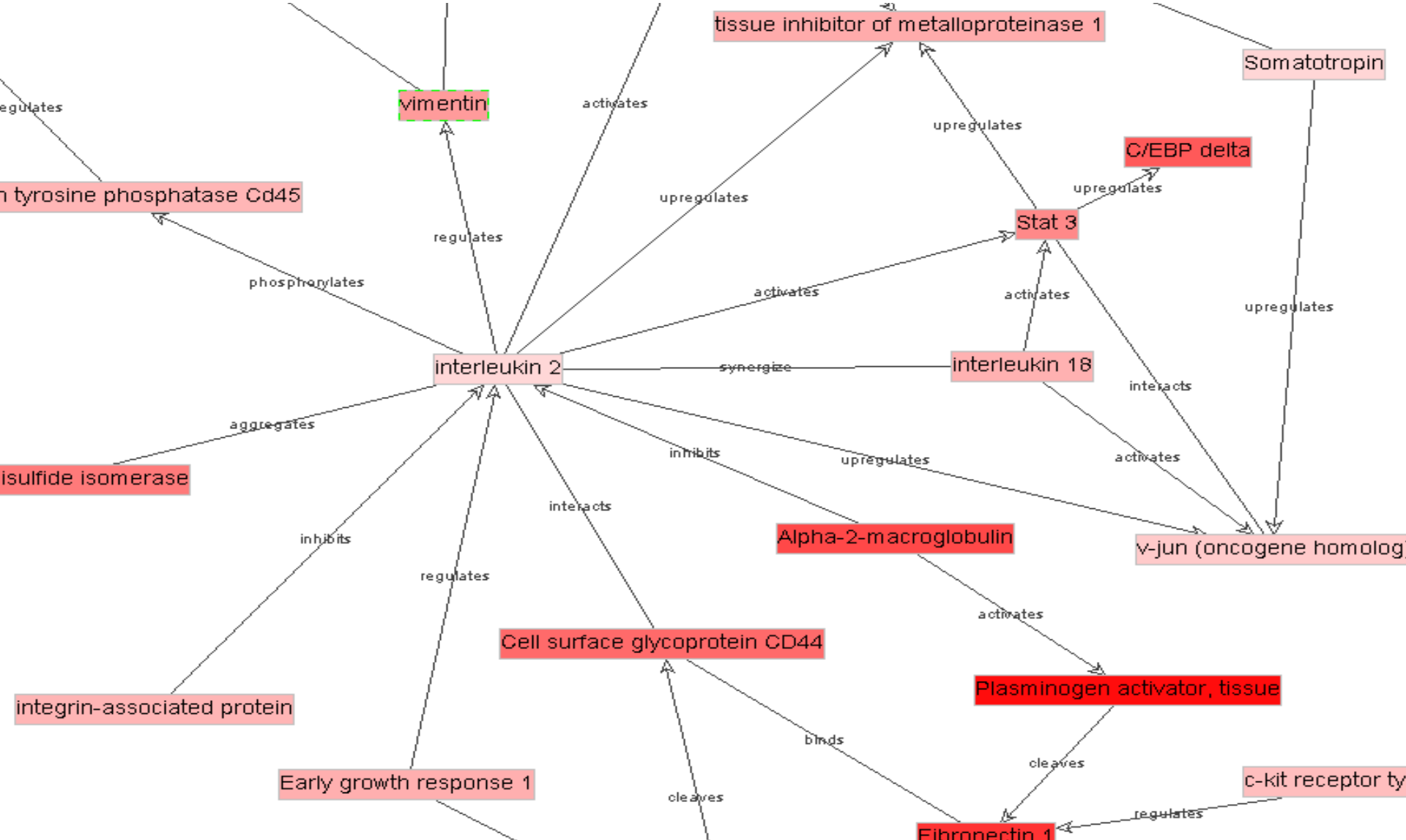
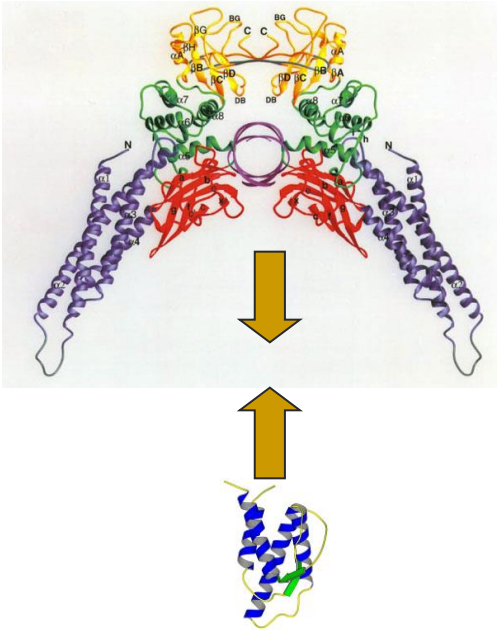
Background: Research in Molecular Biology on Protein Interactions



Protein-Protein Interactions

- Interaction:
  - Binding
  - Upregulation
  - Downregulation
  - Activation
  - Inhibition
  - Phosphorylation
  - …



Relevance for Ontology in Practice ??

- Huge amount of data on protein-protein-interactions
- Vast majority of this data stored in printed journal articles
- Use of text mining approaches
- Text mining typically fills template such as:
  `[Interaction, Protein1, Protein2]`
  `[Binding, Lmo-2, Elf-2]`
- Is this an issue of Ontology in Practice ?

“*Lmo-2 interacts with Elf-2*”

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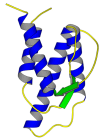
Referents of Protein names

- “Lmo-2” may refer to
  - One single Lmo-2 molecule



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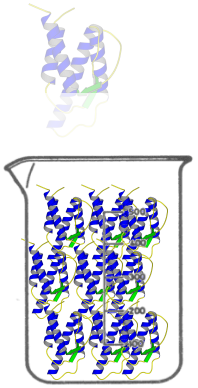

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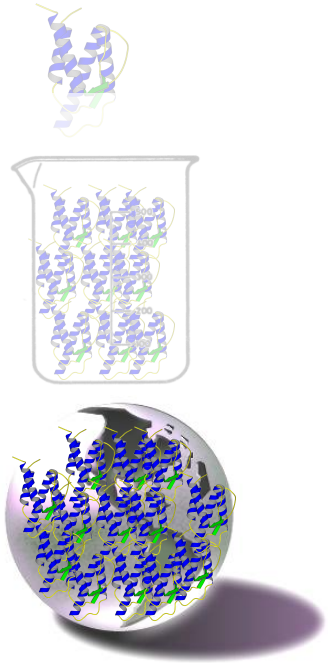

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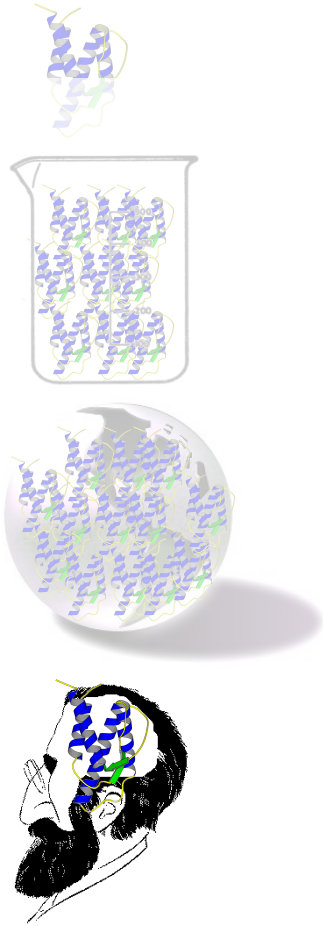

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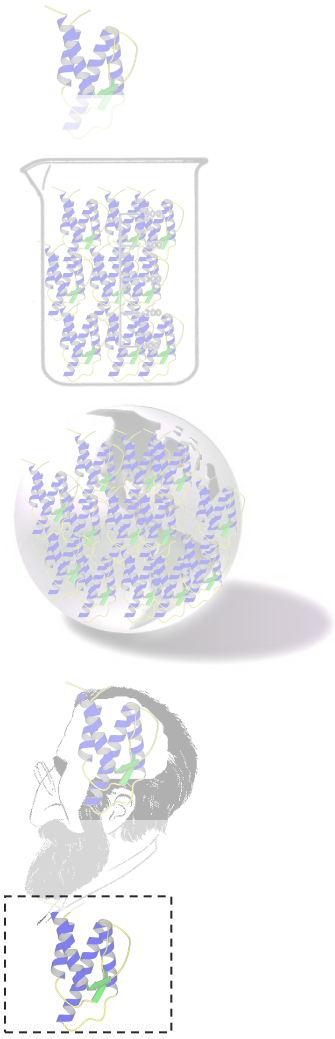
  - The universal (type) “Lmo-2”

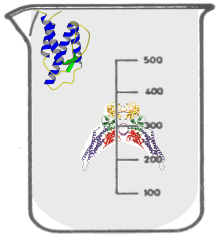


“*Lmo-2 interacts with Elf-2*”

“*Lmo-2 interacts with Elf-2*”: Existential interpretation of single events

"*Lmo-2 interacts with Elf-2*": Existential interpretation of single events

1. There is one interaction event which involves one single Lmo-2 molecule and one single Elf-2 molecule



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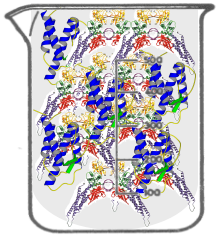

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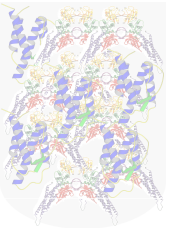

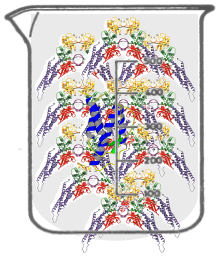

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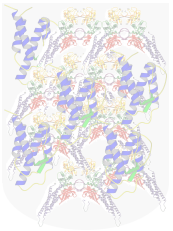

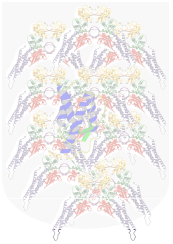

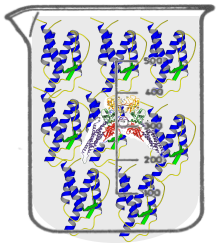

“*Lmo-2 interacts with Elf-2*”: Existential interpretation of collective events

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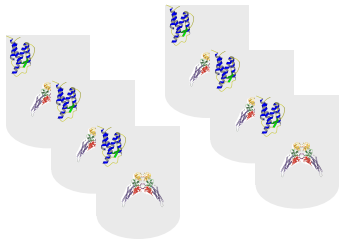

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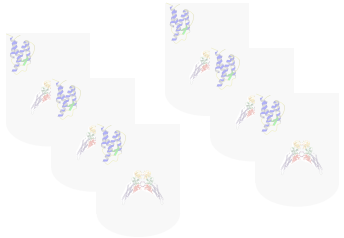
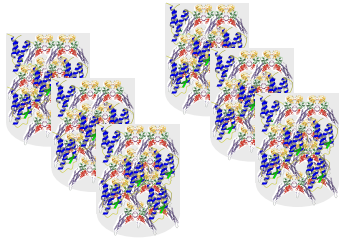


2. There are multiple interactions which involve amounts of Lmo-2 and amounts of Elf-2



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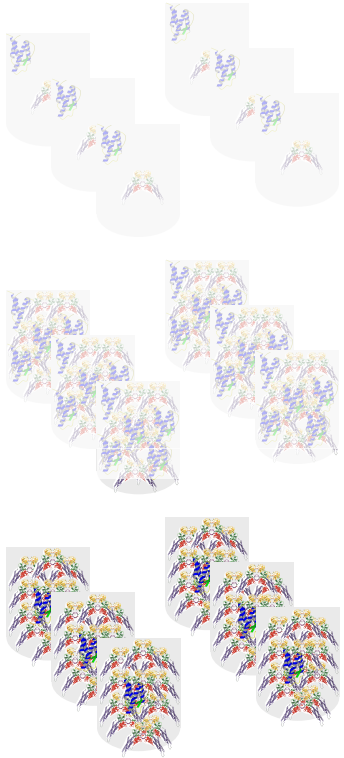

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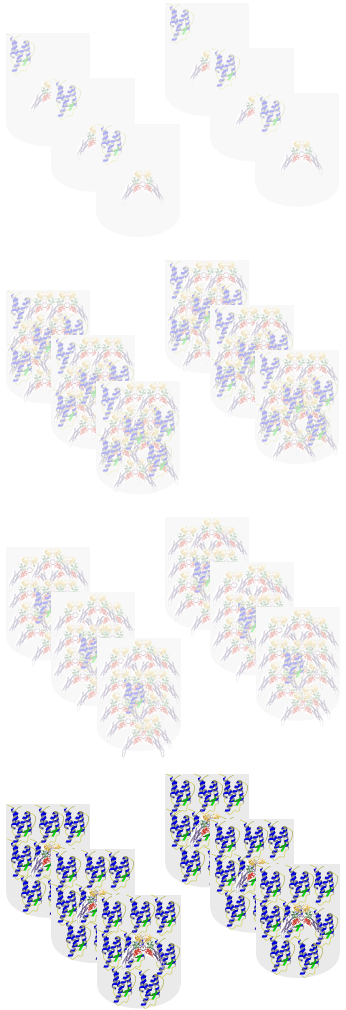

Generic Interpretations ?

“*Lmo-2 interacts with Elf-2*”: Generic interpretation of events

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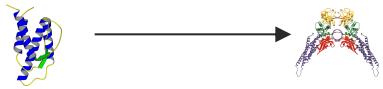

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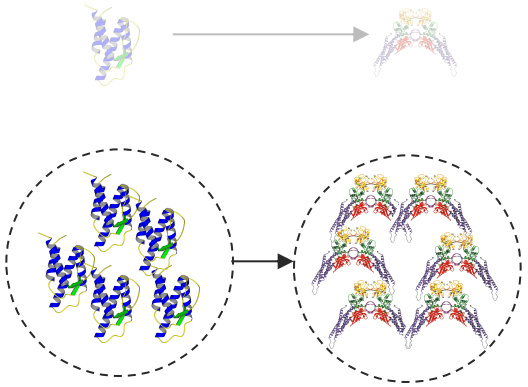

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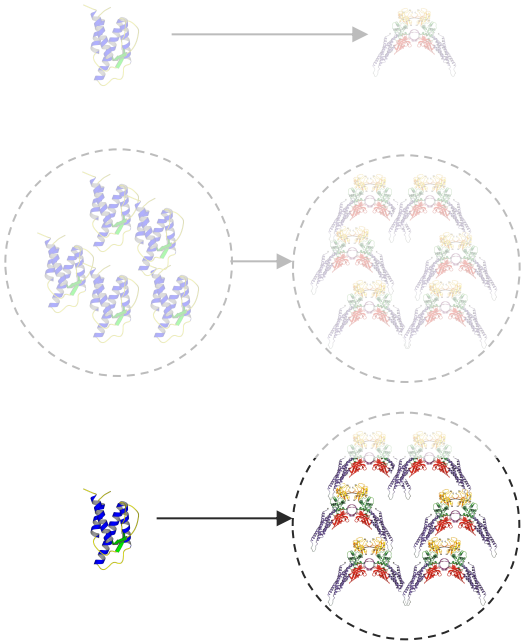

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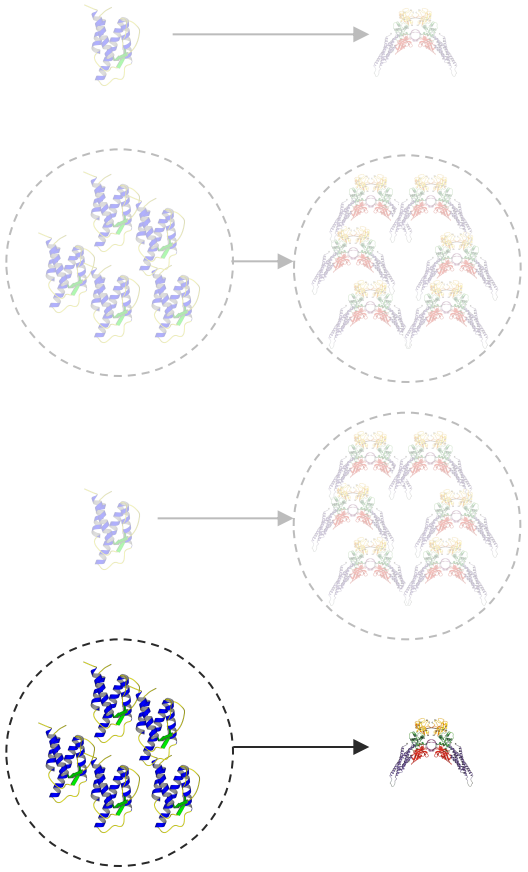

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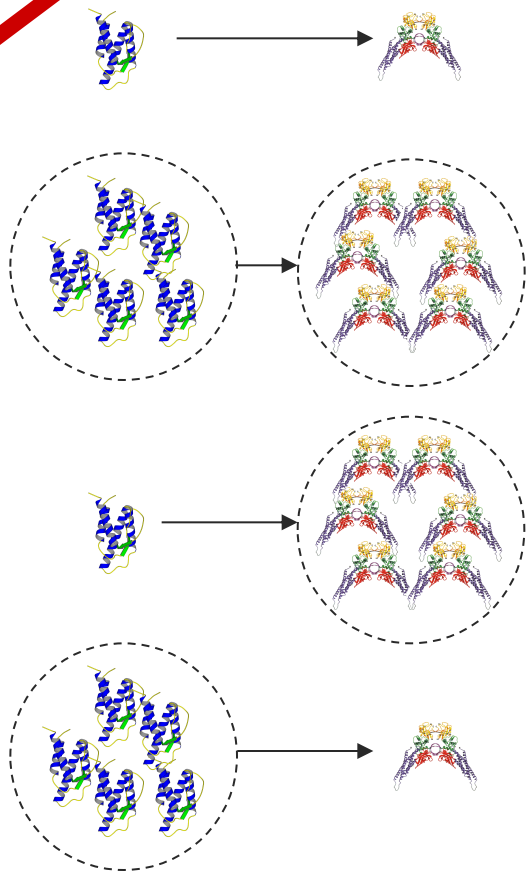

"*Lmo-2 interacts with Elf-2*": Generic interpretations by introducing new event types

1. All instances of *Lmo-2/Elf-2 Interaction*

   have one Lmo-2 and one Elf-2 molecule

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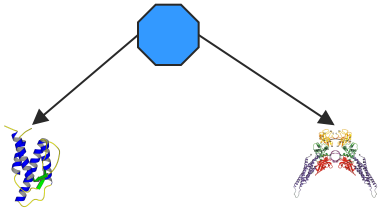

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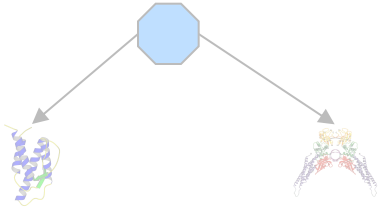
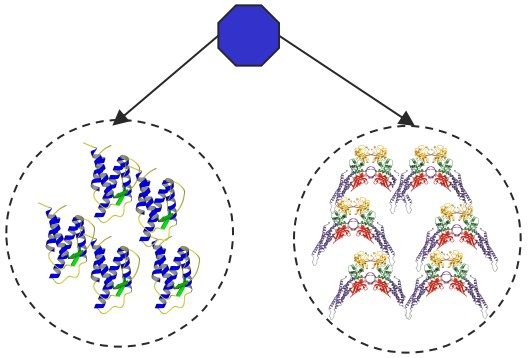


2. All instances of *Lmo-2/Elf-2 Interaction'* have one amount of Lmo-2 and one amount of Elf-2 as participants



3. (…)

… but this does not
further describe generic behaviour
of the proteins involved either

So far…

- Valid existential statements on
  - instances of molecules
  - instances of amounts of molecules
  - instances of events
- Valid universal statements on
  - subtypes of events
- Invalid universal statements on
  - molecules
  - amounts of molecules

Are there universally true properties of molecules or amounts of molecules regarding interaction ?

Dispositional Reading

- Authors of "*Lmo-2 interacts with Elf-2*" possibly do not want to refer to accidental occurrences
- They may want to express a disposition (the capability of an entity of doing sth.) *"Lmo-2 molecules have the disposition to interact with Elf-2 molecules"*

Ambiguities dispositional readings

1. Which event is it exactly that the property in question is meant to cause?
   A: Single events / Collective events
2. What is thought to be the bearer of this property
   A: Single molecules / Collectives of molecules
3. Which kind of property is in fact intended to be ascribed? …

Surefire dispositions (tendencies)

- Dispositions to react invariably in a certain way under specific circumstances
- Problem: Which are the circumstances for the realization of a disposition?
  - Under “all” circumstances: already discarded
  - Under “some” circumstances: considering extreme circumstances, (nearly) any interaction is possible
  - How to define “normal circumstances” ? (range of normality wrt concentration, pressure, temperature, pH etc.)

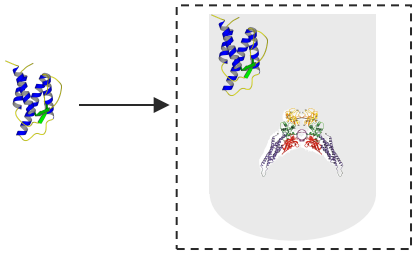
Probabilistic Dispositions (propensities)

- Dispositions which get realized with a certain probability under given circumstances
- Two patterns
  - Real stochastic behavior, e.g. low concentrations of one reagent
  - Hidden distinguishing characteristics, e.g. different subtypes of molecules: wildtype interacts, mutant does not

“*Lmo-2 interacts with Elf-2*”: Generic dispositions

"*Lmo-2 interacts with Elf-2*": Generic dispositions

1. All single Lmo-2 molecules have the disposition to react with some single Elf-2 molecule



"*Lmo-2 interacts with Elf-2*": Generic dispositions

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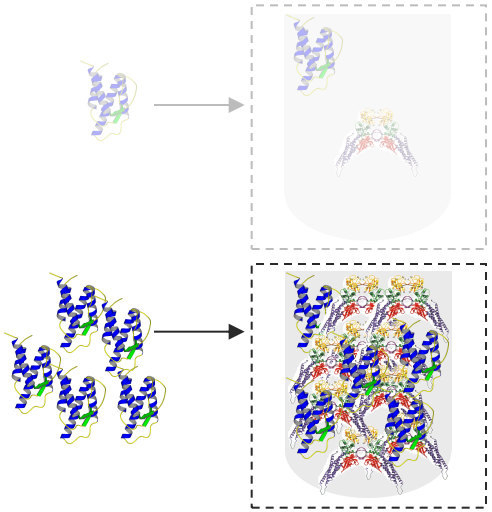

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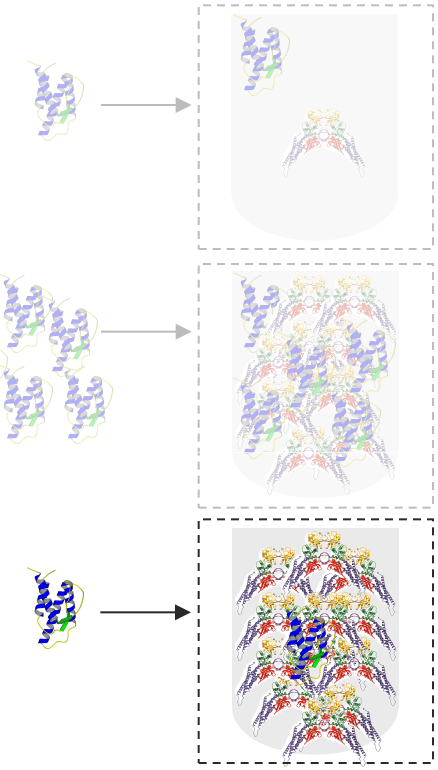

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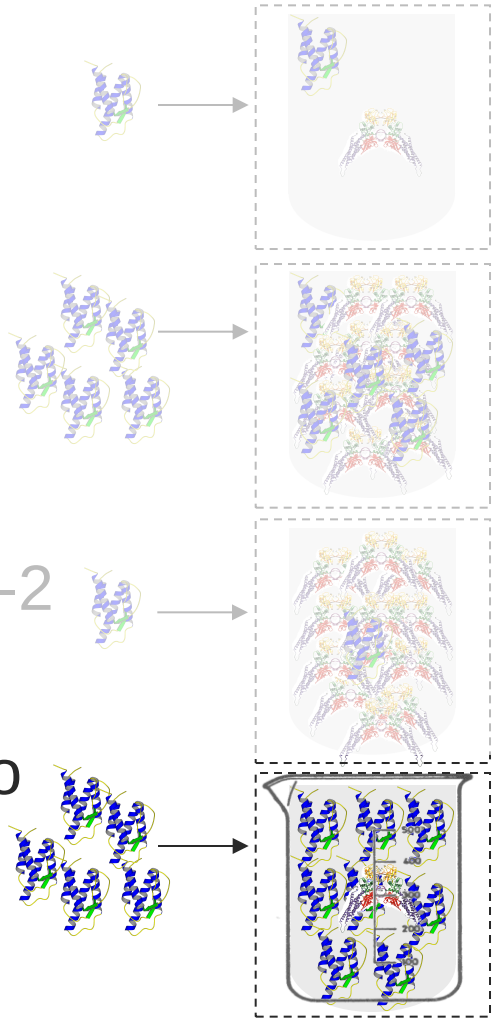

Finally…

- Valid existential statements on
  - instances of molecules
  - instances of amounts of molecules
  - instances of events
- Valid universal statements on
  - subtypes of events
- Valid universal statements about dispositions of
  - molecules
  - amounts of molecules

Ontology in Practice
=
Biologists' Nightmare ?

Simplifying matters and maintaining ontological correctness

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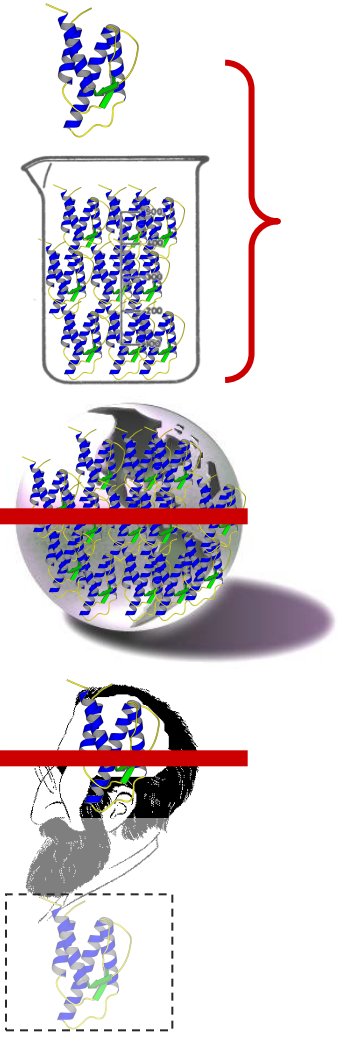


Referents of Protein names

- Proposal:

  “Lmo-2” refers to

  - The universal (type) Lmo-2 molecule

    Or

  - An undefined number (n>0) of instances of Lmo-2

Referents of Interaction Assertions

- Proposal:

  “Interacts” refers to

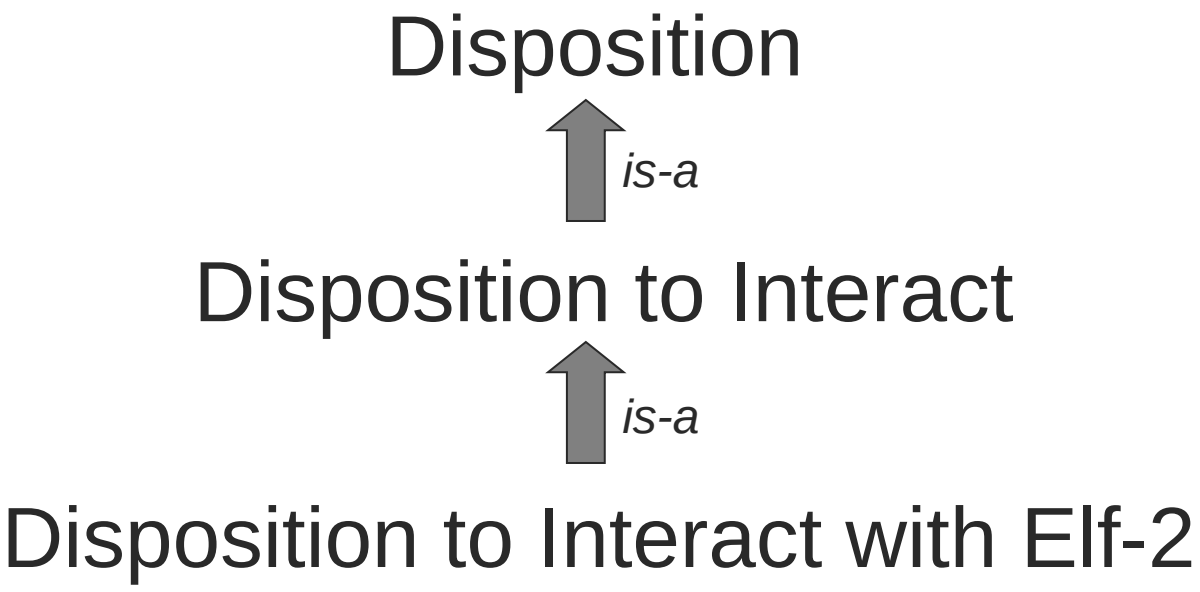
  - A plurality of interaction events

- Reason: Unique interaction events

  cannot be detected and are irrelevant

Introducing Dispositions

Disposition taxonomies:



Conclusion:

"*Lmo-2 interacts with Elf-2*" has the following two readings:

1. There are a plurality of interaction events each of them has one or many Lmo-2 molecules and one or many Elf-2 molecules as participants
2. Every single Lmo-2 molecule or plurality thereof has the disposition to interact with one or many Elf-2 molecules

Thank You !

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"*Lmo-2 interacts with Elf-2*" On the Meaning of Common Statements in Biomedical Literature

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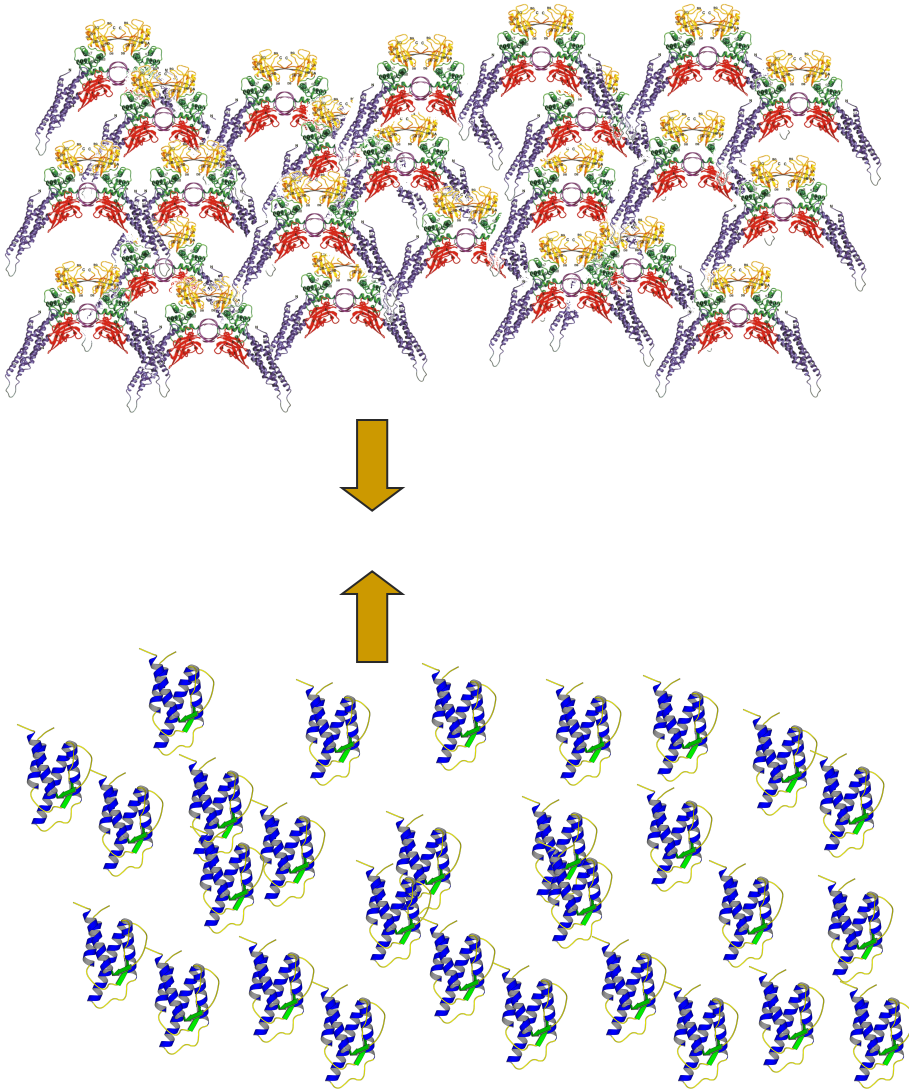
Department of Medical Informatics, Freiburg University Hospital, Germany

Ludger Jansen
Department of Philosophy, University of Rostock, Germany

Occurrents involving collectives (pluralities) of continuants

- Existence of a plurality of Lmo-2 molecules and another instance of Elf-2 molecules, both involved in one interaction event

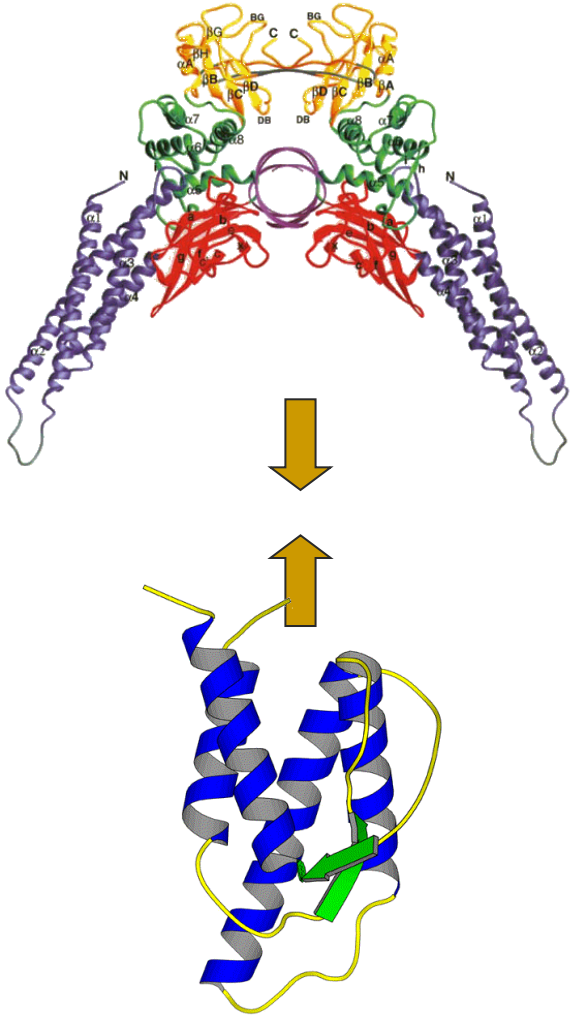


Occurrents involving collectives of continuants

Dispositional Readings

Occurrents involving single continuants

- Existence of at least one interaction event involving one instance of Lmo-2 and one instance of Elf-2



Occurrents involving collectives (pluralities) of continuants

- Existence of a plurality of interaction events each of the involving exactly one Lmo-2 molecule and one Elf-2 molecule

Occurrents involving collectives of continuants

$$
\begin{aligned}
&\exists p, i_1, i_2, \ldots i_n, n > 1 : \\
&\quad \bigwedge_{\nu=1}^{n} (inst(i_\nu, I) \wedge has\text{-}grain(p, i_\nu) \wedge \\
&\quad \exists l_\nu, e_\nu : inst(l_\nu, Lmo\text{-}2) \wedge inst(e_\nu, Elf\text{-}2) \wedge \\
&\qquad has\text{-}participant(i_\nu, l_\nu) \wedge \\
&\qquad has\text{-}participant(i_\nu, e_\nu) \wedge \\
&\quad \forall x : (has\text{-}participant(i_\nu, x) \rightarrow \\
&\qquad inst(x, Lmo\text{-}2) \vee inst(x, Elf\text{-}2)) \wedge \\
&\quad \forall l^*_\nu, e^*_\nu : ((inst(l^*_\nu, Lmo\text{-}2) \wedge \\
&\qquad inst(e^*_\nu, Elf\text{-}2) \wedge has\text{-}participant(i_\nu, l^*_\nu) \wedge \\
&\qquad has\text{-}participant(i_\nu, e^*_\nu)) \rightarrow (e^*_\nu = e_\nu \wedge l^*_\nu = l_\nu)))
\end{aligned}
$$

Occurrents involving single continuants

$$Is\text{-}a(Lmo\text{-}2, ProteinMolecule) \wedge$$
$$Is\text{-}a(Elf\text{-}2, ProteinMolecule) \wedge$$
$$Is\text{-}a(ProteinMolecule, Molecule) \wedge$$
$$Is\text{-}a(Molecule, Continuant) \wedge$$
$$\exists l, e : inst(l, Lmo\text{-}2) \wedge inst(e, Elf\text{-}2)$$

$$\exists l, e : inst(l, Lmo\text{-}2) \wedge$$
$$inst(e, Elf\text{-}2) \wedge interacts(l, e)$$

Occurrents involving single continuants

$$\exists l, e : inst(l, Lmo\text{-}2) \wedge inst(e, Elf\text{-}2) \wedge$$
$$interacts(l, e) \wedge$$
$$\forall l^*, e^* : (inst(l^*, Lmo\text{-}2) \wedge inst(e^*, Elf\text{-}2) \wedge$$
$$interacts(l^*, e^*)) \rightarrow (l^* = l \wedge e^* = e)$$

$$\exists l, e, i : inst(l, Lmo\text{-}2) \wedge inst(e, Elf\text{-}2) \wedge$$
$$inst(i, Interaction) \wedge$$
$$has\text{-}participant(i, l) \wedge has\text{-}participant(i, e)$$

$$\exists l, e, i : inst(l, Lmo\text{-}2) \wedge inst(e, Elf\text{-}2) \wedge$$
$$inst(i, Interaction) \wedge$$
$$has\text{-}participant(i, l) \wedge has\text{-}participant(i, e) \wedge$$
$$\forall x : (has\text{-}participant(i, x) \rightarrow$$
$$inst(x, Lmo\text{-}2) \vee inst(x, Elf\text{-}2))$$

Occurrents involving single continuants

$$
\begin{aligned}
&\exists l, e, i : inst(l, Lmo\text{-}2) \wedge inst(e, Elf\text{-}2) \wedge \\
&\quad inst(i, Interaction) \wedge \\
&\quad has\text{-}participant(i, l) \wedge has\text{-}participant(i, e) \wedge \\
&\quad \forall x : (has\text{-}participant(i, x) \rightarrow \\
&\qquad inst(x, Lmo\text{-}2) \vee inst(x, Elf\text{-}2)) \wedge \\
&\quad \forall l^*, e^* : (inst(l^*, Lmo\text{-}2) \wedge inst(e^*, Elf\text{-}2) \wedge \\
&\qquad has\text{-}participant(i, l^*) \wedge has\text{-}participant(i, e^*)) \\
&\qquad \rightarrow (e^* = e \wedge l^* = l))
\end{aligned}
$$

Occurrents involving collectives of continuants

$$\forall c : inst(c, X_{COLL}) \rightarrow \exists e_1, e_2, ..., e_n, n > 1 : \bigwedge_{\nu=1}^{n} inst(e_\nu, X) \wedge has\text{-}grain(c, e_\nu)$$

$$\exists l, e, i : inst(l, Lmo\text{-}2_{COLL}) \wedge inst(e, Elf\text{-}2_{COLL}) \wedge inst(i, Interaction) \wedge has\text{-}participant(i, l) \wedge has\text{-}participant(i, e)$$

Occurrents involving collectives of continuants

$$
\begin{aligned}
&\exists p, i_1, i_2, \ldots i_n, n > 1 : \\
&\quad \bigwedge_{\nu=1}^{n} (inst(i_\nu, I) \wedge has\text{-}grain(p, i_\nu) \wedge \\
&\quad \exists l_\nu, e_\nu : inst(l_\nu, Lmo\text{-}2) \wedge inst(e_\nu, Elf\text{-}2) \wedge \\
&\qquad has\text{-}participant(i_\nu, l_\nu) \wedge \\
&\qquad has\text{-}participant(i_\nu, e_\nu) \wedge \\
&\quad \forall x : (has\text{-}participant(i_\nu, x) \rightarrow \\
&\qquad inst(x, Lmo\text{-}2) \vee inst(x, Elf\text{-}2)) \wedge \\
&\quad \forall l^*_\nu, e^*_\nu : ((inst(l^*_\nu, Lmo\text{-}2) \wedge \\
&\qquad inst(e^*_\nu, Elf\text{-}2) \wedge has\text{-}participant(i_\nu, l^*_\nu) \wedge \\
&\qquad has\text{-}participant(i_\nu, e^*_\nu)) \rightarrow (e^*_\nu = e_\nu \wedge l^*_\nu = l_\nu)))
\end{aligned}
$$