Modeling cell dynamics using graph rewriting

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Goal

- High-resolution simulation of cellular and molecular biology
  - If model is correct, point predictions may be more accurate than available in wetlab
  - Easier and cheaper to alter the model than in wetlab
Example: EGF Pathway

Exterior

Cytosol
Example: EGF Pathway
Example: EGF Pathway
Example: EGF Pathway
Example: EGF Pathway
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Signaling
Our Work

• New domain-specific language EasyCell for expressing cell dynamics
• Implemented by translating into a graph rewriting language, GrGen
GrGen

- Graph rewriting environment
- Requires .NET 2.0 or Mono 1.2.5+
  - (and java 1.5+)
- Open source

Biologists are not programmers
GrGen:

rule EGFBinding {
    a:EGF;
    b:EGFR;
    negative {
        a --> b1:EGFR;
    }
    negative {
        a1:EGF --> b;
    }
    modify {
        a --> b;
    }
}
GrGen:

rule EGFBinding {
    a: EGF;
    b: EGFR;
    negative {
        a --> b1: EGFR;
    }
    negative {
        a1: EGF --> b;
    }
    modify {
        a --> b;
    }
}

EasyCell:

binding EGF binds EGFR produces ActiveEGFR;
domain SH2;
domain SH3;
domain PS;

protein EGF;
protein EGFR;

protein GRB2 {
    domain SH2[2];
    domain SH3;
};

protein SOS;

binding EGF binds EGFR produces ActiveEGFR;

binding ActiveEGFR binds ActiveEGFR produces EGFRDimer;
generator
    EGFR in ActiveEGFR in EGFRDimer
    produces PS;

binding
    SH3 in GRB2
    binds PS in EGFR in ActiveEGFR in EGFRDimer
    produces EGFRGRB2;

binding
    (SH2,SH2) in gg:GRB2
    where sh:SH3 in gg and sh in EGFRGRB2
    bind SOS
    produces EGFRGRB2SOS;

environment {
    EGF[2];
    EGFR[2];
    GRB2[6];
    SOS[6];
};
Demo
Future work

- ‘Inhibits’ statement
- Preferential binding
- Parameterized rules
- Standard library
- Scalability