Compilers Without Borders
Repurposing Paper, Plastic, and Household Devices as Computational Substrates

Bill Thies

Joint work with Saman Amarasinghe, Vaishnavi Ananthanarayanan, Andrew Cross, Shubhranshu Choudhary, Ed Cutrell, Krittika D'Silva, Nakull Gupta, Swati Ittan, Meghana Marathe, Jacki O'Neill, Paromita Pain, Gaurav Paruthi, Todd Thorsen, J.P. Urbanski, & Aditya Vashistha

Microsoft®
Research

StreamIt: A Language and Compiler for Streaming Applications

- **Key idea:** design language that enables static analysis
  - To improve programmer productivity
  - To enable automatic parallelization

- Project contributions:
  - Language design for streaming [CC'02, CAN'02, PPoPP'05, IJPP'05]
  - Automatic parallelization [ASPLOS'02, G.Hardware'05, ASPLOS'06, MIT'10]
  - Domain-specific optimizations [PLDI'03, CASES'05, MM'08]
  - Cache-aware scheduling [LCTES'03, LCTES'05]
  - Extracting streams from legacy code [MICRO'07]
  - User + application studies [PLDI'05, P-PHEC'05, IPDPS'06, PACT'10]

I hate it when my house is so big,
I need two wireless routers.

Microsoft Research India

Microsoft Research India

Photo: Natalie Linnell (courtesy Kentaro Toyama)

CGNet Swara:
A Voice Portal for Citizen Reporting

Photo: Purushottam Singh Thakur

No handpump in Baiga adivasi village of 25 families, Pls call officers to help...

▶ ⬤━━ 2:43 🔊 ⬤
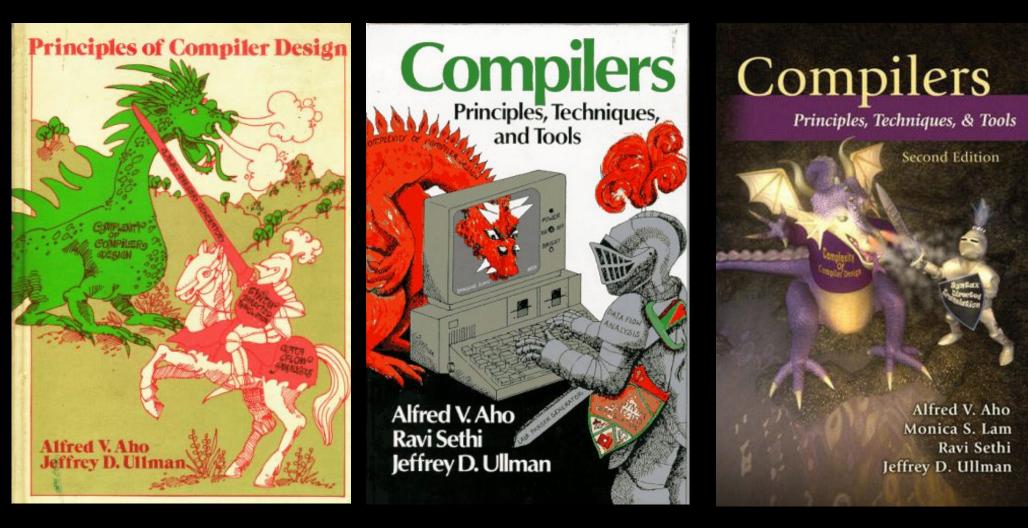
Naresh Bunkar is visiting Tikarapara mohalla in Mahuamancha village, Bijarakachhar panchayat Lormi block Mungeli district in Chhattisgarh where adivasi women tell him there is no hand pump in their village of 25 Baiga families. They fetch water from river 1.5 km away. People fall ill due to dirty water. Health center is 15 km away . They complained to officials many times but no one listens. Pls call P.H.E officer@8878832200 and collector@9425280067. Naresh Bunkar@8720822286

What are the Skills of Programming Language and Compiler Writers?
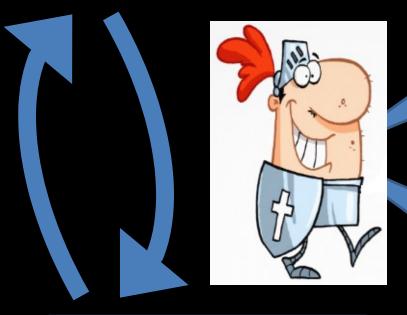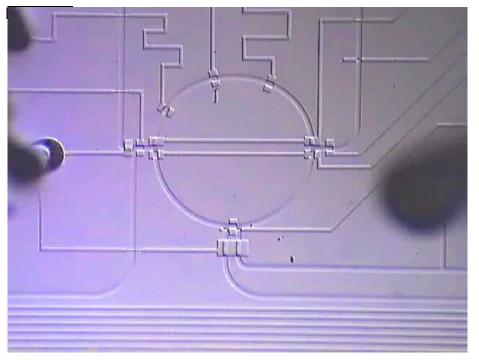
Microfluidic Chips
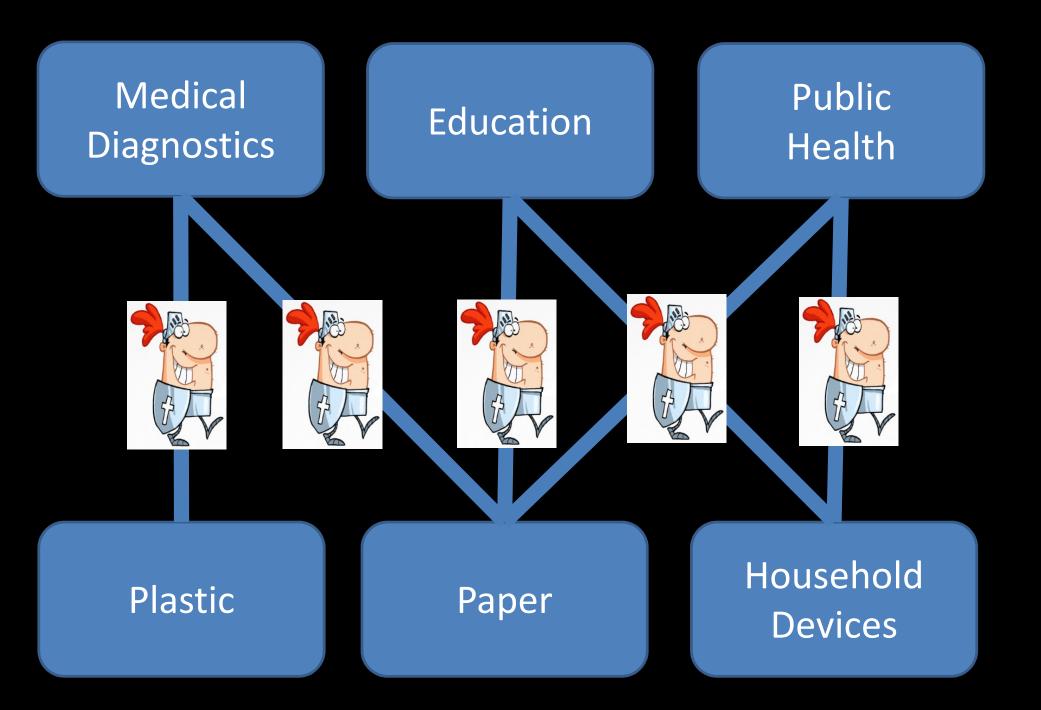
- **Idea: a whole biology lab on a single chip**
  - Input/output
  - **Sensors**: pH, glucose, temperature, etc.
  - **Actuators**: mixing, PCR, electrophoresis, cell lysis, etc.

- **Benefits:**
  - Small sample volumes
  - High throughput

- **Applications:**
  - Biochemistry   - Cell biology
  - Biological computing

1 mm   *10x real-time*

Application to Rural Diagnostics

Disposable Enteric Card

*PATH,
Washington U.
Micronics, Inc.,
U. Washington*

Targets:
- E. coli, Shigella,
  Salmonella,
  C. jejuni

DxBox

*U. Washington,
Micronics, Inc.,
Nanogen, Inc.*

Targets:
- malaria (done)
- dengue, influenza,
  Rickettsial diseases,
  typhoid, measles
  (under development)
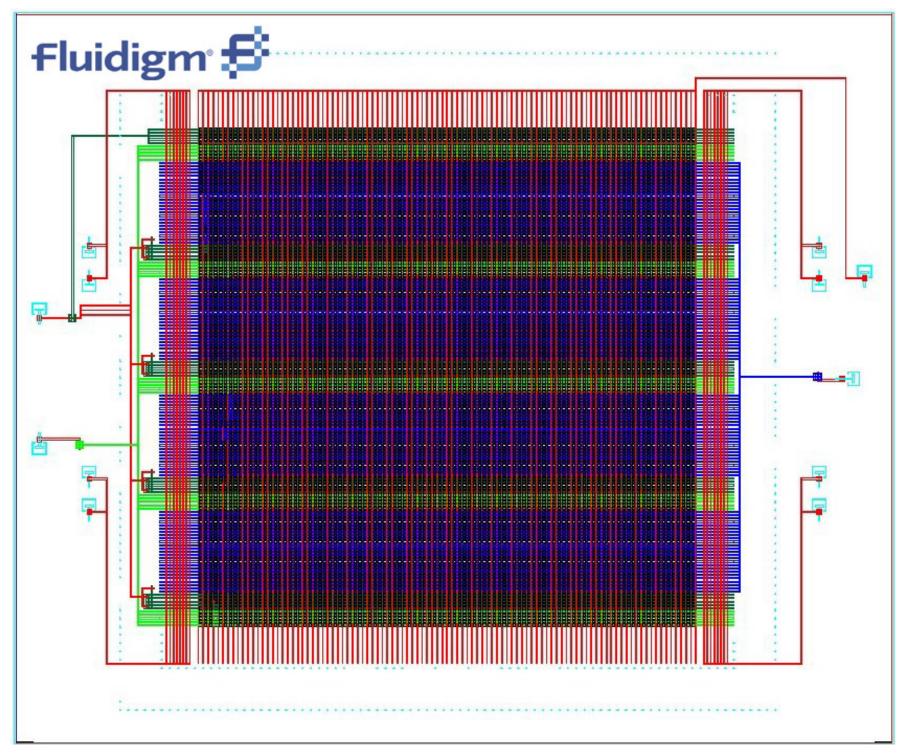
CARD

Rheonix, Inc.
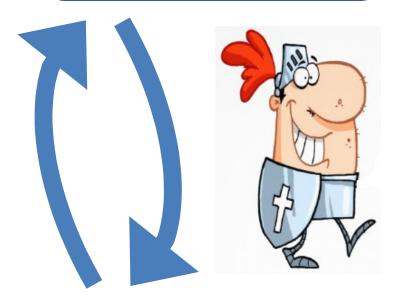
Targets:
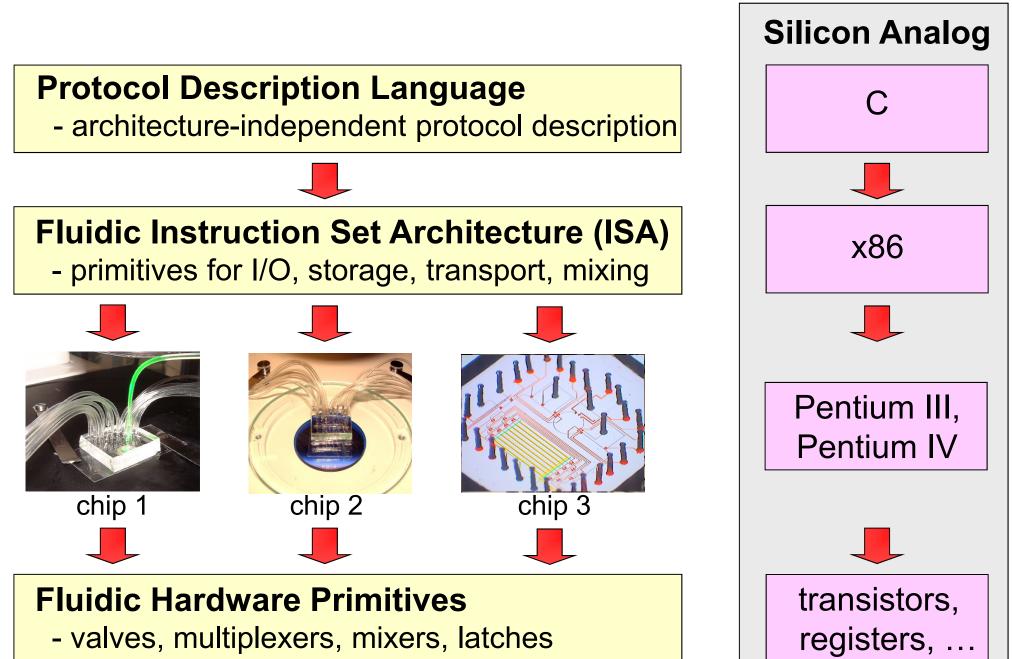- HPV diagnosis
- Detection of
  specific gene
  sequences

Source: Fluidigm Corporation (http://www.fluidigm.com/didIFC.htm)

Abstraction Layers for Microfluidics

Protocol Description Language
- architecture-independent protocol description

Fluidic Instruction Set Architecture (ISA)
- primitives for I/O, storage, transport, mixing

chip 1

chip 2

chip 3

Fluidic Hardware Primitives
- valves, multiplexers, mixers, latches

Silicon Analog

C

x86

Pentium III,
Pentium IV

transistors,
registers, …

Abstraction Layers for Microfluidics

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Contributions

BioCoder Language
[J.Bio.Eng. 2010]

Optimized Compilation
[Natural Computing 2007]

Demonstrate Portability
[DNA 2006]

Micado AutoCAD Plugin
[MIT 2008, ICCD 2009]

Digital Sample Control
Using Soft Lithography
[Lab on a Chip '06]

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Implementation: Oil-Driven Chip

	Inputs	Storage Cells	Background Phase	Wash Phase	Mixing
Chip 1	2	8	Oil	—	Rotary

Implementation: Oil-Driven Chip
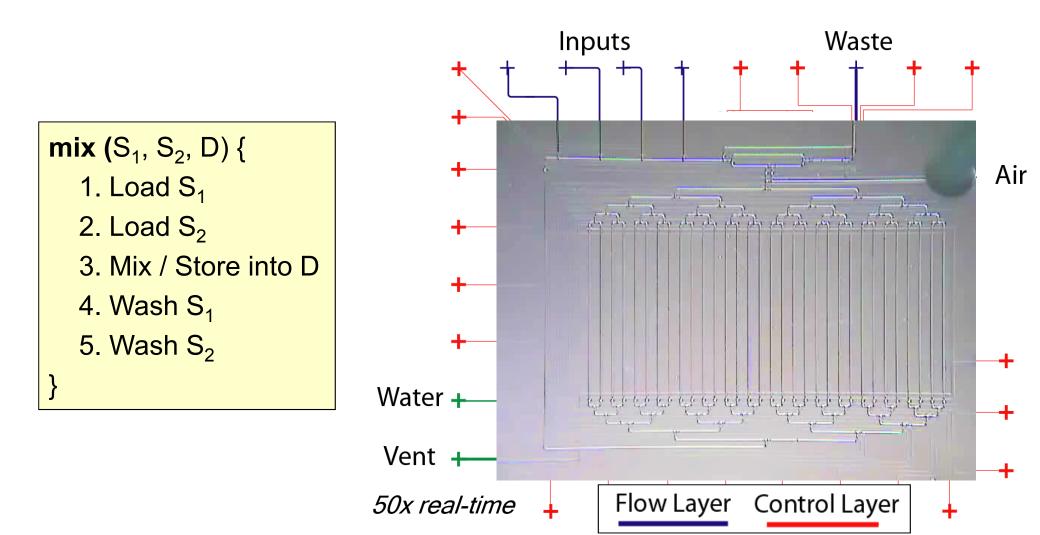
mix (S_1, S_2, D) {

➡️ 1. Load S_1

    2. Load S_2

    3. Rotary mixing

    4. Store into D

}

50x real-time

	Inputs	Storage Cells	Background Phase	Wash Phase	Mixing
Chip 1	2	8	Oil	—	Rotary

Implementation 2: Air-Driven Chip

	Inputs	Storage Cells	Background Phase	Wash Phase	Mixing
Chip 1	2	8	Oil	—	Rotary
Chip 2	4	32	Air	Water	In channels

Implementation 2: Air-Driven Chip
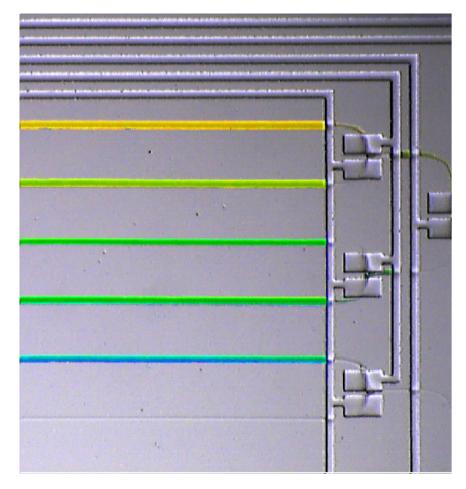
```
mix (S₁, S₂, D) {
    1. Load S₁
    2. Load S₂
    3. Mix / Store into D
    4. Wash S₁
    5. Wash S₂
}
```


Inputs   Waste   Air

Water

Vent

50x real-time

Flow Layer   Control Layer

	Inputs	Storage Cells	Background Phase	Wash Phase	Mixing
Chip 1	2	8	Oil	—	Rotary
Chip 2	4	32	Air	Water	In channels

"Write Once, Run Anywhere"
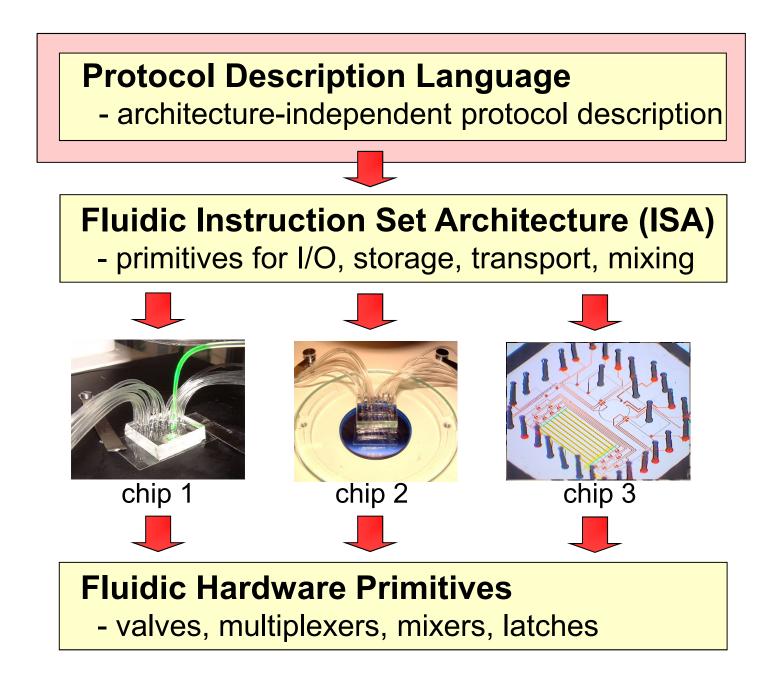
- **Example: Gradient generation**

```
Fluid yellow = input (0);
Fluid blue = input(1);
for (int i=0; i<=4; i++) {
    mix(yellow, 1-i/4, blue, i/4);
}
```

- **Hidden from programmer:**
  - Location of fluids
  - Details of mixing, I/O
  - Logic of valve control
  - Timing of chip operations

450 Valve Operations

Abstraction Layers for Microfluidics

Protocol Description Language
- architecture-independent protocol description

Fluidic Instruction Set Architecture (ISA)
- primitives for I/O, storage, transport, mixing

chip 1   chip 2   chip 3

Fluidic Hardware Primitives
- valves, multiplexers, mixers, latches

Genetic Control of Surface Curvature

Utpal Nath, Brian C. W. Crawford, Rosemary Carpenter,
Enrico Coen*

Genetic Control of Surface Curvature

Utpal Nath, Brian C. W. Crawford, Rosemary Carpenter, Enrico Coen*

Material and Methods

In situ **Hybridization.** The methods used for tissue preparation, digoxigenin-labelling of RNA probes, and *in situ* hybridisation were as described previously *(S13)*. The probe used

florica

Flowe

Enrico S. Co
Robert Elliot
and Rosema

Dual ro
genes a

Gwyneth
Rosemary
Rüdiger Si

John Innes Centre

[1]Present address:
École Normale S
France
[2]Present address:
Lethbridge, 4401
Canada
[3]Present address:
Köln, Gyrhofstras

[4]Corresponding a

"Immu
describ
acid d

The Expression of *D-Cyclin* Genes Defines Distinct Developmental Zones in Snapdragon Apical Meristems and Is Locally Regulated by the *Cycloidea* Gene[1]

Valérie Gaudin[2], Patricia A. Lunness, Pierre R. Fobert[3], Matthew Towers, Catherine Riou-Khamlichi, James A.H. Murray, Enrico Coen, and John H. Doonan*

Three D-cyclin genes are expressed in the apical meristems of snapdragon (*Antirrhinum majus*). The *cyclin D1* and *D3b* genes are expressed throughout meristems, whereas *cyclin D3a* is restricted to the peripheral region of the meristem, especially the organ primordia. During floral development, *cyclin D3b* expression is: (a) locally modulated in the cells immediately surrounding the base of organ primordia, defining a zone between lateral organs that may act as a developmental boundary; (b) locally modulated in the ventral petals during petal folding; and (c) is specifically repressed in the dorsal stamen by the *cycloidea* gene. Expression of both *cyclin D3* genes is reduced prior to the cessation of cell cycle

pacity for continued proliferation throughout the lifetime of the plant. Other tissues, such as secondary meristems, may remain dormant for some time before re-activation.

The molecular basis for localized differences in cell proliferation within the meristem is unclear, but could, as in other organisms, involve changes in the length of the cell division cycle. For example, the duration of the cell cycle in *Drosophila* is increased by the successive addition of G2 and then G1 phases (Edgar and O'Farrell, 1989). An alternative, but not exclusive, control mechanism operates later in larval development, when entry into and exit from the cycle is modulated, leading to localized differences in cell prolifer-

- Main paper
- References
- Ref. papers

BioCoder: A High-Level Programming Language for Biology Protocols

In biology publications, can we replace the textual description of the methods used with a computer program?

1. Enable automation
via microfluidic chips

2. Improve reproducibility
of manual experiments

Example: Plasmid DNA Extraction

I. Original protocol *(Source: Klavins Lab)*

Add 100 ul of 7X Lysis Buffer (Blue) and mix by inverting the tube 4-6 times. *Proceed to step 3 within 2 minutes.*
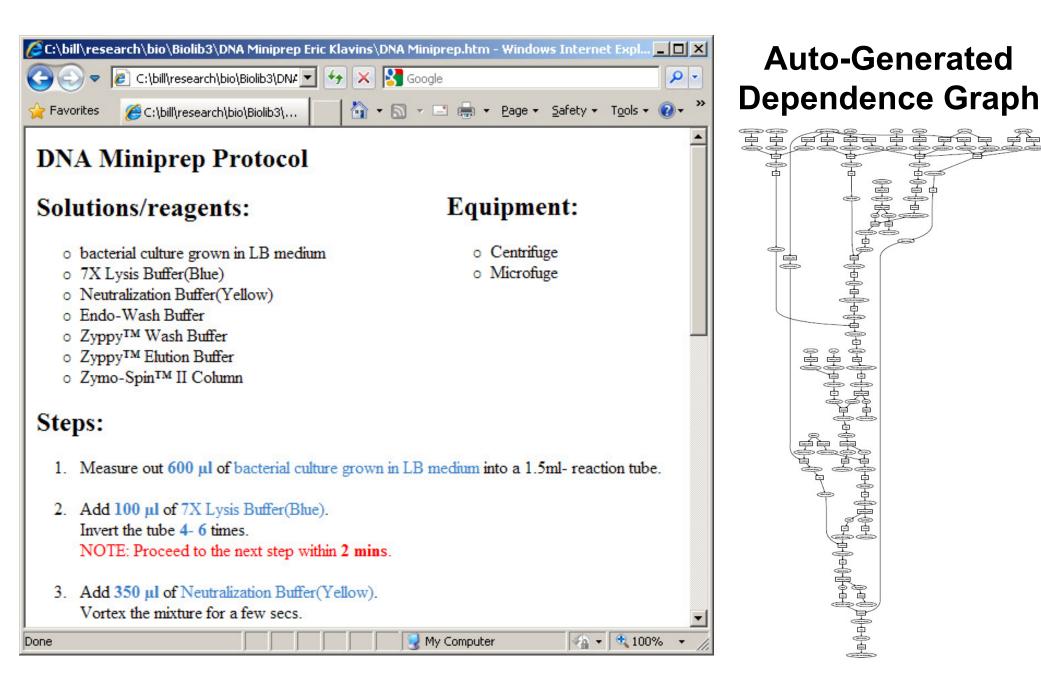
II. BioCoder code

```
FluidSample f1 = measure_and_add(f0, lysis_buffer, 100*uL);
FluidSample f2 = mix(f1, INVERT, 4, 6);
time_constraint(f1, 2*MINUTES, next_step);
```

III. Auto-generated text output

Add 100 ul of 7X Lysis Buffer (Blue).
Invert the tube 4-6 times.
NOTE: Proceed to the next step within **2 mins.**

Example: Plasmid DNA Extraction

Auto-Generated Dependence Graph

BioCoder Language Primitives

- **Declaration / measurement / disposal**
  - declare_fluid
  - declare_column
  - measure_sample
  - measure_fluid
  - volume
  - discard
  - transfer
  - transfer_column
  - declare_tissue

- **Combination / mixing**
  - combine
  - mix
  - combine_and_mix
  - addto_column
  - mixing_table

- **Centrifugation**
  - centrifuge_pellet
  - centrifuge_phases
  - centrifuge_column

- **Temperature**
  - set_temp
  - use_or_store
  - autoclave

- **Timing**
  - wait
  - time_constraint
  - store_until
  - inoculation
  - invert_dry

- **Detection**
  - ce_detect
  - gas_chromatography
  - nanodrop
  - electrophoresis
  - mount_observe_slide
  - sequencing

Standardizing Ad-Hoc Language

- **Need to convert qualitative words to quantitative scale**

- **Example: a common scale for mixing**
  - When a protocol says "mix", it could mean many things
  - Level 1:   tap
  - Level 2:   stir
  - Level 3:   invert
  - Level 4:   vortex / resuspend / dissolve

- **Similar issues with temperature, timing, opacity, …**

Benchmark Suite
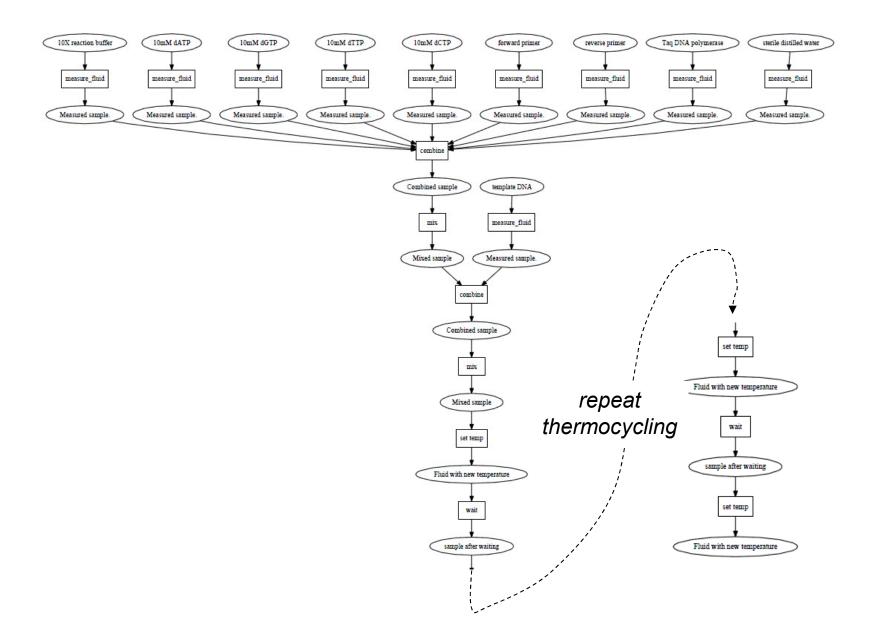
PROTOCOL	TOTAL INSTR.
Source: Academic Laboratory	
★ CTAB DNA Plant Miniprep (Utpal Nath Lab)	225
✓ 2ab Assembly Protocol (Douglas Densmore)	90
✓ DNA Miniprep (Eric Klavins Lab)	50
✓ Ligation (Eric Klavins Lab)	21
✓ Protein in situ localization (Utpal Nath Lab)	81
✓ Restriction Digestion (Eric Klavins Lab)	20
Transformation (Eric Klavins Lab)	33
Source: Textbook	
✓ Alkaline lysis with SDS - miniprep (Mol. Cloning)	21
Alkaline lysis with SDS - maxiprep (Mol. Cloning)	67
Alkaline lysis with SDS - midiprep (Mol. Cloning)	33
Large-scale plasmid prep by boiling (Mol. Cloning)	64
Plasmid prep by lysis w/ SDS (Mol. Cloning)	83
Purification of plamid DNA w/ PEG (Mol. Cloning)	64
Removal of small nucleic acid w/ LiCl (Mol. Cloning)	41
Removal of small nucleic acid w/ NaCl (Mol. Cloning)	36
Small-scale plasmid prep by boiling (Mol. Cloning)	34
Toothpick miniprep (Mol. Cloning)	38
Transformation of E.coli using CaCl2 (Mol. Cloning)	59
Yeast transformation (Methods in Yeast Genetics)	89
Source: Published Paper	
Molecular barcodes (Miner et al., 2004)	75
Plant RNA isolation (Bilgin et al., 2009)	66
SIRT1 redistribution (Oberdoerffer et al., 2008)	107
Splinkerette PCR (Uren et al., 2009)	80
Touchdown PCR (Korbie & Mattick, 2008)	21
Transcriptional instability (Warren et al., 2007)	84
Source: OpenWetWare	
Blackburn - yeast colony PCR	44
Chromosomal DNA isolation from E.coli	52
DNA extraction - salting out	63
DNA extraction from tissue	51
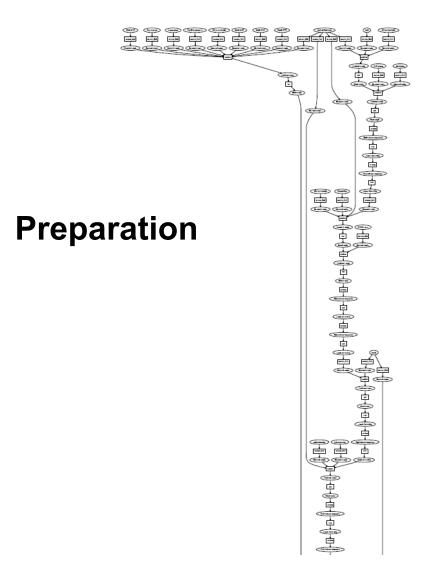
DNA precipitaion	39
Endy - colony PCR	22
Endy restriction digestion	31
Engineering BioBrick restriction digest	18
Engineering BioBricks - colony PCR	16
Ermans lab - DNA miniprep with alkaline lysis	57
Ethanol precipitation of nucleic acids	35
Ethanol precipitation of small DNA fragments	28
Filamentous fungi genomic DNA isolation	79
Freimoser: Fast Yeast Transformation	38
Imaging probe synthesis	23
Kafatos - minipreps	58
Knight colony PCR	17
Knight in vitro transcription	45
Maxiprep of plasmid DNA from E.coli	121
Miniprep GET buffer	77
Miniprep kit-free high-throughput protocol	42
Mouse tissue lysis for genotyping	21
One-step miniprep	43
PCR assay	12
PNK treatment of DNA ends	12
Restriction Digest (Richard Lab)	30
Separation based sensing of neurotransmitter	14
Size selective DNA precipitation	23
Small-scale plasmid isolation - Maxiprep	71
Small-scale plasmid isolation - Miniprep	74
Streptomyces PCR	22
Studier lysate prep	24
Transformation inoue	33
Transforming chemically competent cells	34
Yeast DNA prep	43
Source: Commercial Kit	
AllPrep RNA protein protocol (Qiagen)	93
DNA sequencing by capillary elec. (App. Biosystems)	60
Miniprep (Qiagen)	54
Plasmid purification high yield (Qiagen)	81
Plasmid purification standard (Qiagen)	81

**65 protocols
5800 LOC**

Example: PCR
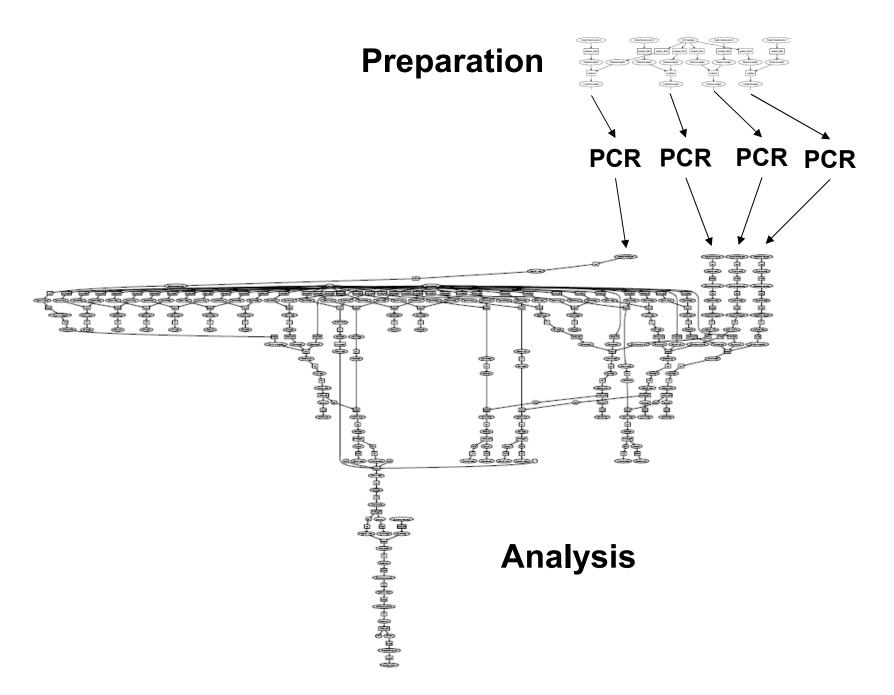
Example: Molecular Barcodes

Preparation
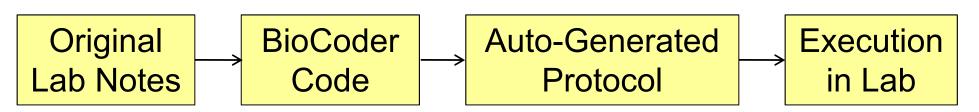
+ PCR (2)

Example: DNA Sequencing

Preparation

PCR **PCR** **PCR** **PCR**

Analysis

Validating the Language

- **Eventual validation: automatic execution**
  - But BioCoder more capable than most chips today
  - Need to decouple language research from microfluidics research

- **Initial validation: human execution**
  - In collaboration with Prof. Utpal Nath's lab at IISc
  - Target Plant DNA Isolation, common task for summer intern

| Original Lab Notes | → | BioCoder Code | → | Auto-Generated Protocol | → | Execution in Lab |

Biologist is never exposed to original lab notes

- **To the best of our knowledge, first execution of a real biology protocol from a portable programming language**

Growing a Community

Growing a Community

Growing a Community

Future Work

ADD — 100 µl 7x Lysis Buffer (Blue) — MIX — invert 4-6 times

- **Backends for BioStream**
  - Generate graphical protocol
  - Generate a microfluidic chip to perform protocol
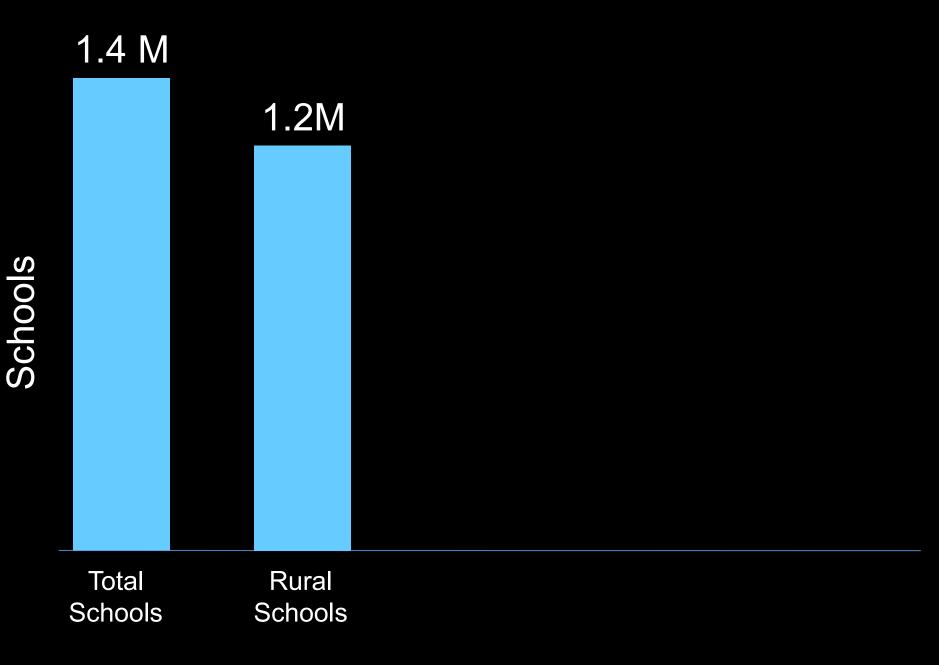
- **Reliability and troubleshooting**
  - Verify that protocol is safe, correct, obeys timing constraints
  - If protocol fails, automatically suggest troubleshooting routine
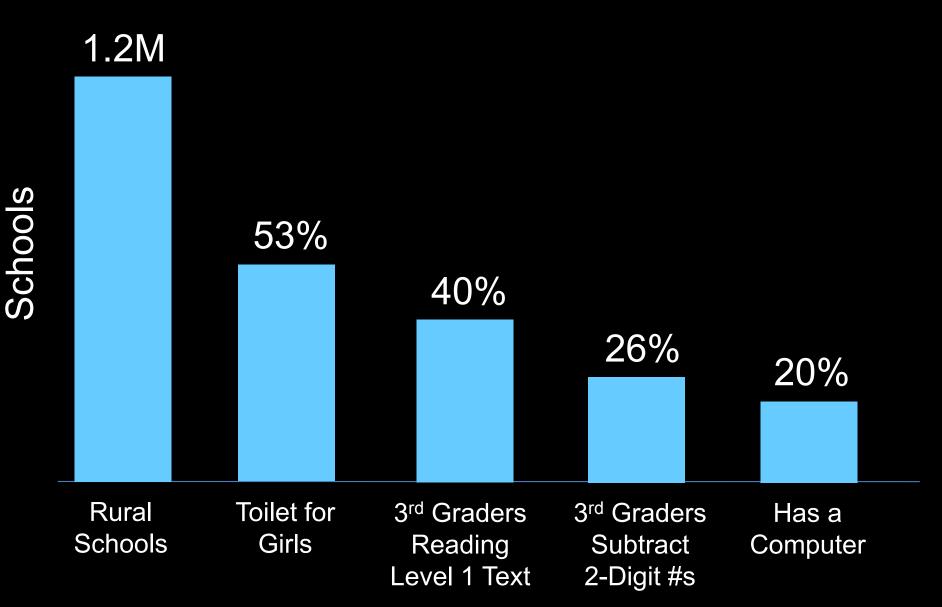
- **Building a knowledge base**
  - Encode experimental results in addition to protocols
  - Search for a protocol based on input/output relationship
  - Revision control for biology protocols

Part 2: Education

Classroom Environment in India

Classroom Environment in India

Source: DISE 2012-2013, ASER 2013

Classroom Environment in India

Schools

1.2M	53%	40%	26%	20%
Rural Schools	Toilet for Girls	3rd Graders Reading Level 1 Text	3rd Graders Subtract 2-Digit #s	Has a Computer

Source: DISE 2012-2013, ASER 2013
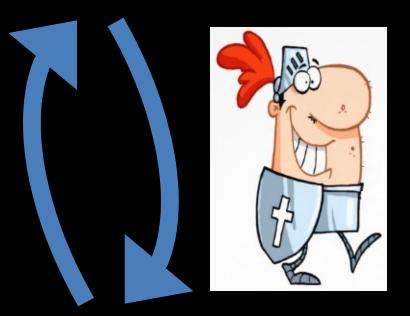
Some photos courtesy Nithya Sambasivan

DVD Player as a Programmable Device

- 16 general-purpose 16-bit registers
  - (No heap/stack)
- Virtual machine instructions
  - Arithmetic   - Comparison   - Branch/Jump   - Timing
  - (No indirect jump)
- Display:
  - Pre-built MPEG-2 videos with mask and highlight layers
- Constrained and specialized internal organization

5,500 articles from
Schools-Wikipedia.org
on TV-DVD

Make a selection or wait for help:
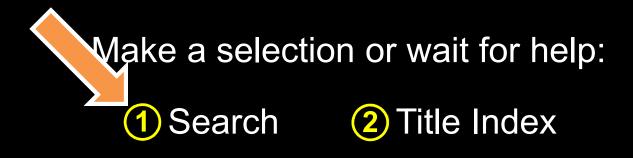
① Search   ② Title Index

5,500 articles from
Schools-Wikipedia.org
on TV-DVD

Make a selection or wait for help:

① Search   ② Title Index

Search

A B C D E F

G H I J K L

M N O P Q R

S T U V W X

Y Z DONE

POWER OPEN/CLOSE

1 2 3

4 5 6

7 8 9

+10

ENTER

Search

A B C D E F
G H I J K L
M N O P Q R
S T U V W X
Y Z DONE

POWER OPEN/CLOSE

1 2 3
4 5 6
7 8 9

+10

ENTER

Search

A B C D E F

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M N O P Q R

S T U V W X

Y Z DONE

C

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H   [I] [ ] [ ] [L]

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7 8 9

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DONE   BKSP

POWER   OPEN/CLOSE

1 2 3
4 5 6
7 8 9

+10

ENTER
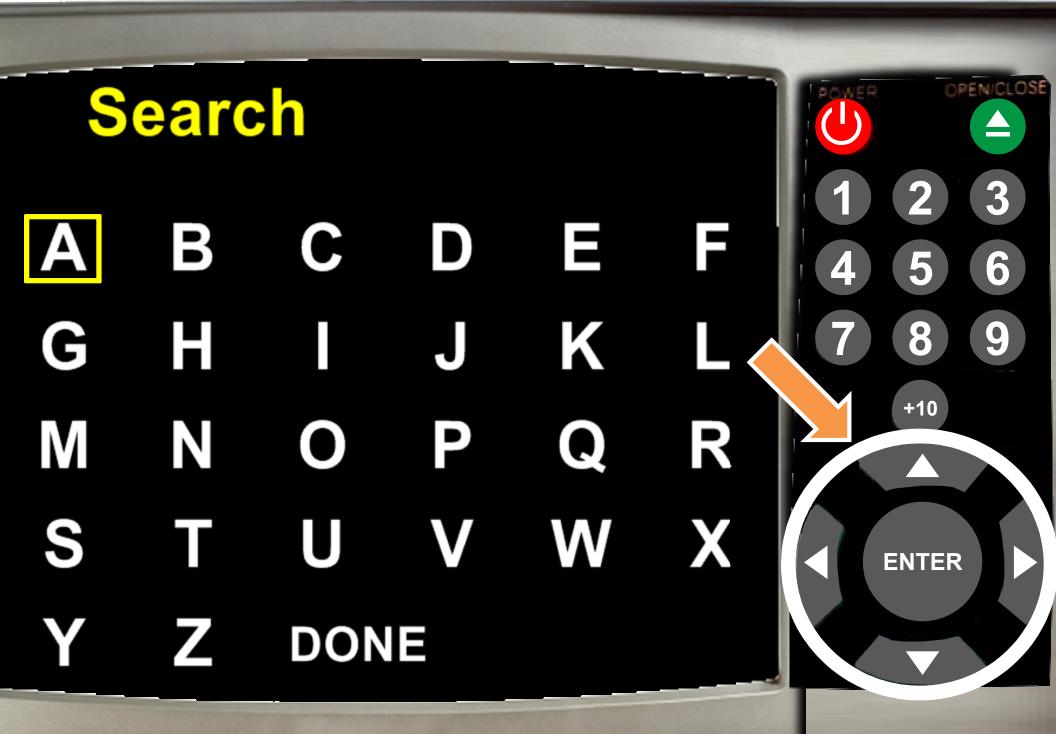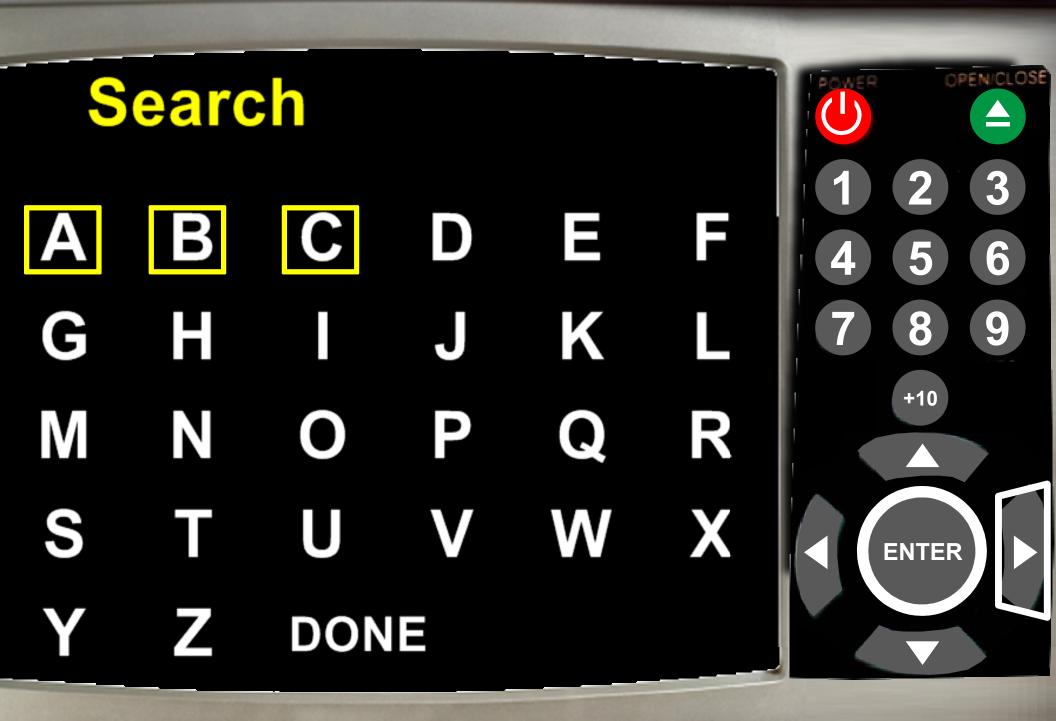
5 **Close, Brian**

6 **Clothing**

7 **Cloud**

8 **Club Band, Sgt. Pepper's Lonely Heart**

9 **cluster, Globular**

10 **cluster, Open**

11 **cluster, Tone**

12 **Coal**

13 **Coal Tit**

14 **Cobalt**

15 **Cobra**

16 **Coccinellidae**

Cloud

Wikipedia. Related subjects: Climate and the Weather

A cloud is a visible mass of droplets or frozen crystals floating in the atmosphere above the surface of the ⑤Earth or another ⑥planetary body. A cloud is also a visible mass attracted by gravity (clouds can also occur as

Stratocumulus perlucidus clouds, as seen from an aircraft window.

Cloud

Wikipedia. Related subjects: Climate and the Weather

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Stratocumulus perlucidus clouds, as seen from an aircraft window.

Navigation Buttons

POWER   OPEN/CLOSE

1 2 3
4 5 6
7 8 9

+10

ENTER

Cloud

Wikipedia. Related subjects: Climate and the Weather

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Scrolling Buttons

Cloud

Wikipedia. Related subjects: Climate and the Weather

A cloud is a visible mass of droplets or

Hyperlinks

floating in the atmosphere above the surface of the ⑤Earth or another ⑥planetary body. A cloud is also a visible mass attracted by gravity (clouds can also occur as

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①

④ Scroll Down

Stratocumulus perlucidus clouds, as seen from an aircraft window.

POWER   OPEN/CLOSE

1 2 3
4 5 6
7 8 9

+10

ENTER

attracted by gravity (clouds can also occur as masses of material in interstellar space, where they are called interstellar clouds and nebulae.) The branch of meteorology in which clouds are studied is nephology.

On Earth the condensing substance is typically water vapor, which forms small droplets or ice crystals, typically 0.01 mm in diameter. When surrounded by billions of other droplets or crystals they become visible as clouds. Dense deep clouds exhibit a high reflectance (70% to 95%) throughout the visible range of wavelengths: they thus appear white, at least from the top. Cloud droplets tend to scatter light efficiently, so

attracted by gravity (clouds can also occur as masses of material in interstellar space, where they are called interstellar clouds and nebulae.) The branch of ⑤meteorology in which clouds are studied is nephology. On ⑥Earth ... substance is typically ⑦water vapor, which forms small droplets or ⑧ice crystals, typically 0.01 mm in diameter. When surrounded by billions of other droplets or ⑨crystals they become visible as clouds. Dense deep clouds exhibit a high reflectance (70% to 95%) throughout the visible range of wavelengths: they thus appear white, at least from the top. Cloud droplets tend to scatter light efficiently, so

Crystal

Wikipedia. Related subjects: Materials science

In chemistry, mineralogy, and materials science, a crystal is a solid in which the constituent atoms, molecules, or ions are packed in a regularly ordered, repeating pattern extending in all three spatial dimensions.

① ④

Quartz crystal

Crystal

Wikipedia. Related Subjects: Materials science

In chemistry, mineralogy, and materials science, a crystal is a solid in which the constituent atoms, molecules, or ions are packed in a regularly ordered, repeating pattern extending in all three spatial dimensions.

Quartz crystal

Back Button

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Scroll Up

Cloud

Wikipedia. Related subjects: Climate and the Weather

A cloud is a visible mass of droplets or frozen crystals floating in the atmosphere above the surface of the ⑤Earth or another ⑥planetary body. A cloud is also a visible mass attracted by gravity (clouds can also occur as

Stratocumulus perlucidus clouds, as seen from an aircraft window.

Cloud

Home Button

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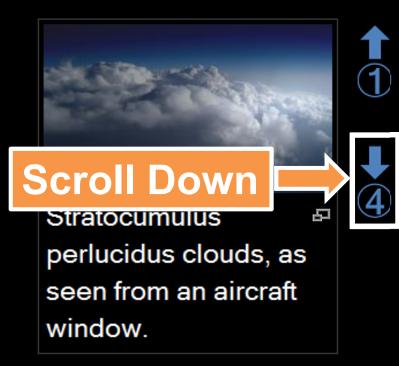
Stratocumulus perlucidus clouds, as seen from an aircraft window.

Key Challenge: Addressing A Large Number of Menus

"I am not familiar with another customer trying to create a disc with the maximum number of menu allowable in the DVD specification."

— Scenarist Support

Key Challenge: Addressing
A Large Number of Menus

$$ButtonHandler \rightarrow Register := Value;\ \textbf{jump}\ Label$$

16 registers!   16 bits   very constrained

Children's Books on TV-DVD [ICTD 2010]

$0.50 for 1 book in print

$0.50 for 10,000 books on DVD

Wikipedia Subset on TV-DVD

[CHI 2011]

Cloud

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A cloud is a visible mass of droplets or frozen crystals floating in the atmosphere above the surface of the ⑤Earth or another ⑥planetary body. A cloud is also a visible mass attracted by gravity (clouds can also occur as

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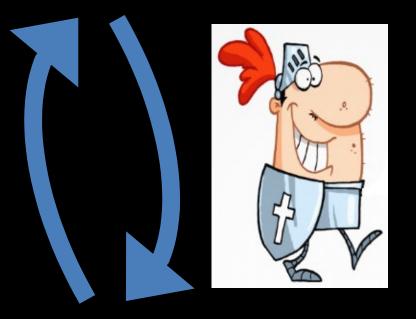
Clickers for Classroom Polling

+ Pedagogical benefits

– Very expensive

Is There a Cheaper Solution?

Audience Polling

At Most One
Electronic Device
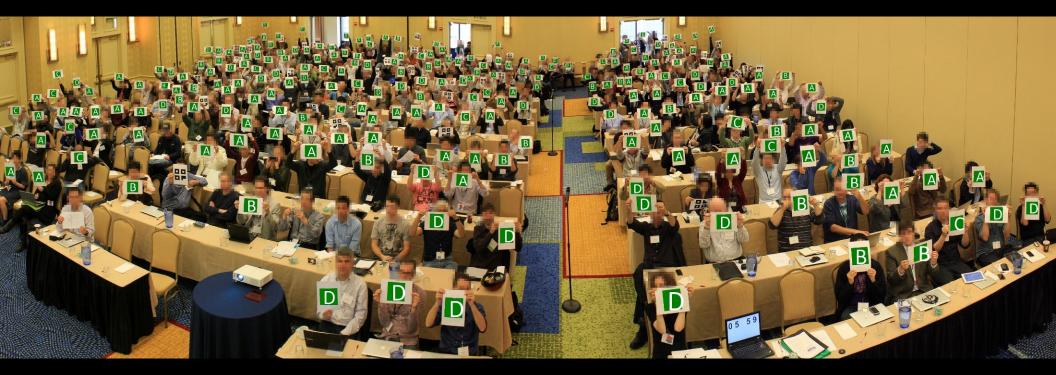
qCards: Low-Cost Audience Polling Using Computer Vision

Polling an Audience of 300
[UIST 2012]

Polling an Audience of 300
[UIST 2012]

90% of people captured
98% of those captured accurately

Polling an Audience of 1,800

Part 3: Public Health

The Problem of Medication Adherence

- WHO: In developed countries, 50% having chronic disease take medication as directed
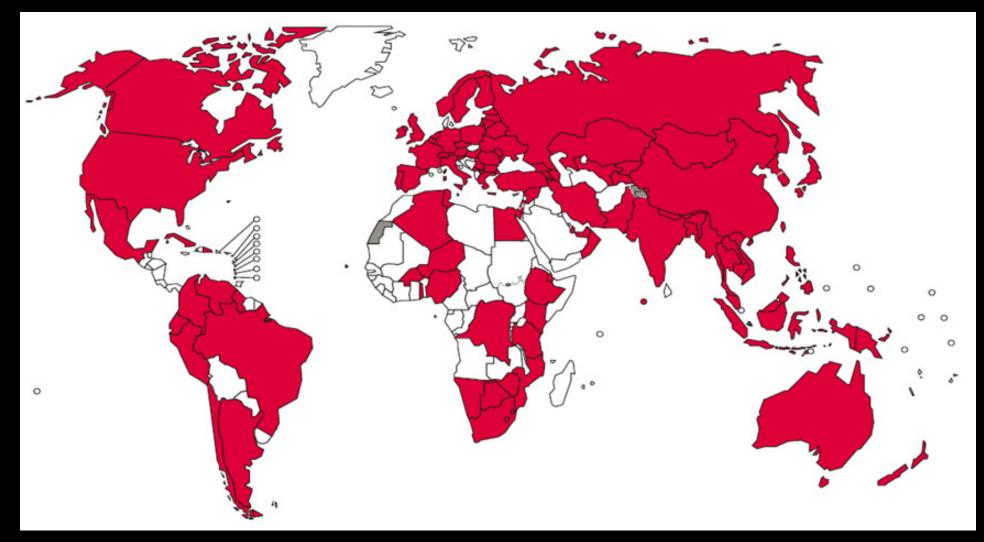
- In US, non-adherence causes:
  - $300 billion annual cost to healthcare system
  - 10% of hospital admissions
  - 23% of nursing home admissions

- Globally, non-adherence claims millions of lives and poses threat of untreatable diseases

Vermeire, E., Hearnshaw, H., Van Royen, P., & Denekens, J. (2001). Patient adherence to treatment: three decades of research. A comprehensive review. *Journal of Clinical Pharmacy and Therapeutics, 26*(5), 331-342.

Extensively Drug-Resistant Tuberculosis (XDR-TB)

Countries Notifying At Least One Case by the End of 2013
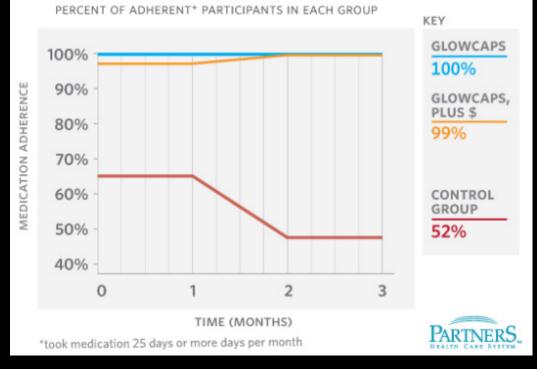
TB Control Strategy in India:
Directly Observed Therapy (DOTS)

Photo: Operation ASHA

Electronic Pillboxes:
Effective but Very Costly
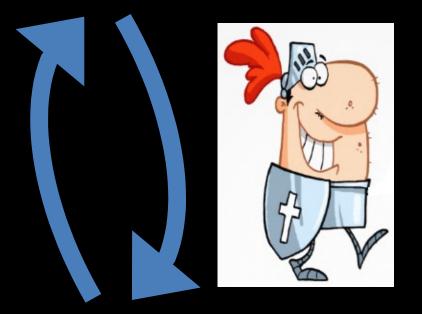
Vitality Glowcap
$99 + $15 / month

Clinical trial shows significant improvement in adherence to hypertension medication (2012)

Is There a Cheaper Solution?

Pill-in Hand Adherence Monitoring

Common Supplies
(Incl. basic mobile phones)

99DOTS

- Overview
- Calendar
- Patients
- Reports
- Profile

Dashboard / Calendar

Adherence

☁ Download adherence calendar

■ **Wednesday, January 14, 2015**

2 of 51 patients have responded today

+ Mark dose taken

| today | ‹ | January ▾ | › | 2015 ▾ |

■ correct   ■ manual   ■ incorrect   ■ missed   ■ first/last day of treatment

RNTCP Program

Patient	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Gopi Kumar																															
Kabutri Devi																															
Md. Ali																															
Anita Devi																															
Binda Devi																															
Panchu Das																															
Smriti Kumari																															
Vishnudev Malik																															
Md. Ahmad																															
Tuntun Paswan																															
Ram Pari Devi																															

Deployments in Treatment Programs

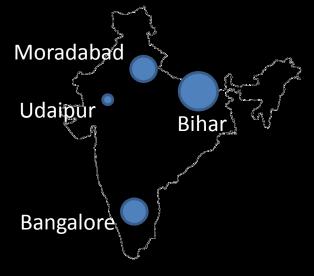Enrolled 80 patients and counting
- Across public and private programs
- In five urban and rural sites
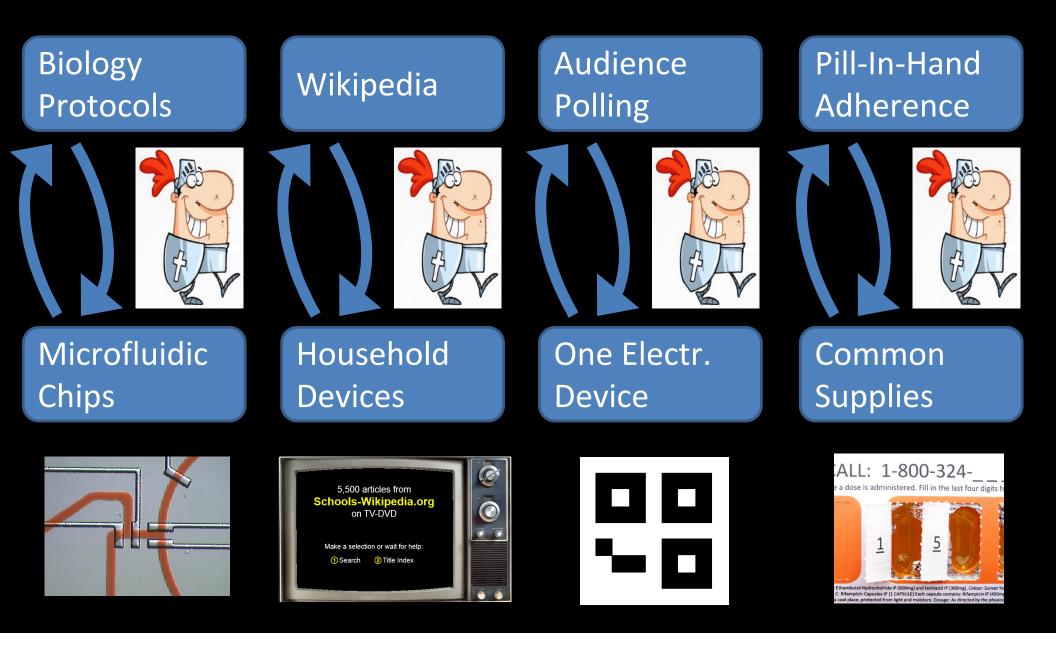- High acceptance by all partners

Support of Key Stakeholders

Future Directions

- Crowdsourcing
- Compiling to living systems
- Personalized education
- More microfluidics

- Problem discovery

Thank you