# PROGRAMS = DATA = FIRST-CLASS CITIZENS IN A COMPUTATIONAL WORLD

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IMDEA and UCM Madrid (March 2012)

Sources:

- Conference CS2BIO Computer Science to Biology (ENTCS proceedings June 2010)
- Journal Scientific Annals of Computer Science (2011, Vol. XXI)
- Festschrift for Carolyn Talcott (November 2011, Springer Festschrift Series, LNCS vol. 7000)
- Article accepted to appear in Philosophical Transactions A of the Royal Society

## ALAN TURING STARTED THE BALL ROLLING (IN 1936)

1. A convincing analysis of the nature of computation
2. A very early model of computation (MOC)
3. The first programmers' manual
4. Undecidability of the halting problem
5. Universal Turing machine (a self-interpreter)
6. Contributor to the "Confluence of ideas'": that

   all sensible models of computation are equivalent, e.g.,

   - Turing machine
   - Lambda calculus
   - Recursive function definitions
   - String rewrite systems

## 75 YEARS OF MODELS OF COMPUTATION (just a few)

| | |
|---|---|
| Lambda calculus | Church 1936 |
| Turing machine | 1936 |
| von Neumann architecture | 1945 |
| Finite automata | Rabin and Scott |
| Counter machine | Lambek and Minsky |
| Random access machine (RAM) | Cook and Reckhow |
| Random access stored program (RASP) | Elgot and Robinson |
| Cellular automaton, LIFE,.. | von Neumann, Conway, Wolfram |
| Abstract state machine | Gurevich et al |
| Text register machine | Moss |
| Blob model | 2010 |

## ABOUT MOCS (MODELS OF COMPUTATION)

### Criteria

- How to compare
- How to improve
- Lacks, failings, inconveniences
- What are they suitable for?

  Programming? Theorem proving ? Modeling ? . . .

### New direction: biological computing

- Enormous potential (price, concurrency, automation, . . . )
- Many as-yet-unclear concepts
- Modeling versus(?) programming

## SOME DIMENSIONS OF OF MOCS

- "Reasonable" machines? (van Emde Boas, Ugo dal Lago)

  PTIME **is the same** on Turing machine and $\lambda$-calculus
- General problem-solving?
- Programmability
- Binding times
- Finiteness and uniformity
- Turing completeness
- Universal machine / self-interpreter

**The Blob MOC:**

- Originally motivated by biological computing.
- a different set of dimensions; may give some insight.

## A RECENT VISIT TO STANFORD RESEARCH INSTITUTE

SRI is doing quality work to model biological systems using Maude, a term rewriting system implementation.

My reaction after a 2 month visit: where are the programs?

- ▶ Many, at the simulation level, i.e., Maude programs.
- ▶ But I could see $\boxed{\text{no programs at the biological level}}$.

A difference in perspective:

- ▶ Natural science is analytic: how does nature really work?
- ▶ Computer science is synthetic: build programmable systems.

This research project:

design a biology-like computing model with programs.

## TWO DIFFERENT MEANINGS OF THE WORD "MODEL"

1. Analytic viewpoint common to the natural sciences: a "model" describes an already-existing reality.

   A good model describes the real world well, e.g., is usable to predict the outcome of not-yet-performed experiments.

2. Synthetic viewpoint in computer science or engineering ("model checking"). Given a problem specification, build a computer program or a hardware device to solve it.

   A good model satisfies the problem specification.

Context:

- The "confluence of ideas" had analytic overtones, suggesting that computability is a natural phenomenon.
- Turing's work (machine design, programming) was synthetic.

## CONNECTIONS EXIST BETWEEN BIOLOGY AND COMPUTATION

**Turing completeness results for biomolecular computation:**

- **Cardelli, Chapman, Danos, Reif, Shapiro, Wolfram,. . .**
- **Net effect: any computable function can be computed, in some sense, by various biological mechanisms.**
- **Not completely compelling from a programming perspective.**

  **(Gödel numbers, 2-counter machine simulation, . . . )**
- **Our aim: a computation model where**
  - **“program” is clearly visible and natural, and**
  - **Turing completeness is not artificial or accidental or horribly inefficient, but a natural part of biomolecular computation**

## OUR PROPOSAL

A model of computation that is

- ▶ biochemically plausible: semantics by chemical-like reaction rules;
- ▶ programmable (a bit like low-level computer machine code);
- ▶ uniform: new "hardware" not needed to solve new problems;
- ▶ stored-program: programs = data;

  programs are executable and compilable and interpretable
- ▶ universal: all computable functions can be computed
- ▶ Turing complete in a strong sense: $\exists$ a universal algorithm

  (able to execute any program, asymptotically efficient)

## SETTING THE CONTEXT

Does it make sense to have

$\boxed{\text{program execution in a biological context}}$ ?

Evidence for “yes”: program-like behavior, e.g.,

▶ genes that direct protein fabrication

▶ “switching on” and “switching off”

▶ reproduction, . . .

There are many not-yet-well understood analogies to the world of programs.

## WHERE ARE THE PROGRAMS?

**In existing models of biomolecular computation**

**it's hard to see anything like a program that realises or directs a computational process.**

- **Many examples: given a problem, the researchers cleverly devise a biomolecular system that can solve this particular problem**
- **The algorithm being implemented is hidden in the details of the system's construction, hard to see.**

**Our purpose is to fill this gap,**

- **to establish a biologically feasible framework in which**
- **programs are first-class citizens.**

## OTHER COMPUTATIONAL FRAMEWORKS

**Circuits, BDDs, finite automata:** Nonuniform, Turing incomplete!

**Turing machine:**

- Pro Visible program; complete; universal machine exists
- Con Asymptotically slow: universal machine takes time $O(n^2)$ to simulate a program running in time $O(n)$

**Other program-based models:** Post, Minsky, LISP, RAM, RASP...

Complex, biologically implausible

**Cellular automata:** von Neumann, LIFE, Wolfram,...

- Pro: Can simulate a Turing machine
- Con: Complex, biologically implausible (synchronisation!)
- Program = start cell pattern? global transition function?
- There seems to be no natural universal cellular automaton.

## PROGRAM EXECUTION IN GENERAL

Natural question: “can” program execution take place?

What is a program ? Roughly . . .

- A set of instructions
- that specify a series (or set) of actions
- Actions are carried out when the instructions are executed (activated. . . )

In stored-program computation models (e.g., von Neumann)

- A program is a concrete object (a form of data)
- that can be replaced to specify different actions.

Thus the program is software and not hardware

## “DIRECT” PROGRAM EXECUTION

**Write $[\![\texttt{program}]\!]$ for the meaning or net effect of running `program`:**

$$[\![\texttt{program}]\!](\texttt{data}_{in}) = \texttt{data}_{out}$$

- `program` **is an active agent.**
- **It is activated (run) by applying the semantic function $[\![\_]\!]$.**
- **Some mechanism is needed to execute `program`, i.e., to apply $[\![\_]\!]$ to `program` and $\texttt{data}_{in}$ :**

  **hardware (“wetware”?).**

**The task of programming is, given a desired semantic meaning, to devise a program that computes it.**

## THE BIOLOGICAL WORLD IS NOT HARDWARE!

We must re-examine programming language assumptions. Computers have programmer-friendly conveniences, e.g.,

- A large address space of randomly accessible data
- Pointers to data, perhaps at a great "distance" from the current program or data
- address arithmetic, index registers,. . .
- Unbounded fan-in: many pointers to the same data item

None of these is biologically plausible!

Workarounds are needed

if we want to do biological programming.

## FOR BIOCHEMICAL PLAUSIBILITY

- $\boxed{\text{There is no action at a distance}}$ **all effects achieved via chains of local interactions.** `Biological analog:` **signaling.**

- $\boxed{\text{There are no pointers to data}}$ **(addresses, links, list pointers): To be acted on, a data value must be physically adjacent to an actuator.** `Biological analog:` **chemical bond between program and data.**

- $\boxed{\text{There is no nonlocal control transfer}}$**, e.g., unbounded GOTOs or remote procedure calls.** `Biological analog:` **a bond from one part of a program to another.**

- $\boxed{\text{A “yes”}}$ **$\exists$ available resources to tap, i.e., energy to change the program control point, or to add data bonds.**

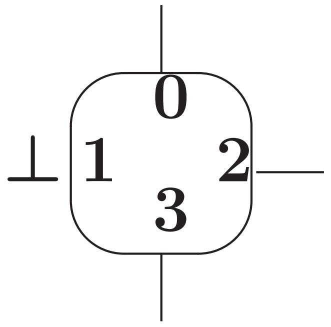
  `Biological analogs:` **ATP, oxygen, Brownian movement.**

## THE BLOB MODEL

Simplified view of a molecule and chemical interactions (Cardelli, Danos, Lanève,...).

Blobs are in a biological "soup" and are connected by symmetrical bonds linking their bond sites.

Picture of a blob: (Bond sites $0, 2$ and $3$ are bound, and $1$ is unbound)



A blob has 4 bond sites and 8 cargo bits (boolean values).

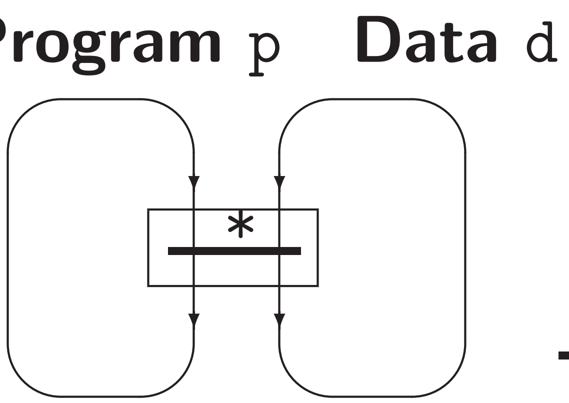
Here: Bond sites $0, 2$ and $3$ are bound, and $1$ is unbound. (Cargo bits not shown)

## KEEPING THE FOCUS

**How to structure a biologically feasible model of computation?**

- **Idea: keep current program cursor and data cursor always close to a focus point where all actions occur.**
- **How? Continually shift both program and data, to keep the active bits near the focus.**

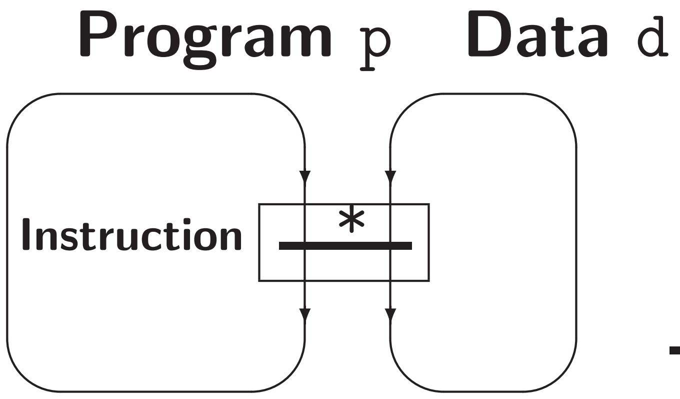
Running program $\mathtt{p}$: computing $[\![\mathtt{p}]\!](\mathtt{d})$



$\square$ = **Focus point for control and data** (connects the PC and the DC)

$\overset{*}{\overline{\phantom{xx}}}$ = **program-to-data bond: "the bug"**

## WHAT HAPPENS AT THE PROGRAM-TO-DATA BOND ?



$\square$ = Focus point for control and data
(connects the PC and the DC)

$\overset{*}{\rule{2em}{1pt}}$ = program-to-data bond

An instruction can . . .

- Move the data cursor along bond 1 (or bond 2 or 3)
- Branch: is data cursor's bond 1 empty or not ? (or 2 or 3)
- Branch: is data cargo bit $i = 1$ or 0 ? $(i = 1, 2, \ldots, 7)$
- Insert a new blob at bond 1 (or 2 or 3)
- Swap: interchange some bonds
- Fan-in: merge control from two predecessor instructions

## A MOVIE IS WORTH DURATION$\times$FRAMERATE$\times$1000 WORDS

**(Circle.avi)**

## PROGRAM BLOBS AND DATA BLOBS

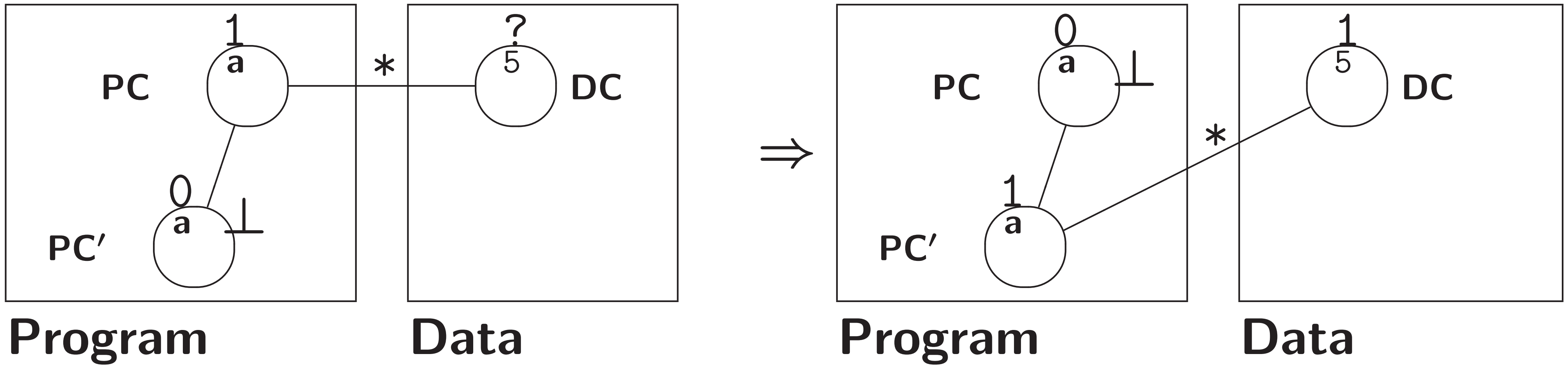
- A program $p$ is (by definition) a connected assembly of blobs.

- The data space is (also) a connected assembly of blobs.

At any moment during execution, i.e., computation of $[\![p]\!](d)$:

- The program cursor (PC) is in $p$.
- The data cursor (DC) is in $d$.
- There is a bond $*$ ("the bug") between the PC and the DC, at bond sites $0$.

## EXAMPLE INSTRUCTION: SCG 1 5 (SET CARGO BIT 5 TO 1)



- ▶ "The bug" $\overset{*}{—}$ has moved:
  - before execution, it connected PC with DC.
  - After: it connects successor PC′ with DC.
- ▶ Control: activation bits 0, 1 have been swapped.

**Instruction syntax:** the 8-bit string 11001101 is grouped as

$$\overbrace{1}^{a}\ \overbrace{100}^{SCG}\ \overbrace{1}^{v}\ \overbrace{101}^{c}$$

## MORE ABOUT INSTRUCTIONS: (one per blob)

**Instruction form:** (8 control bits and 4 bonds)

```
        opcode parameters (bond0, bond1, bond2, bond3)
```

**Why exactly 4 bonds?**

- Predecessor (1 bond); true and false successors (2 bonds);
- 1 bond to link the program cursor and the data cursor.

**It's almost a von Neumann machine code, but. . .**

- A bond is a two-way link between two adjacent blobs.
- A bond is not an address.
- There is no address space as in conventional computer (and hence: no address decoding hardware).
- Also: no registers (though cargo bits can be used).

## INSTRUCTIONS HAVE 8 BITS

| Instruction | Description | Informal semantics (write :=: for a two-way interchange) |
|---|---|---|
| `SCG v c` | Set CarGo bit | DC.c := v; PC := PC.2 |
| `JCG c` | Jump CarGo bit | if DC.c = 0 then PC := PC.3 else PC := PC.2 |
| `JB b` | Jump Bond | if DC.b = ⊥ then PC := PC.3 else PC := PC.2 |
| `CHD b` | CHange Data | DC := DC.b; PC := PC.2 |
| `INS b1 b2` | INSert new bond | DC-new.b2 :=: DC.b1; DC-new.b1 :=: DC.b1.bs; |
| | — | PC := PC.2 |
| `SBS b1 b2` | SWap Bond Sites | DC.b1 :=: DC.b2; PC := PC.2 |
| `SWL b1 b2` | SWap Links | DC.b1 :=: DC.b2.b1; PC := PC.2 |
| `SWP3 b1 b2` | Swap bs3 on linked | DC.b1.3 :=: DC.b2.3; PC := PC.2 |
| `FIN` | Fan IN | PC := PC.2 (two predecessors: bond sites 1 and 3) |
| `EXT` | EXiT program | |

| | |
|---|---|
| `SCG,...,EXT`: | Operation codes |
| `b, b1, b2`: | Bond site numbers |
| `c`: | Cargo site number |
| `v`: | A one-bit value |

## TURING COMPLETENESS as by Cardelli, Zavattaro,. . .

**Language $M$ is as powerful as $L$ (write $L \leq M$) if**

$$\forall p \in L\text{−programs } \exists q \in M\text{−programs } ( \, [\![p]\!]^L = [\![q]\!]^M \, )$$

$L$ and $M$ are languages (biological, programming, whatever).

**Aim: show that an interesting $M$ is Turing complete.**

One way: reduce an already Turing complete language , e.g.,

- ▶ $L =$ two-counter machines 2CM. very, very slow!
- ▶ $M =$ a biomolecular system of the sort being studied.
- ▶ The technical trick: show how to construct
  - from any 2CM program,
  - a biomolecular $M$-system that simulates the given 2CM.

## ANOTHER WAY: SIMULATION BY INTERPRETATION

Turing completeness is usually shown by simulation, e.,g.,

- for any 2CM program you build a biomolecular system . . .

But: the biomolecular system is usually built by hand. The effect: hand computation of the ∃ quantifier in

$$\forall p \; \exists q \; (\llbracket p \rrbracket^{L} = \llbracket q \rrbracket^{M})$$

In contrast, Turing's original "Universal machine" (UM) works by interpretation, where ∃ is realised by machine.

- The UM can execute any TM program, if coded on the UM's tape along with its input data.
- Our research follows Turing's line, in a biological context:

  It does simulation by general interpretation, and not by one-problem-at-a-time constructions.

## PROGRAM EXECUTION BY INTERPRETATION

- $$[\![\mathtt{interpreter}]\!](\mathtt{program}, \mathtt{data}_{in}) = \mathtt{data}_{out}$$

- **Now `program` is a passive data object: both `program` and $\mathtt{data}_{in}$ are data for the interpreter.**

- **`program` is now executed by running the interpreter program.**

  **(Of course, some mechanism will be needed to run the interpreter, e.g., hard-, soft- or wetware.)**

- **Self-interpretation is possible, and useful in practice.**

- **Turing's original "Universal machine" was a self-interpreter.**

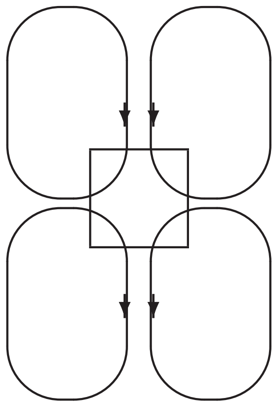
## A “BLOB UNIVERSAL MACHINE”

**We have programmed a self-interpreter for the blob formalism – analogous to Turing’s original universal machine.**

**This gives: Turing-completeness in a new biological framework.**

## SELF-INTERPRETATION IN THE BLOB WORLD

**Interpreter and its data**



**Program $p$ Data $d$**

**Picture of the computation: $[\![\texttt{interpreter}]\!](\boldsymbol{p}, \boldsymbol{d})$**

**The interpreted program $p$ and its data $d$ are both data for** `interpreter`**.**

## A "BLOB UNIVERSAL MACHINE"

We have developed a self-interpreter for the blob formalism – analogous to Turing's original universal machine.

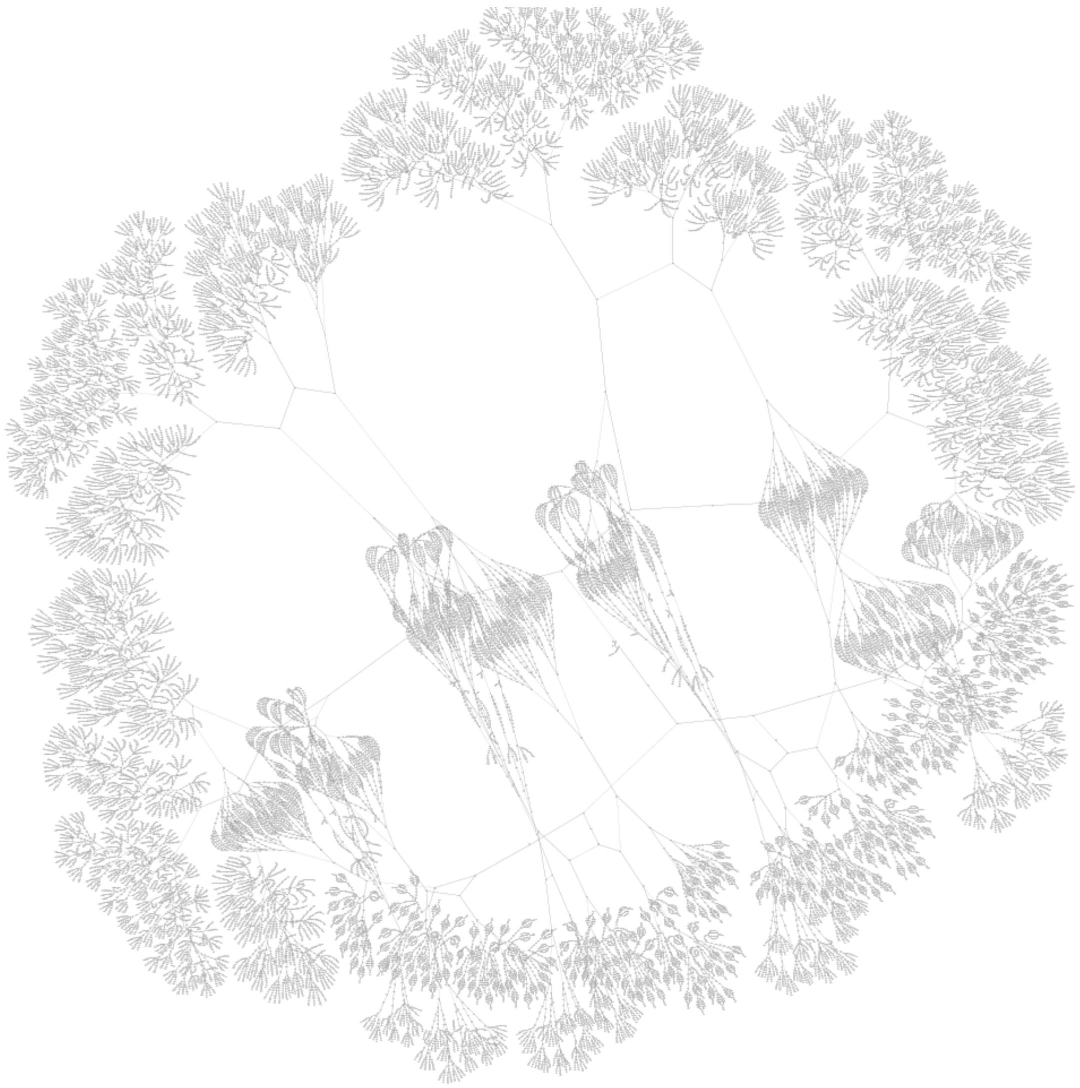
This gives: Turing-completeness in a new biological framework.
Blob programs do not have to be encoded!

Self-interpretation without asymptotic slowdown.
The blob data model (4 bond sites per bob) gives more efficient self-interpretation than Turing's original universal machine.

Overcomes a limitation built-in to the Turing model, namely asymptotic slowdown. The technical reason:

The time to interpret one blob instruction
is bounded by a constant $c$
(that may depend on the program being interpreted)

## BIRDS-EYE VIEW OF THE SELF-INTERPRETER



(Not shown: Each ’finger’ along the periphery has a connection to the main control in the center)

## SOME DESIRABLE PROPERTIES OF A MOC

- **Existence of programs; and general problem solving: a natural path from an informal algorithm to an MOC program.**
- **Turing completeness.**
- **Uniformity and strong finiteness: one set of hardware is enough for all problems.**
- **Physical realizability, e.g., execution possible without action at a distance, e.g., data pointers.**
- **Programs as data objects: Readability for universal machine. Writeability for program generation, e.g., a compiler.**
- **Plausible program running times, e.g., polynomially related to programming languages, e.g., $\lambda$-calculus.**

## A BIT MORE ON FINITENESS AND UNIFORMITY

- **Uniformity: one set of hardware is enough for all problems.**
  - **Classic example: the universal Turing machine**
  - **Non-example: the von Neumann architecture (maybe big, but it is finite!)**
- **Applied to programs, uniformity implies strong finiteness: only an a priori fixed number of possible instructions.**

  **The blob MOC is strongly finite: one fixed set of instructions can compute any computable function.**
- **(This looks unlikely – what about unbounded number of control states, or instruction labels?)**

  **Well. . . we showed how to blob-simulate an arbitrary Turing machine on the architecture, using "fan-in" to implement control transfers.**

## CONTRIBUTIONS OF THIS WORK

- Programmable bio-level computation where programs = data.
- Blob semantics by abstract biochemical reaction rules.
- All computable functions are blob-computable:
  - This can be done with one fixed instruction set (i.e., a “machine language”)
  - We don’t need new rule sets (biochemical architectures) to solve new problems; it’s enough to write new programs.
- (Uniform) Turing-completeness
- Interpreters and compilers make sense at biological level, may give useful operational and utilitarian tools.

## WHAT SEEMS JUST AROUND THE CORNER

- Programs are currently similar to classical machine code; this requires (too much) programmer skill. Possible solutions:
  - Devise an intermediate-level blob programming language.
  - Describe/constrain program behavior, data structures by static program analysis; or a type system.
  - Program activation should be possible: once a program is generated, start executing it. Needs "stored program" model (as in von Neumann architecture or RASP).
- Still to analyse: Time or energy to perform a single program step (may depend on program/data). An appropriate and realistic cost model, including code motion, should be found.
- Concurrency (programs perhaps generated dynamically by one master program, analogous to biological reproduction.)

## WHAT HAS NOT YET BEEN DONE

- Promise of tighter analogy between universality and self-reproduction.
- A usable higher-level programming language
- Find a true, biological (not just “plausible”) implementation of the fixed set of reduction rules in vitro.
- Computational complexity, e.g., limitations imposed by a 3-dimensional blob-space.

## References

[1] Leonard M. Adleman. On constructing a molecular computer. In DIMACS, AMS, pages 1–21, 1996.

[2] Luca Cardelli and G. Zavattaro. Turing universality of the biochemical ground form. MSCS, 19, 2009.

[3] Paul Chapman. Life universal computer. http://www.igblan.free-online.co.uk/igblan/ca/, 2002.

[4] V. Danos, J. Feret, W. Fontana, and J. Krivine. Abstract interpretation of cellular signalling networks. Volume 4905 of VMCAI, Lecture Notes in Computer Science, pages 83–97, October 1970.

[5] Vincent Danos and Cosimo Laneve. Formal molecular biology. TCS, 325:69 – 110, 2004.

[6] Martin Gardner. Mathematical recreations. Scientific American, October 1970.

[7] Masami Hagiya. Designing chemical and biological systems. New Generation Comput., 26(3):295, 2008.

[8] L. Kari and G. Rozenberg. The many facets of natural computing. Commun. ACM, 51(10):72–83, 2008.

[9] Ehud Shapiro. Mechanical Turing machine: Blueprint for a biomolecular computer, Weizmann, 1999.

[10] Ehud Shapiro and Y Benenson. Bringing DNA computers to life. Scientific American, 294:44–51, 2006.

[11] Carolyn Talcott. Pathway logic. Volume 5016 of SFM, LNCS, pages 21–53, 2008.

[12] John von Neumann and A.W. Burks. Theory of Self-Reproducing Automata. Univ. Illinois Press, 1966.

[13] Erik Winfree. Toward molecular programming with DNA. SIGOPS Oper. Syst. Rev., 42(2):1–1, 2008.

[14] Stephen Wolfram. A New Kind of Science. 2002.

## THANK YOU!

**Questions?**