Applications of Rewriting Logic in Biology

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Course Plan

Session I: Background

- Rewriting Logic
- Maude

Session II: Simple Signaling Processes

- Biological processes -- informally
- Pathway Logic representation of signaling
 SmallKB a small network

Session III: Interactive Analysis

- Transformation to Petri nets
- The Pathway Logic Assistant

Session IV: Using the Pathway Logic Assistant

- Demo -- SmallKB live
- The Egf Stimulation Model
 - Curation
 - Demo

Lecture I: Outline

Logic

- Propositional Reasoning
- Equational Reasoning
- · ADTs
- Rewriting Logic

Maude http://maude.cs.uiuc.edu/

- Functional modules (Equational)
- System modules
- Search and model-checking
- Reflection

About Logic

Making description and reasoning precise

- Language
 - for describing things and/or properties
 - given by a signature and rules for generating additional elements (terms, formulas)
- Models--for interpreting to language elements
 - a mathematical structure
 - interpretation of terms
 - satisfaction of formulas: M |= wff
- Reasoning
 - rules for inferring what holds in all models

Propositional/Boolean Logic

- Language
 - Signature -- a set of propositions P,Q, ...
 - Formulas built from propositions using boolean constants and connectives (no terms)
 - true, false, P and Q, not P, ...
- Model-- A valuation of propositions
 - V : Prop -> {T,F}
 - Extended to formulas:
 - V(P and Q) = if (V(P) = T and V(Q) = T) then T else F
 - V |= wff if V(wff) = T
 - •
- Reasoning
 - simplest is truth table

Propositional/Boolean Logic II

• Basic truth table

Α	В	not(A)	A and B
Т	Т	F	Т
Т	F	F	F
F	Т	т	F
F	F	Т	F

Defined operators

•

- A or B := not(not(A) and not(B))
- A impl B := not(A) or B

Propositional/Boolean Logic: Example

- V: A,B,C -> T,T,F
 - V(A and B and not(C)) = T
- otherwise
- V(A and B and not(C)) = F

Note:

A and B and not(C) is equivalent to not(A and B impl C)

Proof: Compute truth table from the basic table

Α	В	С	(A and B)	not(C)	(A and B) and not(C)
Т	Т	Т	Т	F	F
Т	Т	F	Т	т	т
Т	F	Т	F	F	F
Т	F	F	F	т	F
F	т	Т	F	F	F
F	Т	F	F	т	F
F	F	т	F	F	F
F	F	F	F	Т	F

Example as a Boolean Circuit





Equational Logic: Language

Signature

- a set of operation symbols with arity, $o: O_n$
- a set of variable symbols, X
- Terms T
 x : X
 c : O₀
 f(t₁,...,t_n) for f : O_n and t₁,...,t_n : T

•Formulas -- $t_0 = t_1$

Equational Logic: Models

- M = < D, I >
 - D a set (of data)
 - $I : O_0 \rightarrow D$, $I : O_n \rightarrow (D^n \rightarrow D)$
 - V : X -> D variable assignment
 - Interpretation relative to a variable assignment
 I [V] (x) = V(x)
 - $I[V](f(t_1, ..., t_n)) = I(f)(I[V](t_1), ..., I[V](t_n))$
 - Satisfaction
 - $M \models t_0 = t_1 [V] \text{ if } I[V] (t_0) = I[V] (t_1)$

Equational Logic: Reasoning Rules

equivalence

•
$$t_0 = t_1 \mid -- t_1 = t_0$$

• $t_0 = t_1, t_1 = t_2 \mid -- t_0 = t_2$

congruence

•
$$t_1 = t_1' \dots t_n = t_n' | -- f(t_1, \dots, t_n) = f(t_1', \dots, t_n')$$

substitution

• † = †' |-- †[S] = †'[S]

Equational Theory

- ET = Equational Signature + Equational Axioms (E)
- M |= ET if M |= eq for eq : E
- t[E] -- the equivalence class of t wrt E
- Initial model < T/E, I/E>
 - no junk -- every element is denotation of a term
 - no confusion -- terms have equal denotations iff they are in the same equivalence class
 - proof by induction on term structure

Equational Theory: Peano Numbers

- Signature
 - Ops: $0: O_0, s: O_1, +, m: O_2$
 - Vars: x, y, ... : X
- Equations:
 - 1. x + 0 = 0
 - 2. x + s y = s(x + y)
 - 3. $0 \text{ m} \times = 0$

4.
$$s(x) = 0 = s(x)$$

5.
$$s(x) m s(y) = x m y$$

Calculating

 s s s 0 + s s 0
 = s(s s s 0 + s 0) --- 2[x := s s s 0, y := s 0]
 = s s (s s s 0 + 0) --- 2[x := s s s 0, y := 0]
 = s s s s s s 0 --- 1 congruence

ADTs (Abstract Data Types)

An ADT consists of one or more sets of values, together with a set of operations

(D1 ... Dk, c1 ... cm, f1 ... fn)

An initial model of an equational theory

- Values are given by constructors: c(t1,...,tl)
- Functions f1 .. fn are defined by mathematical relations (usually equations).

Equational Logic: Variations

 <u>Sorted EqL</u> -- Signature includes sorts (data types) and operation arity is sorted (+: Nat Nat -> Nat)

 <u>Order Sorted EqL</u> -- SortedEqL with a partial order on the sorts (Zero < Nat, NZNat < Nat)

• <u>Membership EqL</u> -- connected components of the sort partial order become Kinds, which can contain additional `error' elements. Terms are typed at the kind level.

Rewriting Logic

Q: What is rewriting logic?

A1: A logic for executable specification and analysis of software systems, that may be concurrent, distributed, or even mobile.

A2: A logic to specify other logics or languages

A3: An extension of equational logic with local rewrite rules to express

- 1. concurrent change over time
- 2. inference rules

Rewrite Theories

- Rewrite theory: (Signature, Labels, Rules)
- Signature: (Sorts, Ops, Eqns) -- an equational theory
 - Describe data types, system state
- Rules have the form label : t => t' if cond
- Rewriting operates modulo equations
 - Describes computations or deductions, also modulo equations

Deduction/Computation Rules



closed under



Rewriting Logic is Reflective

A reflective logic is a logic in which important aspects of its metatheory (entailment relation, theories, proofs) can be represented at the object level in a consistent way.

This has many applications:

- Transforming, combining rewrite theories
- Execution / proof strategies
- Meta tools: theorem provers, coherence checkers ...
- Language extensions: object-oriented, real-time, ...
- Higher-order capabilities in a first-order framework
- Model of reflection for concurrent objects
- Domain specific assistants

<u>Rewriting Logic as a</u> <u>Semantic Framework</u>

A wide variety of models of computation can be naturally expressed as rewrite theories

- Lambda Calculus, Turing Machines
- O Concurrent Objects and Actors
- CCS, CSP, pi-calculus, Petri Nets
- Chemical Abstract Machine, Unity
- Graph rewriting, Dataflow, Neural Networks
- Real-time Systems
- Physical Systems (Biological processes)

<u>Rewriting Logic as a</u> <u>Logical Framework</u>

A wide variety of logics have a natural representation as rewrite theories

- Equational logic
- Horn logic
- Linear logic
- Quantifiers
- Higher-order logics (HOL, NuPrl)
- Open Calculus of Constructions
- Rewriting logic

What Rewriting Logic Is/IsNot

- A rewrite theory plus a term describes a state transition system
 - states can have rich algebraic structure
 - transitions are local and possibly concurrent
- The equational part of a rewrite theory is similar to a term rewriting system (modulo ACI axioms)
 - it is usually desirable for equations to be CR and terminating
 - rewrite rules are often non-deterministic and non-terminating

Maude

- Maude is a language and environment based on rewriting logic
- See: http://maude.cs.uiuc.edu
- Features:
 - Executability -- position /rule/object fair rewriting
 - High performance engine --- {ACI} matching
 - Modularity and parameterization
 - Builtins -- booleans, number hierarchy, strings
 - Reflection -- using descent and ascent functions
 - Search and model-checking

Maude Formal Methodology



ADTs in Maude

ADTs are specified in Maude using functional modules

fmod <modname> is

<imports></imports>	<pre>*** reuse, modularity</pre>
<sorts></sorts>	<pre>*** data types and subtyping</pre>
<opdecls></opdecls>	*** names/and arities of operations
<eqns></eqns>	*** how to compute functions
endfm	

- The module components can appear interleaved and in any order
- The semantics of an fmod is an initial model
 - no junk---every data value is constructable
 - no confusion---two terms are equal only forced by the equations

Maude System Specifications

- A Maude specification has two parts
- An equational part describing structure and properties of system states (and ADT)
- A rules part specifying how the system might change over time.

Operator declarations

The <opdecls> part of a module consists of operator declarations having the form

op <opname> : <argSorts> -> <resultSort> [<attributes>] .

opname can be an identifier (without special characters) or identifiers interleave with `_'s (mixfix notation).

Including assoc declares the operator to b associative, ...

*** unary constructor op s_ : Nat -> Nat [ctor] . *** unary operator op sub1 : Nat -> Nat . *** associative commutative infix operator with identity op _+_ : Nat Nat -> Nat [assoc comm id: 0] .

The NAT and NATLIST Data Types

The natural numbers are specified by

```
fmod NAT is
        sorts Zero NzNat Nat .
        subsort Zero NzNat < Nat .</pre>
        op 0 : -> Zero [ctor].
        op s : Nat -> NzNat [ctor] .
            . . . .
      endfm
  Examples: 0, s s s 0 (also printed as 3)
Lists of natural numbers are specified by
     fmod NATLIST is
       pr NAT .
        sort NatList . subsort Nat < NatList .
       op nil : -> NatList .
       op : NatList NatList -> NatList [assoc id: nil] .
            . . . .
     endfm
Example lists: nil, 123
```

Defining NatList Functions I

Definition by pattern matching (extending NATLIST)

```
var n: Nat. var nl: NatList .
 op head : NatList ~> Nat .
 op tail : NatList -> NatList .
 eq head(n nl) = n.
 eq tail(n nl) = nl. eq tail(nil) = nil.
Consider the list : 1 2 3
It matches the pattern (n n1) with n := 1, n1 := 2 3
Maude> reduce head(1 2 3) . Maude> red tail(1 2 3) .
result NzNat: 1
                           result NatList: 2 3
Maude> red head(nil) . Maude> red tail(nil) .
result [Nat]: head(nil) result NatList: nil
```

<u>Defining NatList Functions II</u> <u>Definition by recursion</u>

Define a function `sum' that adds the elements of a NatList.

var n : Nat. var nl : NatList .
op sum : NatList -> Nat .
eq sum(nil) = 0 .
eq sum(n nl) = n + sum(nl) .

The equations are used to reduce terms to canonical form $sum(1 \ 2 \ 3) = 1 + sum(2 \ 3) = 1 + 2 + sum(3) = 1 + 2 + 3 = 6$

Maude> reduce sum(1 2 3) .
result NzNat: 6

<u>Defining NatList Functions III</u> <u>Conditional equations</u>

Define a function `isElt' that takes a Nat and a NatList and returns true if the Nat is in the NatList and false otherwise.

Examples: isElt(4, 4 6 3) = true isElt(4, 7 2 4 6) = isElt(4,2 4 6) isElt(4,nil) = false

Defining NatList Functions IV

Alternate definition of `isElt': via AC pattern matching

```
vars n : Nat . vars nl nl': NatList .
op isElt : Nat NatList -> Bool .
eq isElt(n, nl n nl') = true .
eq isElt(n, nl) = false [owise] .
```

Examples:

isElt(4, 7 2 4 6 3) matches the 1st equation
taking n := 4, nl := 7 2, nl' := 6 3
and so reduces to true

isElt(4, 7 2 3) does not match the 1st equation, so reduces to false by the [owise] equation

Using Maude

maude is an alias to the maude executable (maude.linux)

To try the NatList examples:

- 0 \$> cd <pathToExamples>MaudeExamples
- 0 \$> maude nat-list

<u>Caveats</u>

Caveats for writing Maude specifications:

- Don't forget the period at the end of a declaration or statement!
- Check keywords / symbols are correct.
 - correct use of fmod, mod
 - op vs ops
 - variables not used before bound
- Make sure all cases are covered in defining equations.

Specifying behavior/dynamics

System dynamics are specified in system modules using rewrite rules

mod <modname> is</modname>		
*** functional	part	
<imports></imports>	***	reuse, modularity
<sorts></sorts>	***	data types and subtyping
<opdecls></opdecls>	***	names/and arities of operations
<eqns></eqns>	***	how to compute functions

<rules></rules>		
endm		

A system module defines a set of computations (aka derivations) over the ADT specified by the functional part.

Rule declarations

The <rules> part of a system module consists of rule declarations having one of the forms

rl[<id>]: <lh>> => <rh>.

crl[<id>]: <lhs> => <rhs> if <cond> .

<la>, <ras>, <cond> are terms, possibly containing variables.

A rule applies to a term T if there is a substitution S (mapping variables to terms) such that S<lps> is a subterm of T (<lps> matches a subterm of T) and S <cond> rewrites to true.

In this case T can be rewritten by replacing the matched subterm by the matching instance of <rhs> (S <rhs>).

Rule application

Suppose we have the following rules (in a suitable module).

```
rl[fa2b]: f(a,x) => f(b,x).
rl[hh2h]: h h(y) => h(y).
```

then

```
g(c,f(a,d)) => g(c,f(b,d))
```

using [fa2b] and congruence

and

```
h h(g(c,f(a,d))) \implies h(g(c,f(b,d)))
```

also using replacement.

Before applying a rewrite rule, Maude reduces a term to canonical form using equations. The rule lhs is not reduced.

Petri Nets

Petri nets (Place-transition nets) are a formalism for modeling concurrent system behavior.

- Places represent properties or component features.
- System state is represented by marking of places (what properties hold or features are present)
- Transitions specify state change as transfer of marks from one place to another
- Petri nets have a natural graphical representation and a natural representation in Maude

A simple Petri net computation



Petri Net Example A vending machine



The vending machine in Maude

```
mod VENDING-MACHINE is
sorts Coin Item Place Marking .
subsorts Coin Item < Place < Marking .
op null : -> Marking . *** empty marking
ops $ q : -> Coin .
ops a c : -> Item .
op _ : Marking Marking -> Marking
                      [assoc comm id: null] . *** multiset
rl[buy-c]: $ => c .
rl[buy-a]: $ => a q .
rl[change]: q q q q => $ .
endm
```

What about AC Rewriting?

For terms constructed from operators that are declared with attributes such as assoc, comm and / or id, rule matching is extended to match AC terms to segments.

q M:Marking q matches a subterm of a q c \$ q q
with M:Marking := c \$
q M:Marking a M1:Marking matches a subterm of
\$ q c \$ q a
with M:Marking := c \$ q and M1:Marking := nil

Using the vending machine

```
What is one way to use 3 $s?
Maude> rew $ $ $ .
result Marking: q a c c
```

How can I get 2 apples with 3 \$s?

Maude> search \$ \$ =>! a a M:Marking .

```
Solution 1 (state 8)
M:Marking --> q q c
```

```
Solution 2 (state 9)
M:Marking --> q q q a
```

```
No more solutions.
states: 10 rewrites: 12)
```

Model checking

Algorithm for determining if $M \models P$ (M satisfies P) where M is a `model' and `P' is a property.

In our case a model is a Maude specification of a system together with a state of interest.

A property is a `temporal logic' formula to be interpreted as a property of computations of the system (linear sequences of states generated by application of rewrite rules).

Model checking

Temporal formulas are built from propositions about states, using boolean connectives, and temporal operators [] (always) and <> (eventually).

Satisfaction for $M \models A$ is axiomatized by equations

 $M \models P$ if $C \models P$ for every computation C of M

C |= A if the first state of C satisfies A

C |= [] P if every suffix of C satisfies P

C |= <>P if some suffix of C satisfies P

Model checking: Defining properties

```
mod MC-VENDING-MACHINE is
  inc VENDING-MACHINE . inc MODEL-CHECKER . inc NAT .
  op vm : Marking -> State [ctor] .
  op countPlace : Marking Place -> Nat .
  op value : Marking -> Nat . *** in units of quarters
  . . . .
  ops fiveQ lte4Q : \rightarrow Prop .
  ops nCakes nApples val : Nat -> Prop .
  eq vm(M) |= fiveQ = countPlace(M,q) == 5.
  eq vm(M) |= lte4Q = countPlace(M,q) <= 4.
  eq vm(M) = nApples(n) = countPlace(M,a) == n.
  eq vm(M) |= val(n) = value(M) == n.
endm
```

Model checking the vending machine I

Starting with 5 \$s, can we get 6 apples without accumulating more than 4 quarters? Model check the claim that we can't.

Maude>

```
red modelCheck(vm($ $ $ $ $),[]~(lte4Q U nApples(6))) .
result ModelCheckResult: counterexample(
```

```
{vm($ $ $ $ $ $),'buy-a}
{vm($ $ $ $ $ $ q a),'buy-a}
{vm($ $ $ $ q q a a),'buy-a}
{vm($ $ $ q q q a a a),'buy-a}
{vm($ $ q q q q a a a),'buy-a}
{vm($ $ a a a a),'change}
{vm($ $ a a a a a),'buy-a}
{vm($ q a a a a a), 'buy-a},
{vm($ q a a a a a a), deadlock})
```

A counterexample to a formula is a pair of transition lists representing an infinite compution which fails to satisfy the formula. A transition is a state and a rule identifier. The second list (deadlock) represents a loop.

Model checking the vending machine II

```
Starting with 5 $s, can we get 5 quarters then 6 apples?
```

```
Maude>
red modelCheck(vm($ $ $ $ $),
        []~(<>fiveQ /\ (fiveQ |-> nApples(6))) .
result ModelCheckResult: counterexample(...)
```

Is value conserved?
Maude> red modelCheck(vm(\$ \$ \$ \$ \$),[]val(20) .
result Bool: true

Extracting Paths from CounterExamples

A simple path from a given initial state SO, to a state satisfying a property P is a list of rules together with a state S1 satisfying P such that applying the rules starting with SO leads to S1.

One way to find a simple path is to model check the assertion that from SO no state can be reached satisfying P: modelCheck(SO, ~ <> P). If there is a reachable state satisfying P, a counterexample will be returned. The counterexample contains the list of rules applied.

Using findPath

The module SIMPLE defines a function findPath that extracts a simple path from a counterexample and a property.

```
mod FP-VENDING-MACHINE is
inc MC-VENDING-MACHINE .
inc SIMPLE .
endm
Maude> red findPath(vm($ $ $ $), nApples(5)) .
result SimplePath:
  spath(`buy-a `buy-a `buy-a `change `buy-a,
      vm(q a a a a a)) .
```

A Vending Machine Mall

To illustrate systems states with more structure, consider a `Mall' which contains possibly multiple vending machines, each vending a specific item. In addition the Mall contains `Goods', items purchased, and coins available to make purchases.

We add rules to put coins into machines and extract items purchased. The orginial vending machine rules are used to turn coins into items.

The Mall specification

```
mod VENDING-MALL is
  inc VENDING-MACHINE .
  sorts Machine Goods Mall .
  subsort Machine Goods < Mall .
  op mt : \rightarrow Mall .
  op : Mall Mall -> Mall [ctor assoc comm id: mt] .
  op m : Item Marking -> Machine [ctor] .
  op g : Place -> Goods [ctor] .
  var M : Marking . var C : Coin . var I : Item .
  rl [coin-in] : m(I, M) q(C) \Rightarrow m(I, M C).
  rl [apple-out] : m(a, M a) \Rightarrow m(a, M) q(a).
  rl [cake-out] : m(c, M c) \Rightarrow m(c, M) q(c).
endm
```

Shopping in the Mall

Consider an initial state with an two vending machines, one for apples, one for cakes, and 4 \$s.

Default shopping yields 2 apples.

```
Maude> rew m(a,null) m(c,null) g($) g($) g($) g($) .
result Mall: g(a) g(a) m(a, q q c c) m(c, null)
```

Can I get 4 apples and a cake?

```
Maude> search m(a,null) m(c,null) g($) g($) g($) g($) =>! X:Mall g(a) g(a) g(a) g(a) g(c) . No solution.
```

But I can get 4 apples and 4 guarters stuck in the machine!

```
search m(a,null) m(c,null) g($) g($) g($) g($)
=>! m(a, q q q q) X:Mall .
Solution 1 (state 725)
X:Mall --> g(a) g(a) g(a) m(c, null)
```

Reflection: Meta-representation of terms

- A constant is meta-represented by a quoted identifier (qid) where the identifier is its name dotted with the name of its (least) sort.
 - `\$.coin meta-represents the term \$
 - `a.Item meta-represents the term a
- A variable is meta-represented by a qid containing its name and the name of its sort separated by :
- `M:Marking meta-represents the variable M:Marking
 The meta-representation of a composite term has the form op[t1,...,tk] where op is a qid nameing the operator
 - '__['q.Coin, 'q.Coin, 'q.Coin] is the metarepresentation of q q q q.

Reflection: Ascent/Descent functions

 \cdot upTerm(a) = `a.Item the meta-representation of a term

•upRls(modname,bool)

 the set of rules (meta-represented) in the module with name modname (and its imports if bool is true)

- metaReduce(module, term) = {term', type} = res
- metaXapply(module,term,rid,subst,start,bound,n)
 - = res = {term',type,subst',context}
 - start, bound bound the search for a match
 - n is the solution number

•getTerm(res) = term'

Reflection example: Module analysis

```
fmod CONSUMERS is
  inc MY-META .
 var M : Module . var T : Term .
 var R : Rule . var RS : RuleSet .
  op consumes : Module Rule Term -> Bool .
                                  *** assumes M defines 'has
  eq consumes (M, R, T) =
      getTerm(metaReduce(M, 'has[getLhs(R),T]))
        == 'true.Bool .
  op consumerRules : Module Term -> QidSet .
  op consumerRules : Module RuleSet Term -> QidSet .
  eq consumerRules (M,T) =
       consumerRules (M, upRls (getName (M), true), T) .
  eq consumerRules (M, none, T) = none.
  eq consumerRules(M,R RS,T) =
   (if consumes(M,R,T) then getRuleId(R) else none fi);
       consumerRules(M,RS,T) .
endfm
```

Reflection Example: Module analysis cntd.

```
mod VEND-X is
    inc VENDING-MACHINE .
```

vars M0 M1 : Marking .
op has : Marking Marking -> Bool .

```
eq has(M0 M1, M1) = true .
eq has(M0, M1) = false [owise] .
endm
```

select CONSUMERS .

Maude> red consumerRules(['VEND-X],'\$.Coin) .
result: QidSet 'buy-a ; buy-c

```
Maude> red consumerRules(['VEND-X],'q.Coin) .
result: Qid 'change
```

Reflection example: Strategy

```
fmod METAREWRITE-LIST is
  inc MY-META .
 var M : Module . vars T T': Term .
 var res : Result4Tuple? .
  var rid : Qid . var ql : QidList .
  op metaRewList : Module QidList Term -> Term .
  eq metaRewList(M,nil,T) = T .
  ceq metaRewList(M,rid ql,T) = metaRewList(M,ql,T')
    if res := metaXapply(M,T,rid,none,0,unbounded,0)
    /  T' := if res :: Result4Tuple
             then getTerm(res)
             else T fi .
endfm
```

Reflection example: Strategy cntd.

result GroundTerm: '___['q.Coin,'a.Item]

result Constant: '\$.Coin

Maude Exercises

The folder MaudeExamples contains the code for all the examples.

See README.txt for a summary of the file contents

See exercises.txt for instructions