



KR-MED 2006

International Workshop - November 8, 2006 in Baltimore, MD, USA

“Biomedical Ontology in Action”



“Lmo-2 interacts with Elf-2”
On the Meaning of Common Statements
in Biomedical Literature

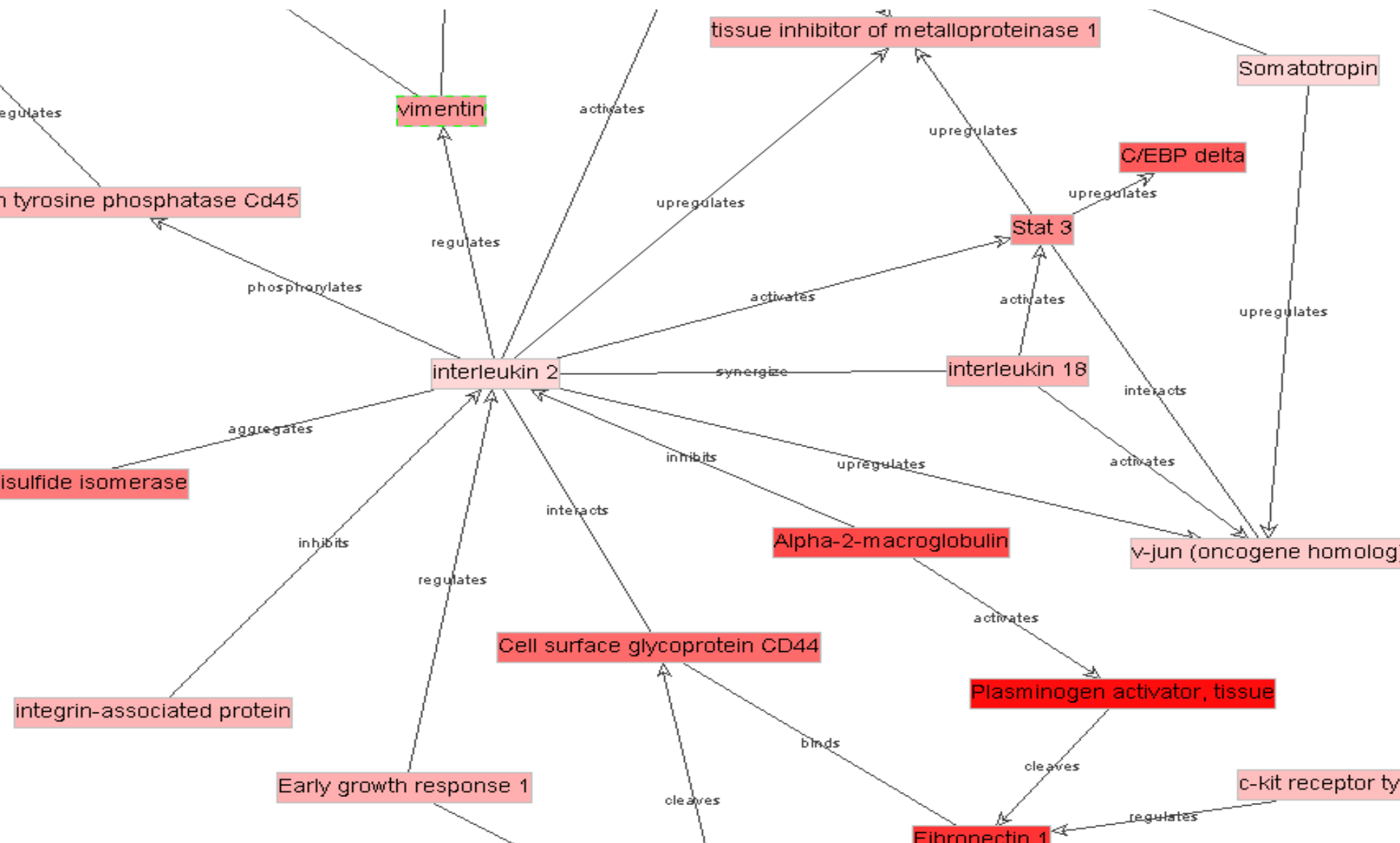
Stefan Schulz

Department of Medical Informatics, Freiburg University
Hospital, Germany

Ludger Jansen

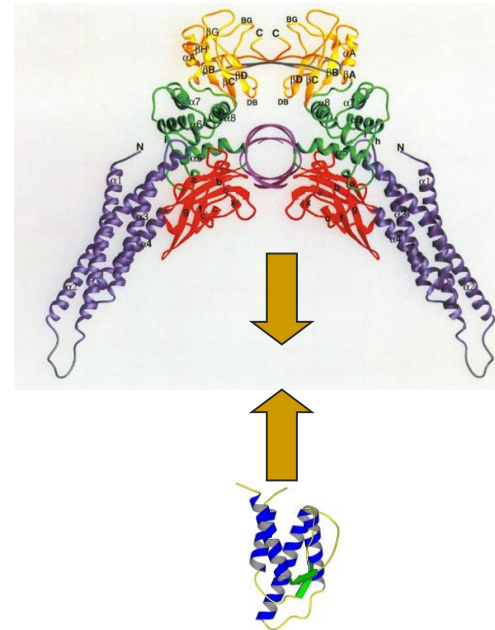
Department of Philosophy, University of Rostock, Germany

Background: Research in Molecular Biology on Protein Interactions



Protein-Protein Interactions

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



Relevance for Ontology in Practice ??

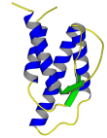
- Huge amount of data on protein-protein-interactions
- Vast majority of this data stored in printed journal articles
- Use of text mining approaches
- Text mining typically fills template such as:
[Interaction, Protein1, Protein2]
[Binding, Lmo-2, Elf-2]
- **Is this an issue of Ontology in Practice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

“Lmo-2 interacts with Elf-2”

“*Lmo-2* interacts with *Elf-2*”

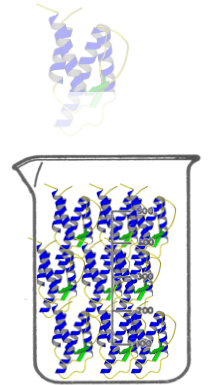
Referents of Protein names

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



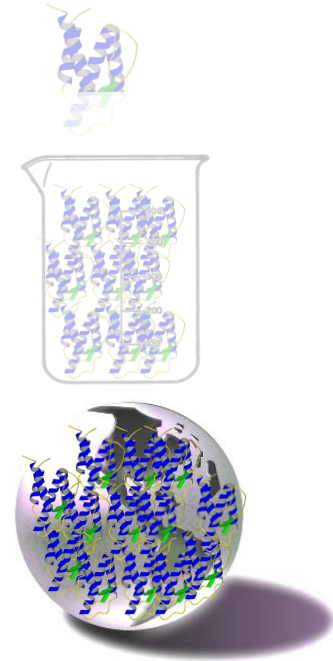
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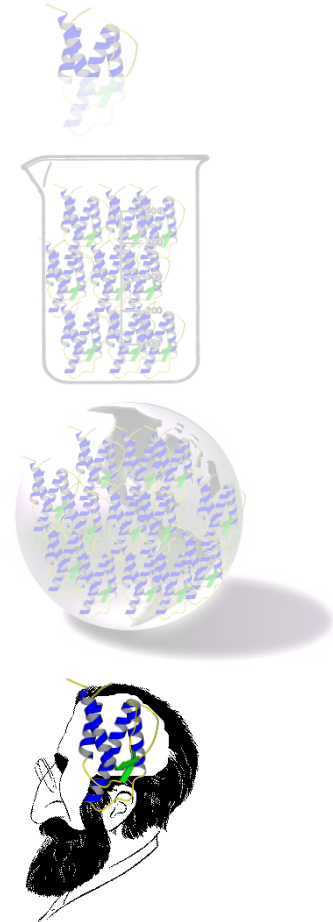
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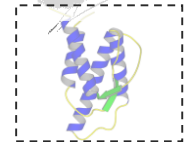
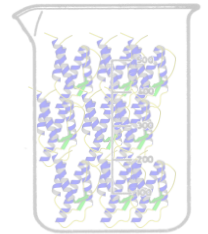
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 - The mental representation of “Lmo-2”



Referents of Protein names

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 - Some amount of Lmo-2, e.g. in an experiment
 - The collection of all Lmo-2 molecules in the world
 - The mental representation of “Lmo-2”
 - The universal (type) “Lmo-2”



“Lmo-2 interacts with Elf-2”

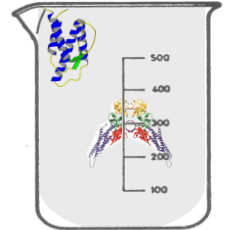
“Lmo-2 interacts with Elf-2”:

Existential interpretation of **single** events

“*Lmo-2 interacts with Elf-2*”:

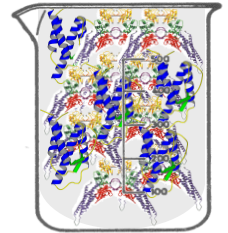
Existential interpretation of **single** events

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



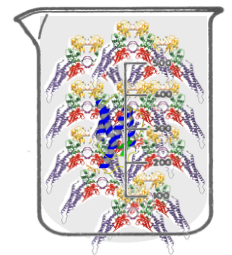
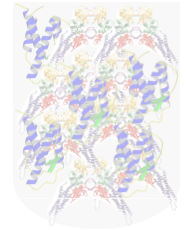
“*Lmo-2* interacts with *Elf-2*”: Existential interpretation of **single** events

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



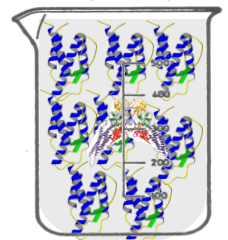
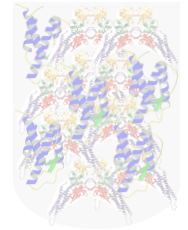
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“*Lmo-2* interacts with *Elf-2*”: Existential interpretation of **single** events

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4. There is one interaction event which involves an amount of *Lmo-2* and an single *Elf-2* molecule



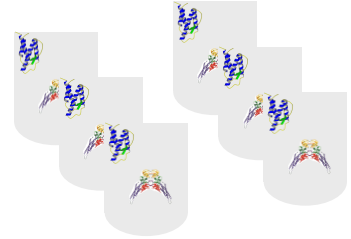
“Lmo-2 interacts with Elf-2”:

Existential interpretation of **collective** events

“*Lmo-2 interacts with Elf-2*”:

Existential interpretation of **collective** events

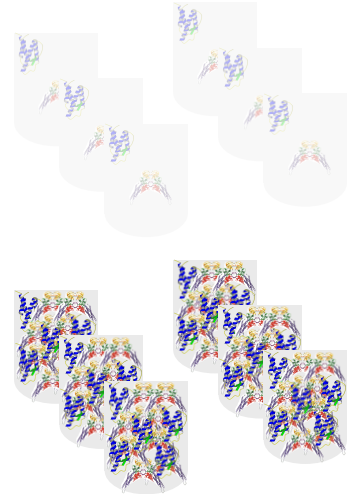
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“*Lmo-2* interacts with *Elf-2*”:

Existential interpretation of **collective** events

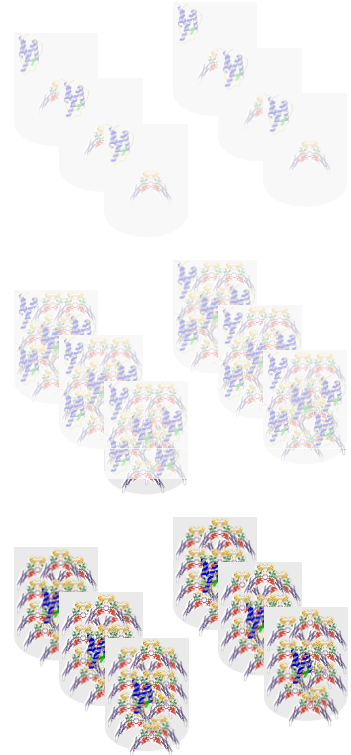
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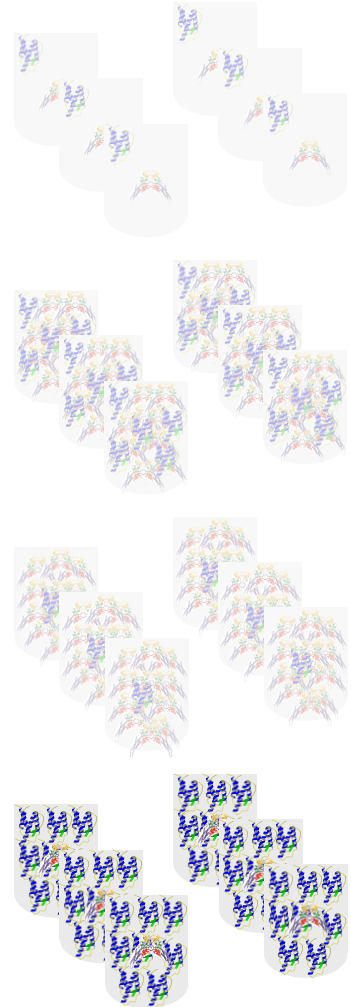
Existential interpretation of **collective** events

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

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4. There are multiple interactions each of which involves an amount of *Lmo-2* and one single *Elf-2* molecule



Generic Interpretations ?

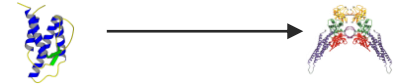
“Lmo-2 interacts with Elf-2”:

Generic interpretation of events

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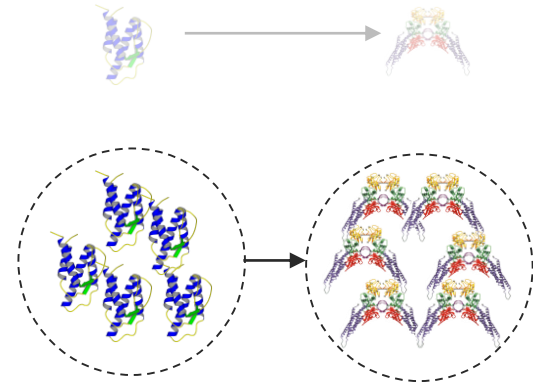
Generic interpretation of events

1. All *Lmo-2* molecules interact with some *Elf-2* molecule



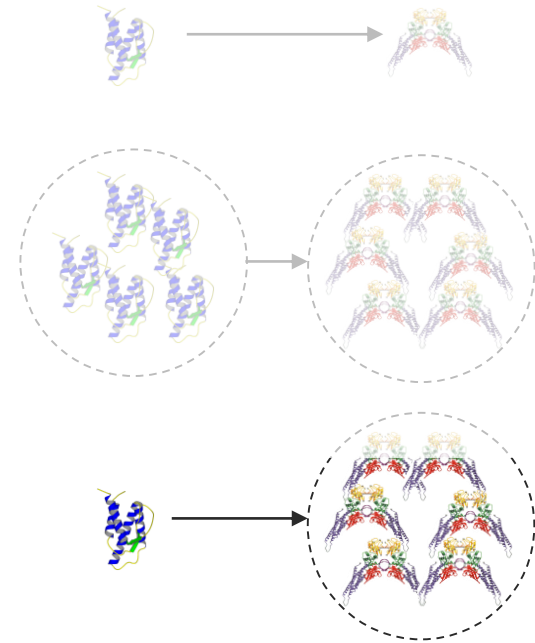
“*Lmo-2* interacts with *Elf-2*”: Generic interpretation of events

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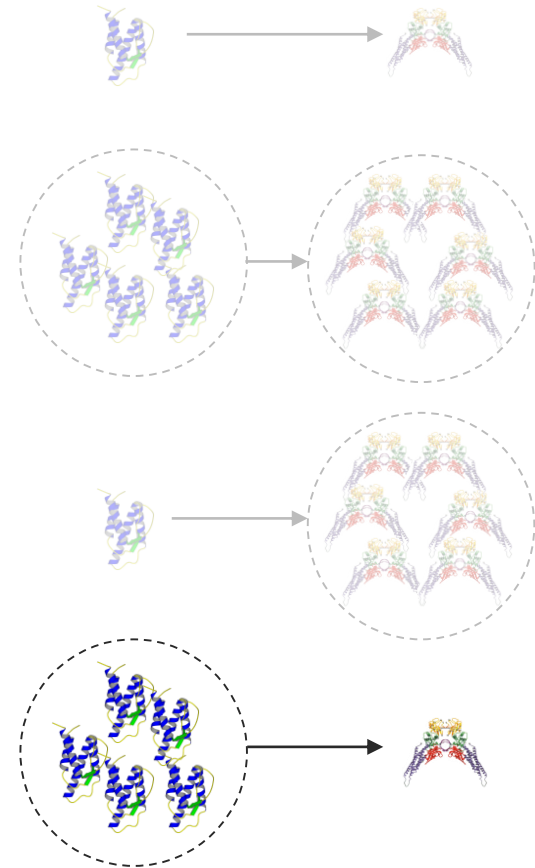
“*Lmo-2* interacts with *Elf-2*”: Generic interpretation of events

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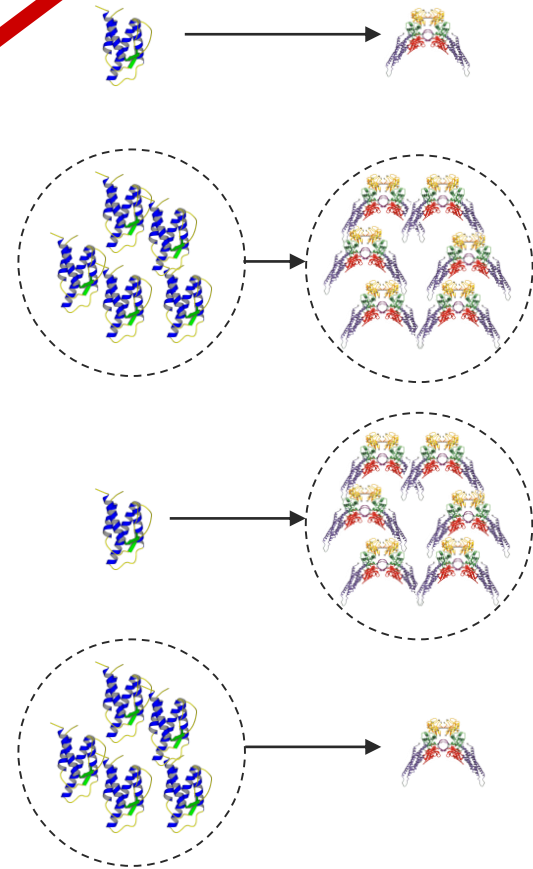
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4. All amounts of *Lmo-2* interact with some *Elf-2* molecule



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

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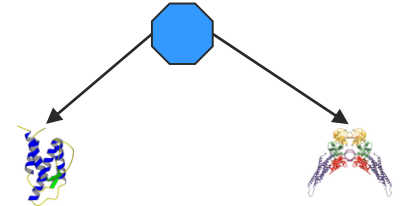


“*Lmo-2 interacts with Elf-2*”: Generic interpretations by introducing new event types

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

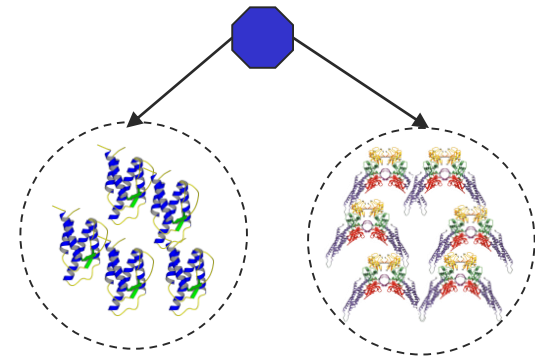
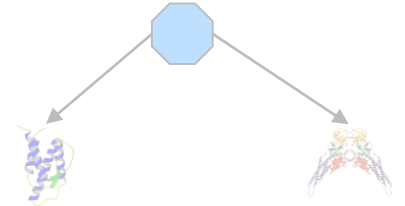
“*Lmo-2* interacts with *Elf-2*”: Generic interpretations by introducing new event types

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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 as participants
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.)

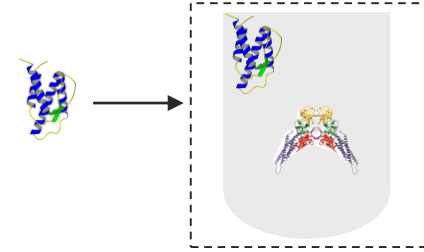
Probabilistic Dispositions (propensities)

- 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

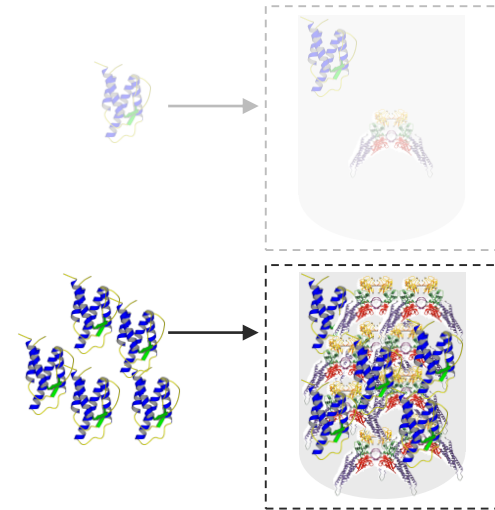
“*Lmo-2* interacts with *Elf-2*”: Generic dispositions

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



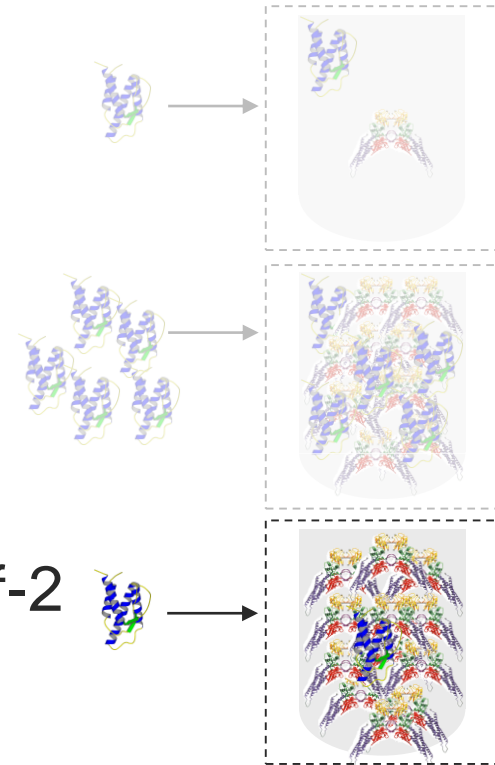
“*Lmo-2* interacts with *Elf-2*”: Generic dispositions

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



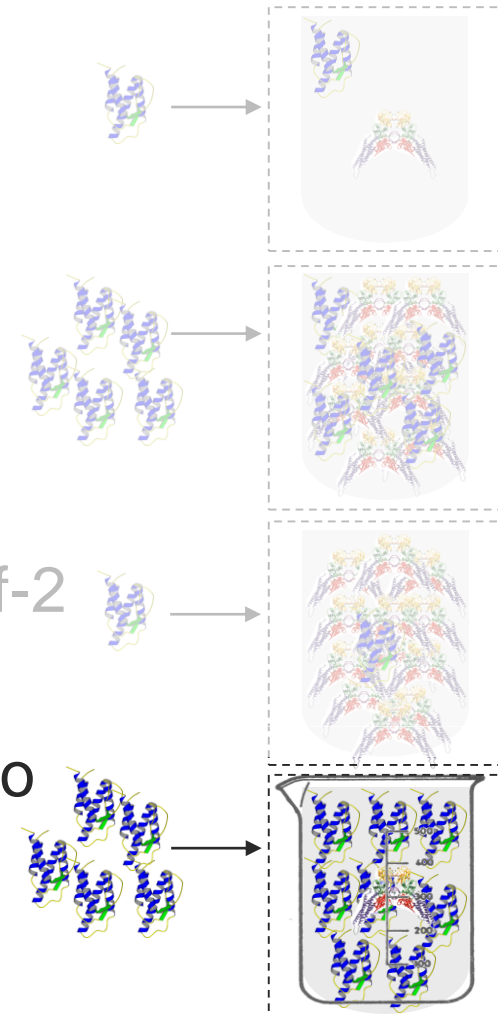
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“*Lmo-2* interacts with *Elf-2*”: Generic dispositions

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Finally...

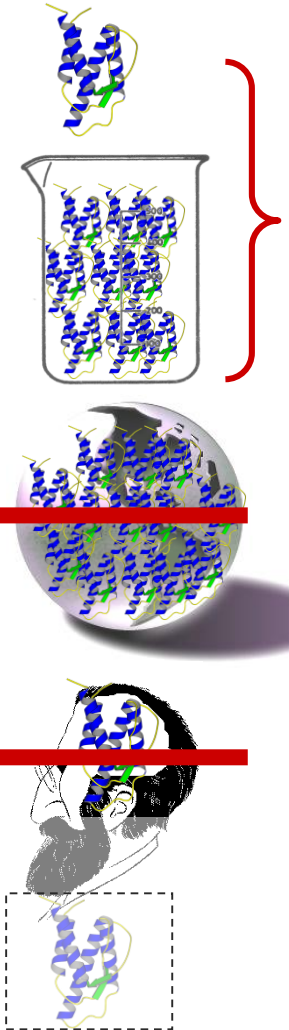
- **Valid existential** statements on
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 - instances of amounts of molecules
 - instances of events
- **Valid universal** statements on
 - subtypes of events
- **Valid universal** statements about dispositions of
 - molecules
 - amounts of molecules

Ontology in Practice
=
Biologists' Nightmare ?

Simplifying matters **and**
maintaining ontological
correctness

Referents of Protein names

- “Lmo-2” may refer to
 - One single Lmo-2 molecule
 - Some amount of Lmo-2 molecules, e.g. in an experiment
 - ~~○ The collection of all Lmo-2 molecules in the world~~
 - ~~○ The mental representation of “Lmo-2”~~
 - The universal (type) “Lmo-2”



Referents of Protein names

- Proposal:

“Lmo-2” refers to

- The universal (type) Lmo-2 molecule

Or

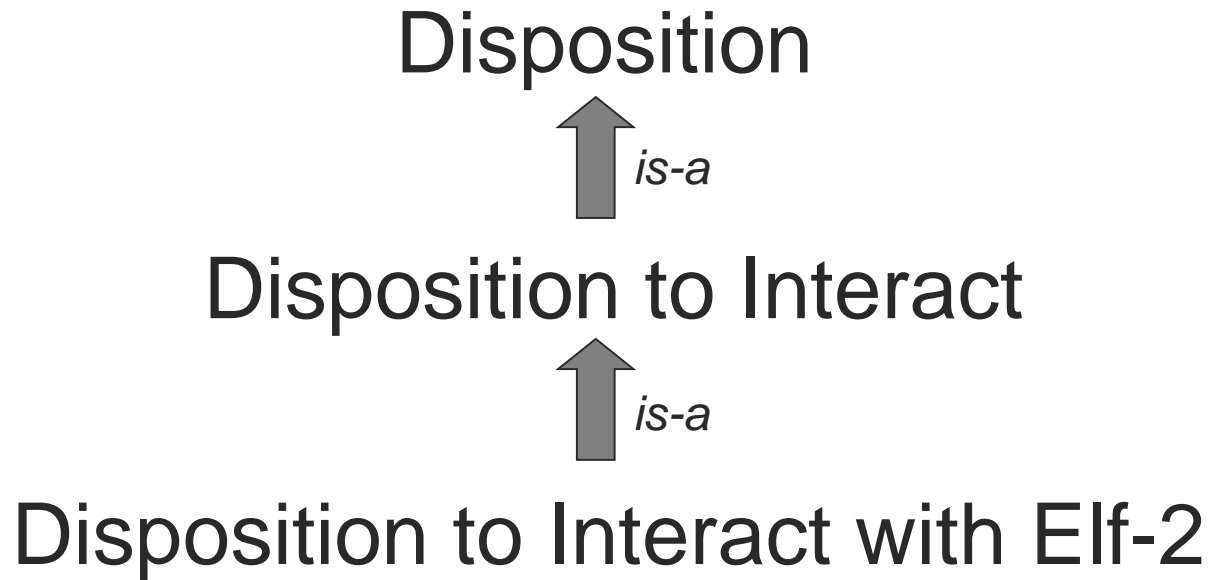
- An undefined number ($n > 0$) of instances of Lmo-2

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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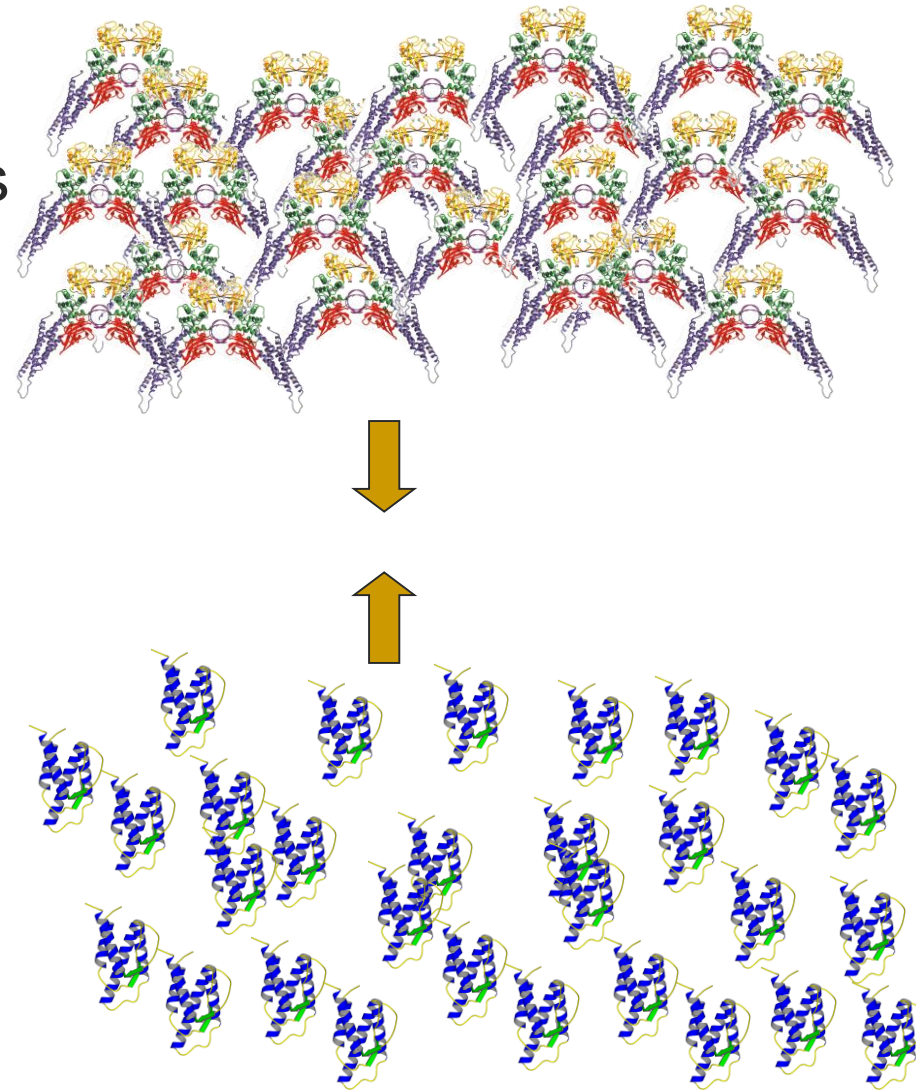
Department of Medical Informatics, Freiburg University
Hospital, Germany

Ludger Jansen

Department of Philosophy, University of Rostock, Germany

Occurrences 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



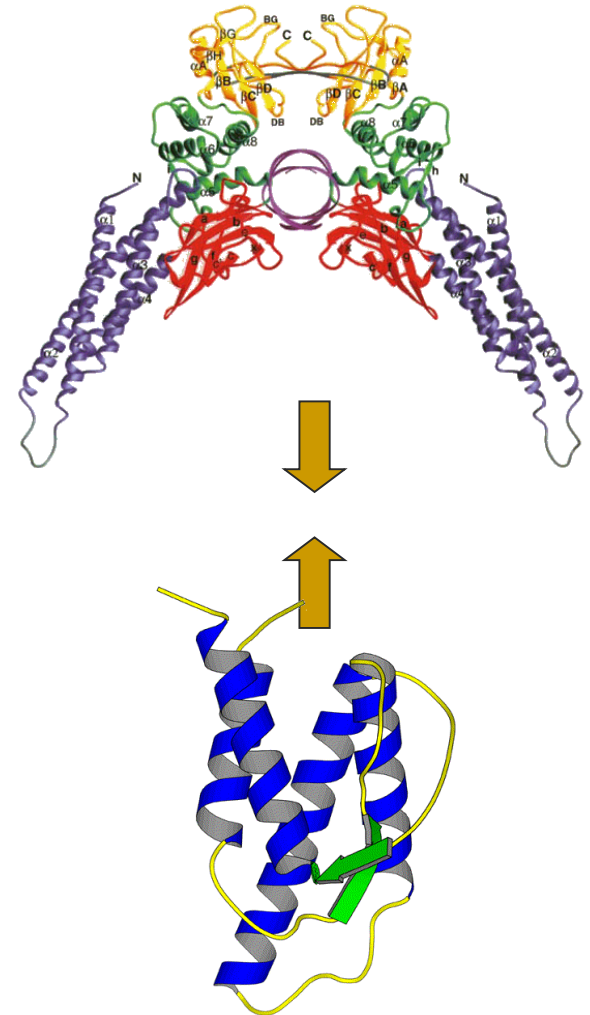
Occurrences involving collectives of continuants

Dispositional Readings



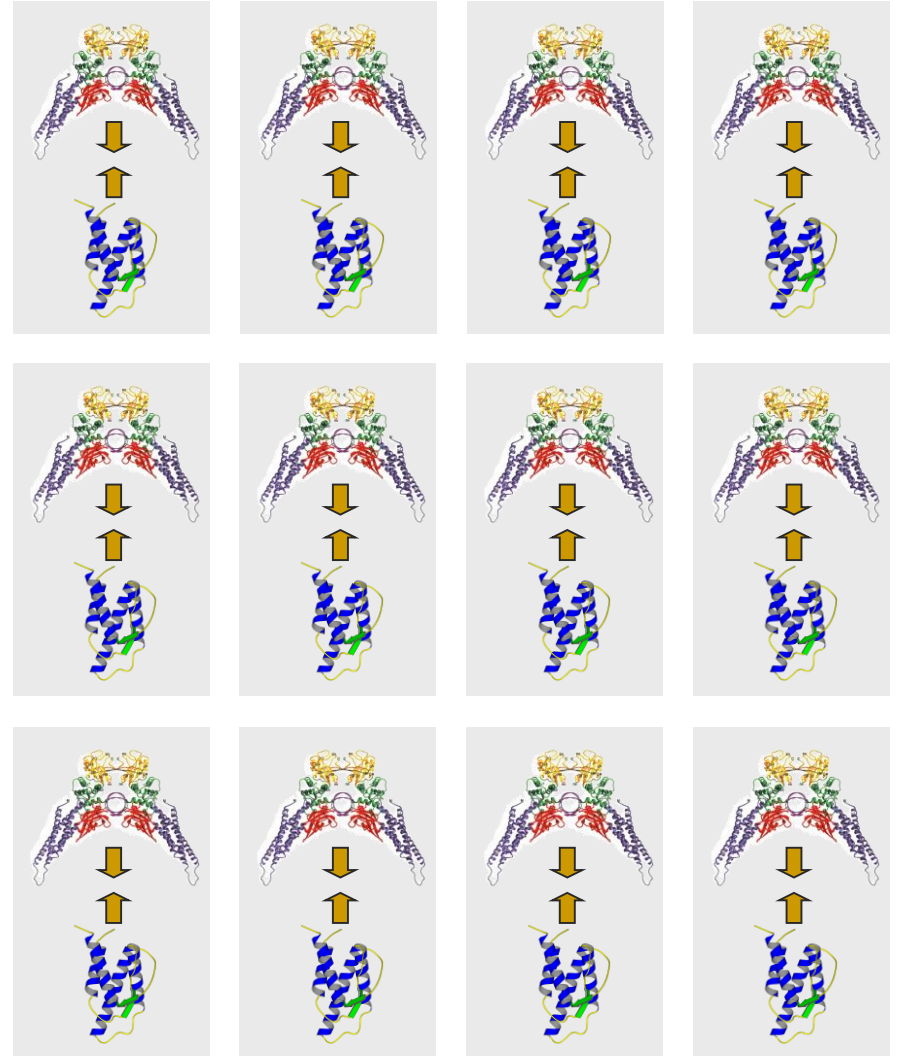
Occurrences involving single continuants

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



Occurrences 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



Occurrences involving collectives of continuants

$\exists p, i_1, i_2, \dots, i_n, n > 1 :$

$\bigwedge_{\nu=1}^n (inst(i_\nu, I) \wedge has-grain(p, i_\nu) \wedge$

$\exists l_\nu, e_\nu : inst(l_\nu, Lmo-2) \wedge inst(e_\nu, Elf-2) \wedge$

$has-participant(i_\nu, l_\nu) \wedge$

$has-participant(i_\nu, e_\nu) \wedge$

$\forall x : (has-participant(i_\nu, x) \rightarrow$

$inst(x, Lmo-2) \vee inst(x, Elf-2)) \wedge$

$\forall l_\nu^*, e_\nu^* : ((inst(l_\nu^*, Lmo-2) \wedge$

$inst(e_\nu^*, Elf-2) \wedge has-participant(i_\nu, l_\nu^*) \wedge$

$has-participant(i_\nu, e_\nu^*)) \rightarrow (e_\nu^* = e_\nu \wedge l_\nu^* = l_\nu)))$

Occurrences involving single continuants

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

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

Occurrences involving single continuants

$$\begin{aligned} & \exists l, e : inst(l, Lmo-2) \wedge inst(e, Elf-2) \wedge \quad (1) \\ & \quad interacts(l, e) \wedge \\ & \quad \forall l^*, e^* : (inst(l^*, Lmo-2) \wedge inst(e^*, Elf-2) \wedge \\ & \quad \quad interacts(l^*, e^*)) \rightarrow (l^* = l \wedge e^* = e) \end{aligned}$$

$$\begin{aligned} & \exists l, e, i : inst(l, Lmo-2) \wedge inst(e, Elf-2) \wedge \quad (2) \\ & \quad inst(i, Interaction) \wedge \\ & \quad has-participant(i, l) \wedge has-participant(i, e) \end{aligned}$$

$$\begin{aligned} & \exists l, e, i : inst(l, Lmo-2) \wedge inst(e, Elf-2) \wedge \quad (3) \\ & \quad inst(i, Interaction) \wedge \\ & \quad has-participant(i, l) \wedge has-participant(i, e) \wedge \\ & \quad \forall x : (has-participant(i, x) \rightarrow \\ & \quad \quad inst(x, Lmo-2) \vee inst(x, Elf-2)) \end{aligned}$$

Occurrences involving single continuants

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

Occurrences involving collectives of continuants

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

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

Occurrences involving collectives of continuants

$\exists p, i_1, i_2, \dots, i_n, n > 1 :$

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$\exists l_\nu, e_\nu : inst(l_\nu, Lmo-2) \wedge inst(e_\nu, Elf-2) \wedge$

$has-participant(i_\nu, l_\nu) \wedge$

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$has-participant(i_\nu, e_\nu^*)) \rightarrow (e_\nu^* = e_\nu \wedge l_\nu^* = l_\nu)))$