Systems Biology on Bio-Linux

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Centre for Ecology & Hydrology
NATURAL ENVIRONMENT RESEARCH COUNCIL

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1. Bio-Linux: A Computational Biology Workstation

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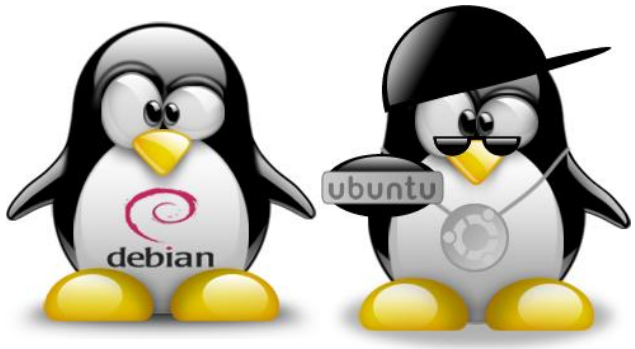
"one-stop-shop computational solution
-- from desktop to the cloud --
for biologists and bioinformaticians alike"

- Free, open source operating system
- Based on Linux (Ubuntu LTS) (64-bit)
- Release cycle in synchronization with Ubuntu
- Free and Open Source Software Advocacy
- 8 years
- 6 major releases, 3 base distributions
- 143 packages, >500 bioinformatics tools



http://nebc.nerc.ac.uk/tools/bio-linux

1.1 Community Outreach

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- Bio-Linux USB Sticks
- Users/Developers Group Meetings (BOSC)
- Mailing lists (Developers, Users)
- HelpDesk for User Support: helpdesk@nebc.ac.uk
- Teaching: “Introduction to Bio-Linux”
- Code Catalogue
  http://nebc.nerc.ac.uk/tools/code-corner

1.2 Bio-Linux Usage Figures

- >2500 registered ISO downloads
- 150 people on discussion list
- >5000 distinct IP hits on package repository (last month)
- 1200 page views (last month)

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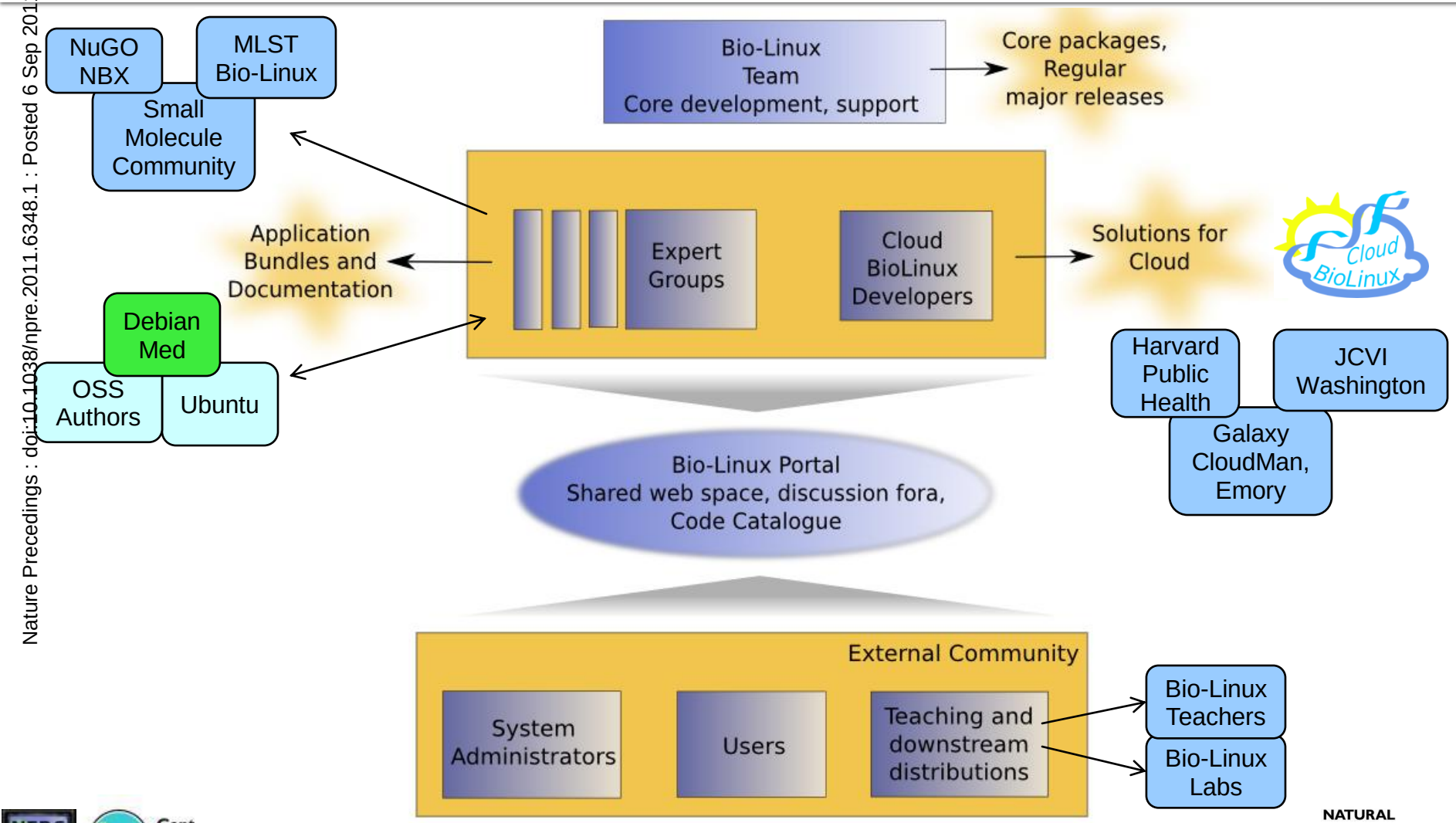
1.3 The Bio-Linux Organogram



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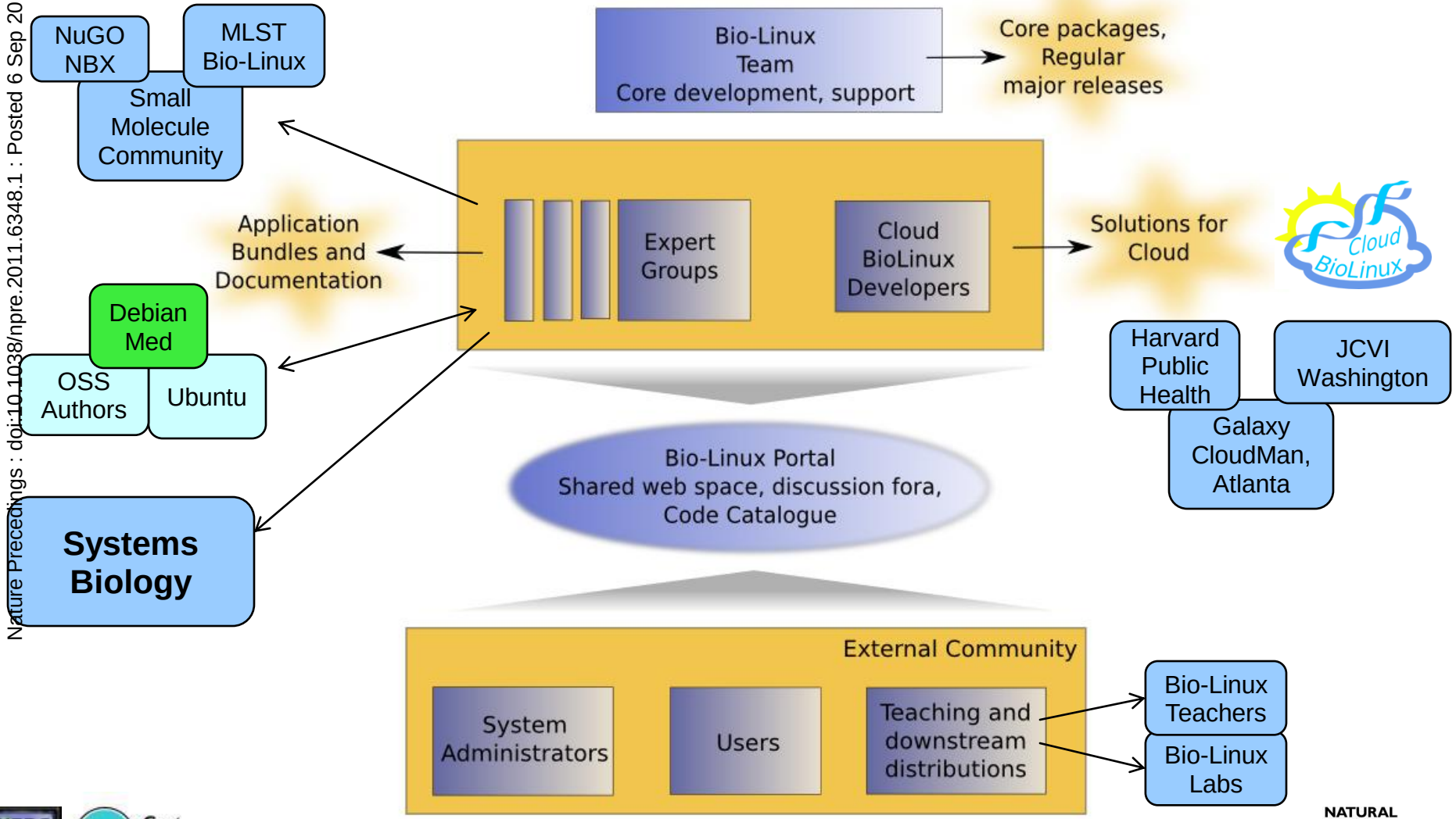
1.3 The Bio-Linux Organogram



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2.1 Modelling Approaches: Top-Down

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Top-Down Modelling (Mathematical modelling)

- Based on ordinary or partial differential equations
- Population of "identical" individuals
- Underlying behavioural rules are treated as a 'black box'

- Essential in formulation of general theories
- Biological systems represent a challenge for mathematical modellers;
  - inherent complexity,
  - non-linear relationships among individual components

2.2 Modelling Approaches: Bottom-Up

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Bottom-Up Modelling (Agent-Based Modelling)

- Models each individual aiming to study:
  - mechanisms for underlying behaviour
  - interactions between individuals/environment
- Treats individuals as unique and discrete entities with properties that can change during their lives
- Once rules are specified, population and community level consequences emerge naturally

2.3 Why ABM

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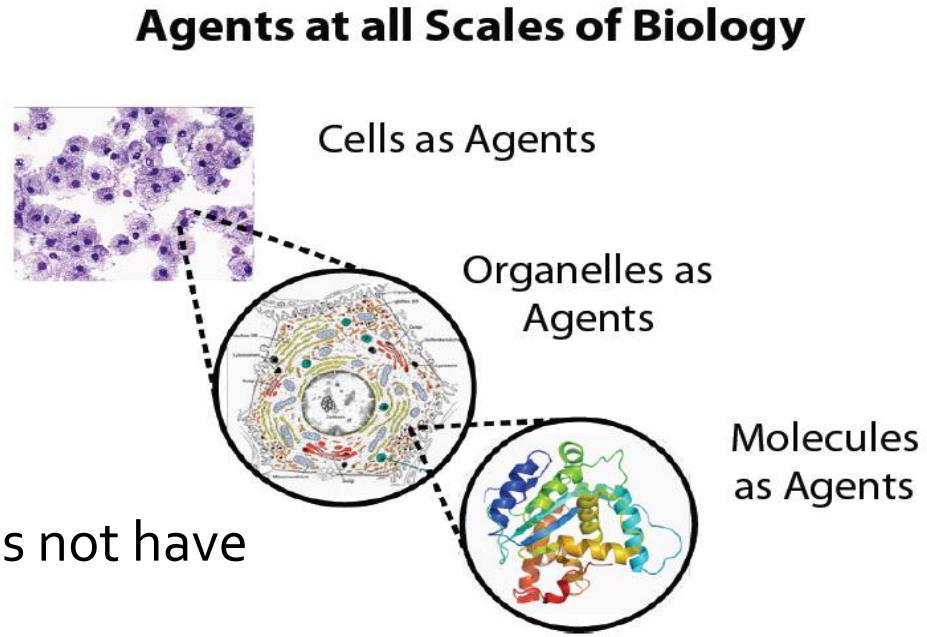
- In heterogeneous populations ability to focus on individuals – in all their variation – and to explore what emerges from their interactions



- Agent-based chemical model does not have same restrictions as ODE models; any number and distribution of molecules can be modelled, spatial concerns can easily be accounted

- Clearer picture of what is actually occurring in the cell

2.4 ABM Framework: FLAME

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FLAME
FLexible Agent Modelling Framework

www.flame.ac.uk

Advantages Of FLAME

1. Multi-Scale & Flexible

- Efficient simulations with many millions of agents
- Can be executed on various platforms

2. X-machine Architecture

- Agents carry an internal memory
- Communication through Message Passing Interface (MPI)

3. Supports Parallelism

- Automatically parallelisable models
- Any model can be run in parallel without any modification

4. Round-Robin & Geometric Partitioning

Two partitioning methods available when run in parallel:

- RR - one agent at a time;
- GEO - based on a common attribute

2.5 Hybrid Modelling: SysMO (SUMO Consortium)

Modelling Regulation of Electron Transport Chain in E. coli

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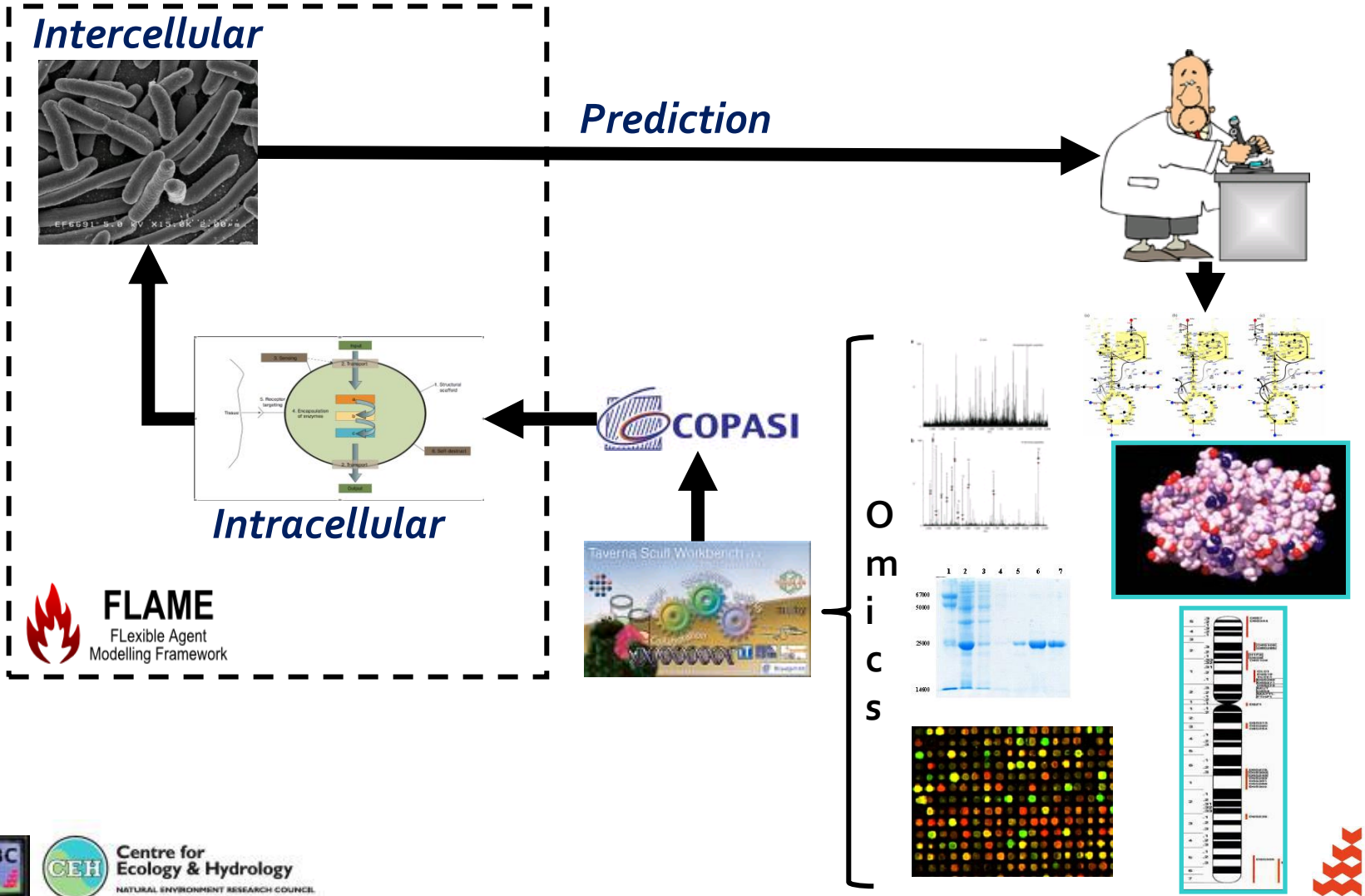

COPASI for SBML Generation

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A

```
<sbml>
  <model>
    <listOfCompartments>
      <compartment id="C1" name="Cytoplasm">
    </listOfCompartments>
    <listOfSpecies>
     <species id="M1" name="Glu"/>
     <species id="E1" name="hexokinase"/>
     ...
    </listOfSpecies>
   <listOfReactions>
     <reaction id="R1" name="reaction1">
       <listOfReactants>
        <speciesReference species="M1"/>
        ...
       </listOfReactants>
     <listOfProducts>
      <speciesReference species="M2"/>
      ...
    </listOfProducts>
    <listOfModifiers>
     <modifierSpeciesReference species="E1"/>
   </listOfModifiers>
    </reaction>
   ...
</sbml>
```

Qualitative SBML model

Parameterisation workflow

B

```
<sbml>
 <model>
  <listOfUnitDefinitions>
    ...
  </listOfUnitDefinitions>
   <listOfCompartments>...</listOfCompartments>
   <listOfSpecies>
    <species id="M1" name="Glu" initialConcentration="10"/>
    <species id="E1" name="hxk" initialConcentration="3"/>
    ...
   </listOfSpecies>
   <listOfReactions>
    <reaction id="R1" name="reaction1">
     <listOfReactants>...</listOfReactants>
     <listOfProducts>...</listOfProducts>
     <listOfModifiers>...</listOfModifiers>
    <kineticLaw>
     <math xmlns="http://www.w3.org/1998/Math/MathML">
      ...
     </math>
     <listOfParameters>
      <parameter id="k1" value="2"/>
      ...
     </listOfParameters>
    </kineticLaw>
    </reaction>
   ...
</sbml>
```

Parameterised SBML model

3.1 Standards: Technical Challenges

- **Support for hierarchical models (Lucian Smith)**
- **Support for dynamic structures (Chris Myers)**
- **What is appropriate for ABMS?**
- **Is an SBML extension for ABMs possible?**

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Collaboration

Biologists

Modellers

Different Domains

3.2 Standards: Sociological Challenges

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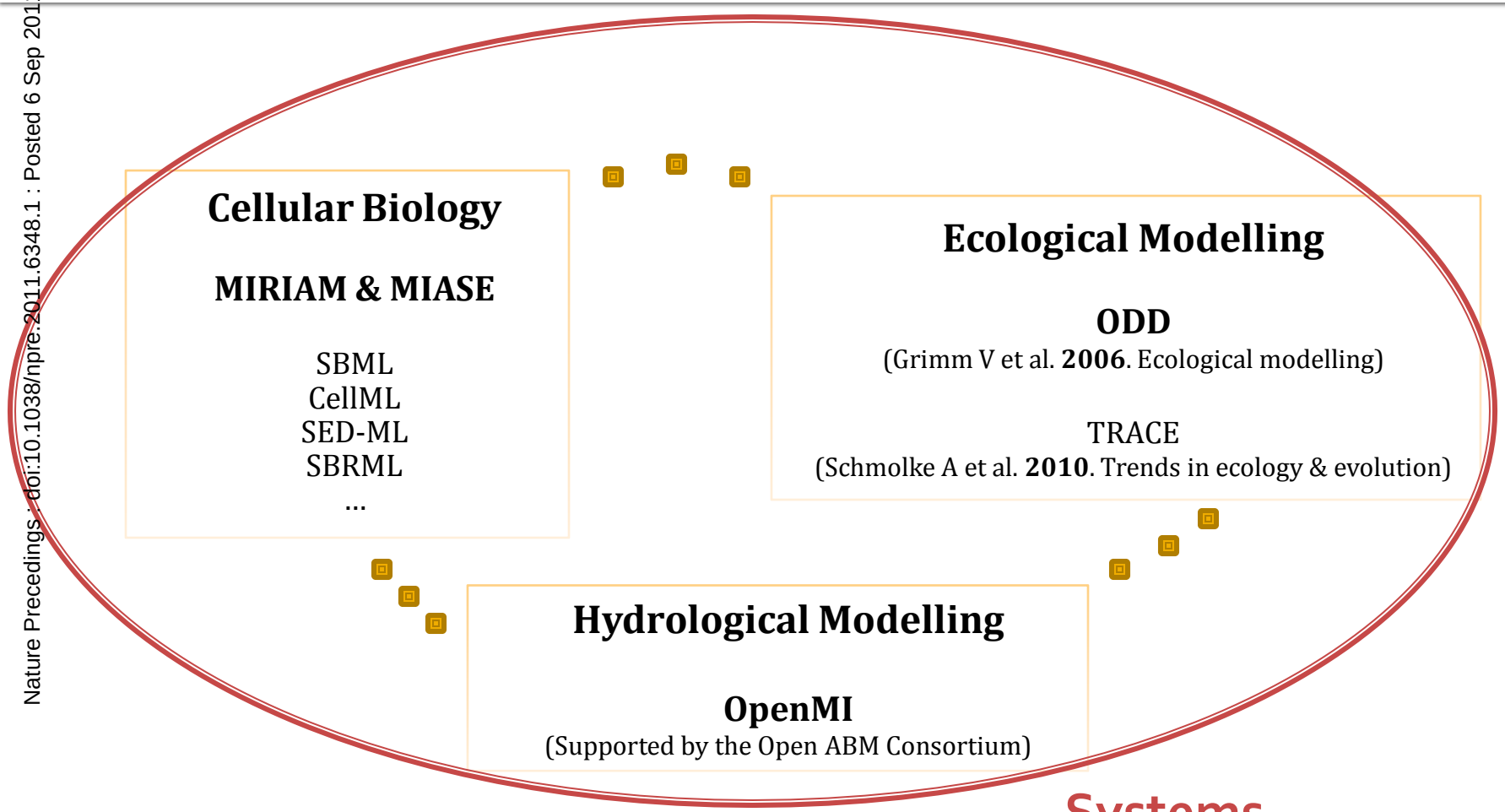

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3.2 Standards: Sociological Challenges

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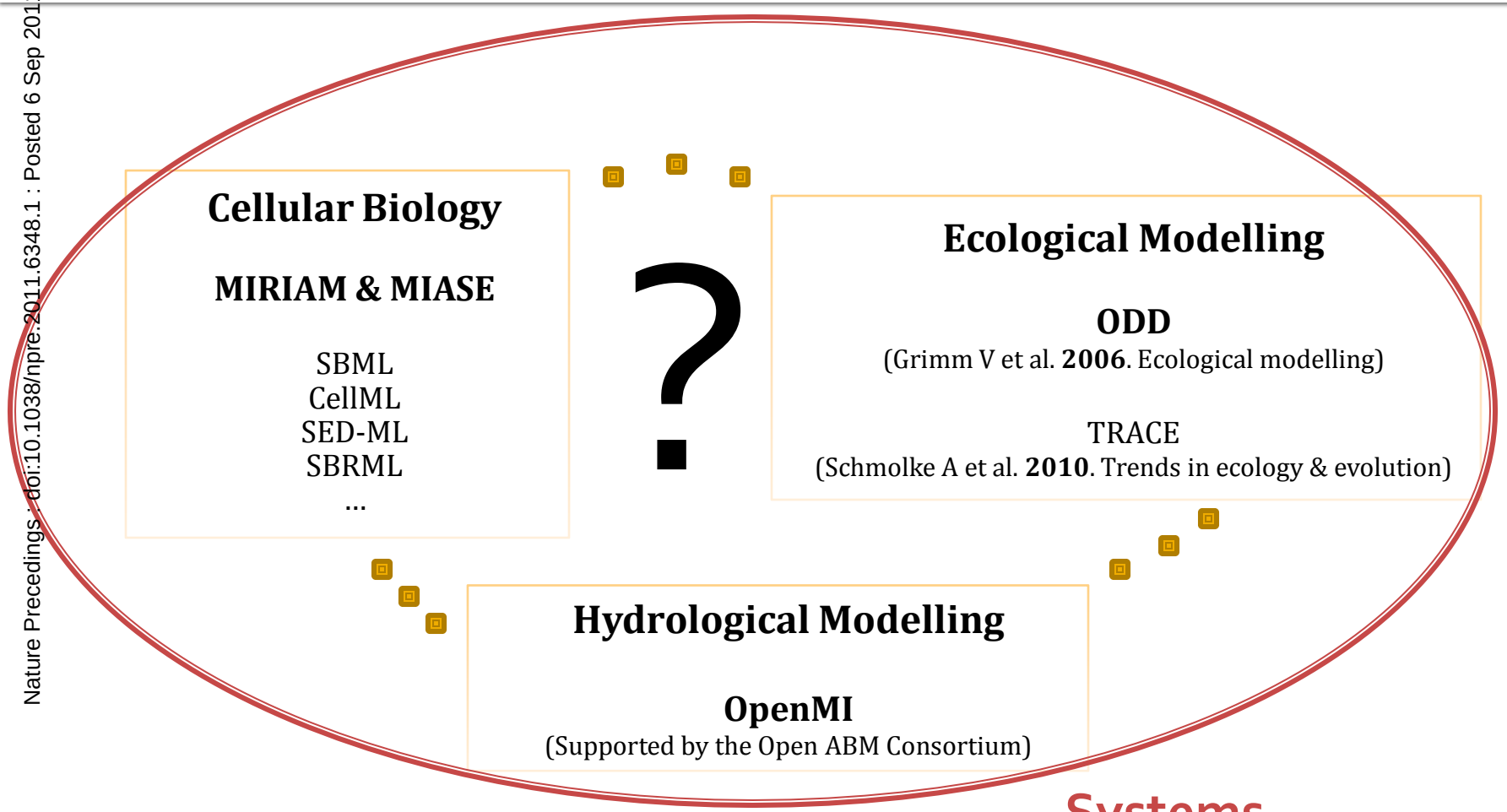

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Conclusive Remarks

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- Is the COMBINE Community willing to help us form a "Systems Biology" software bundle on Bio-Linux?
- How can we integrate Agent-Based Modelling into the wider community?
- How do we think about describing **"A Systems Biology Model"**?

Acknowledgements

- **NEBC Director**
  Professor Dawn Field

- **Lead Bio-Linux Developers**
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  Oliver Buckley
  Tim Booth

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  Dr. Enis Afgan (Emory University, Atlanta)

- **SysMO Consortium**
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  Professor Carol Coble

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