Decision Support for Antibiotic Prescription

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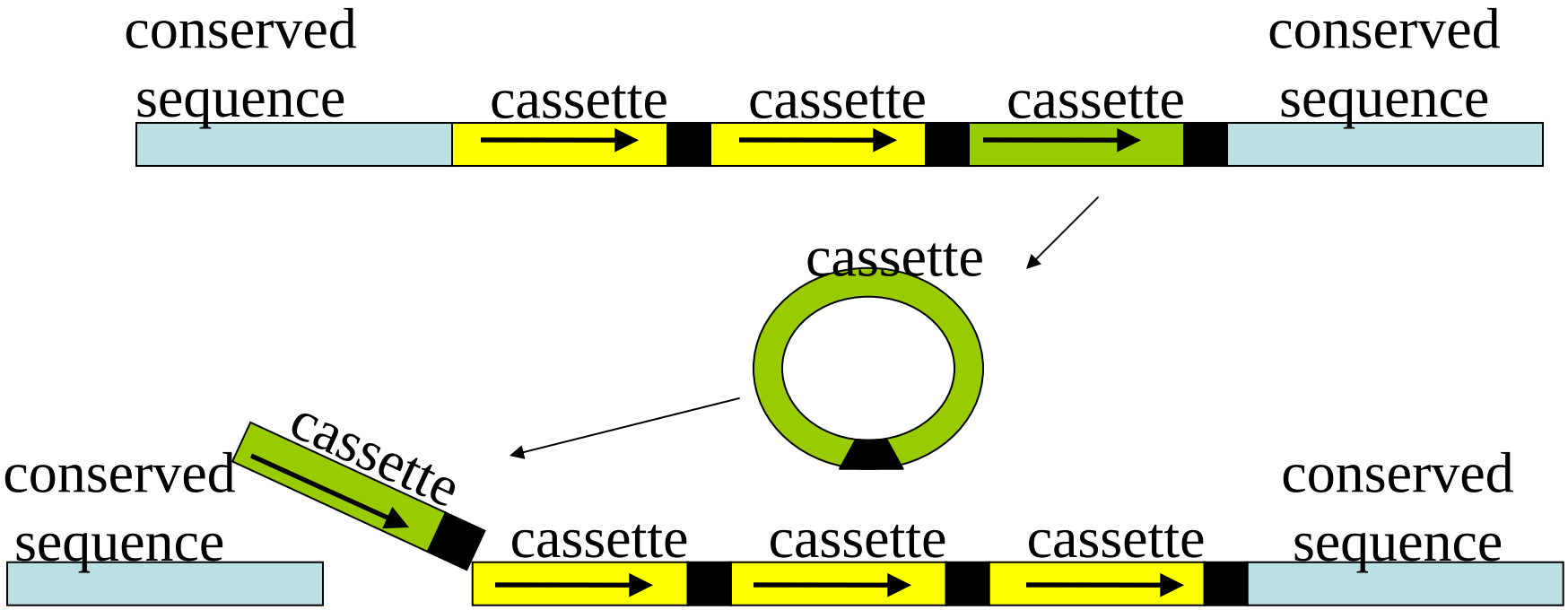
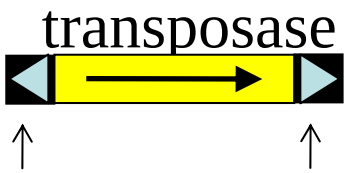
The ABR Problem

- Some bacteria are resistant to some antibiotics
- Antibiotic resistance spreads (horizontal transfer) and aggregates →
  - More multi-resistant infections
  - **Mobile Genetic Elements**
- Nosocomial (hospital acquired) infections
- Estimated (AU)$2.5B per year in Australia
- **According to WHO, ABR is one of top three global health issues**

Gene Cassettes



Insertion Sequence



Transposition

Transposon

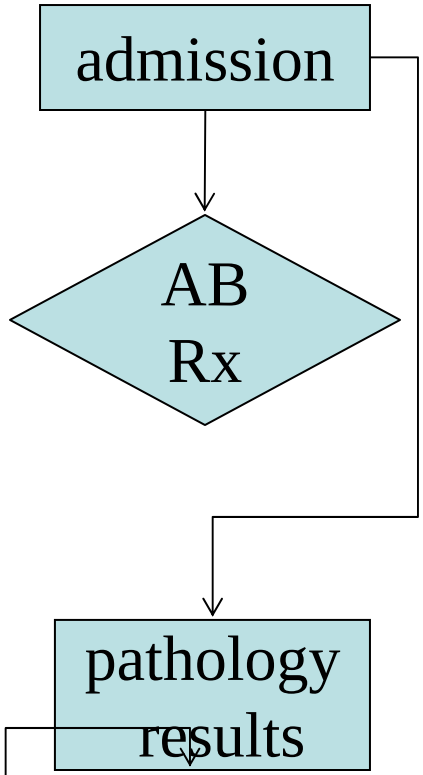
Integron

Composite Transposon

The Challenge

- Most effective therapy for patient
- Minimal ecological impact
- Simple and quick pathology

Current Practice

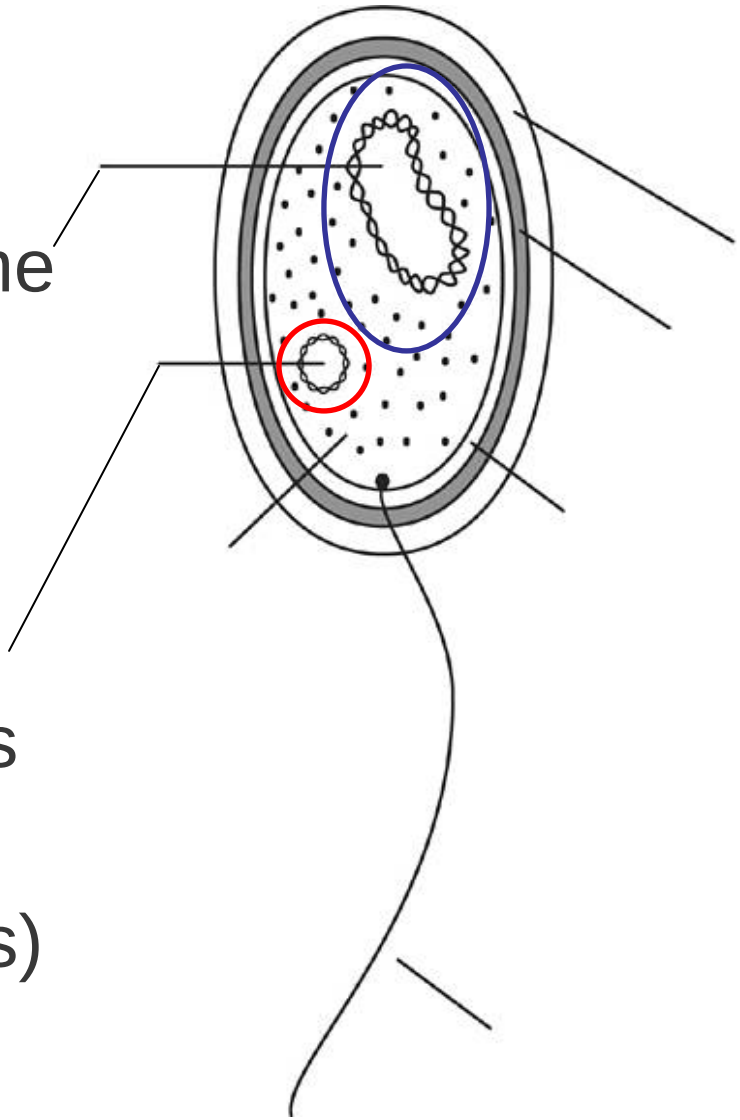


- "given patient symptoms, what is best practice?"
- Guidelines (pink book[1])
- Computed Guideline Support (Shahar et al.)
  - Not yet applied to AB
- Adaptive heuristic models based on any of: symptoms, patient records, pathology, risk
- Delayed pathology (2+ days)

[1] Centers for Disease Control and Prevention. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. Atkinson W, Hamborsky J, McIntyre L, Wolfe S, eds. 10th ed. 2nd printing, Washington DC: Public Health Foundation, 2008.

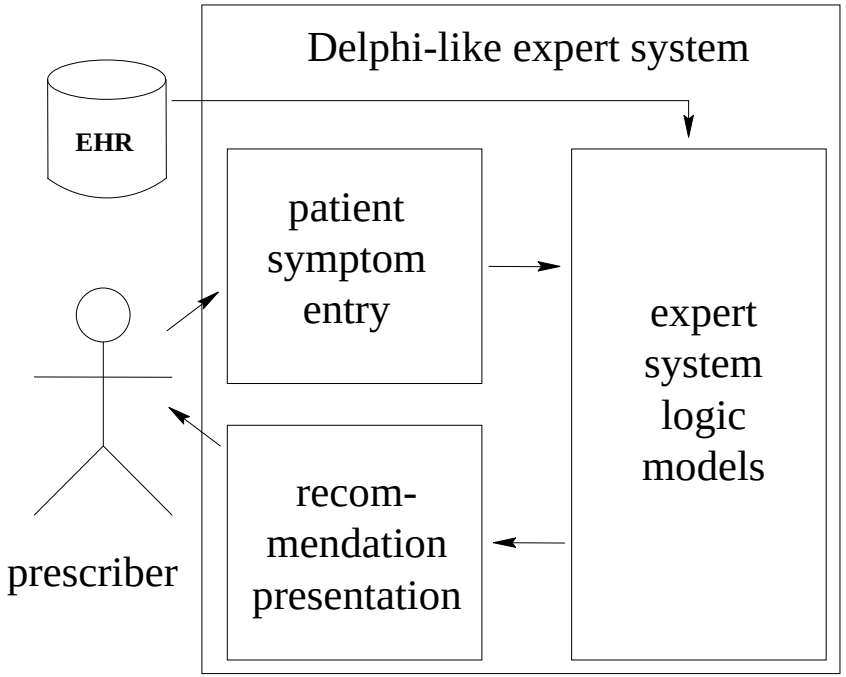
Current Pathology

- Measures the chromosome
  - Species
  - Strand
  - Morphology
  - Symptoms
- Should measure Plasmids
  - Multi-resistance regions
- Requires culturing (2 days)



Computational Support

- First developed 1976 (MYCIN)
  - shown some improvement in practice
- Modern systems:
  - Same model:
    - Clinician enters symptoms
    - Gets recommendations
  - Cost/benefit recommendation
    - Ecological impact
    - Risks to patient
    - Likely outcomes
  - Questionable adoption
  - No pathology

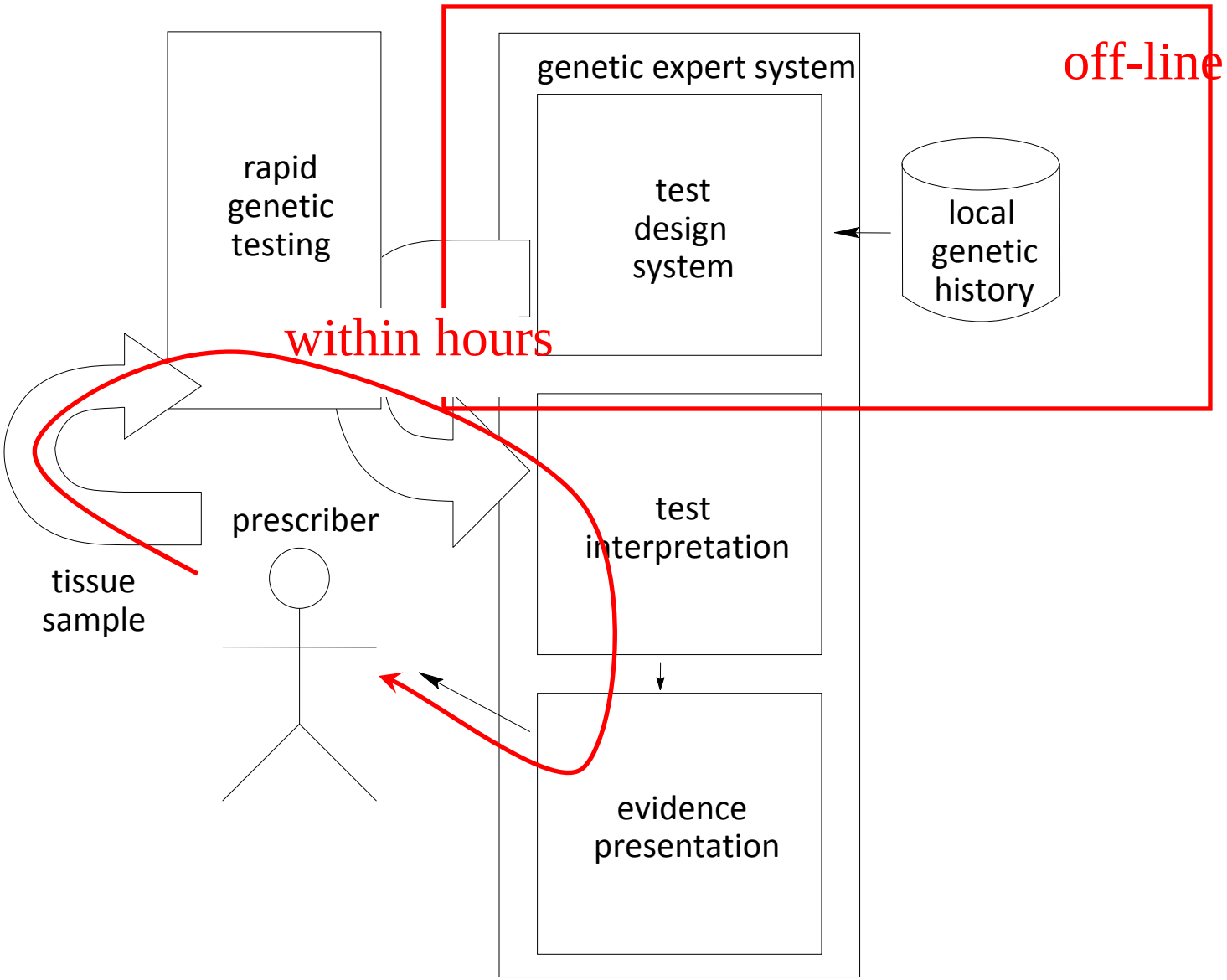


A new DSS Model for AB prescription

- Target the question:
  - "given a patient scenario and an environmental context, what is best action?"
- "Context" here means molecular data in the environment of the patient
  - Temporal
  - Monitored and adjusted
- Complements heuristics from existing systems

Approach

- Catalogue of molecular resistances
  - Mobile Genetic Elements
  - Species independent
  - Co-occurrences
- Specialised catalog per environment
  - Device, ward, hospital, city, country
  - Migration from other environments
  - Emergence from new sequences


off-line
genetic expert system
rapid genetic testing
test design system
local genetic history
within hours
prescriber
tissue sample
test interpretation
evidence presentation

Rapid Testing System

- A system that quickly checks for genes of interest without culturing
- Easily adjustable to new genes, tests
- Most likely PCR (2 under development)

Why PCR?

- PCR is a method for asking DNA yes/no questions for presence of sequence on interest
- Currently (likely always will be) cheaper than sequencing
- Cost per probe can be optimised further
  - [Hejlesen *et al.,* **DNA-Based Bayesian Inference and Analysis of Bacterial Antibiotic Resistance,** Scandinavian Health Informatics 2009]

– Exra probes can be used for monitoring

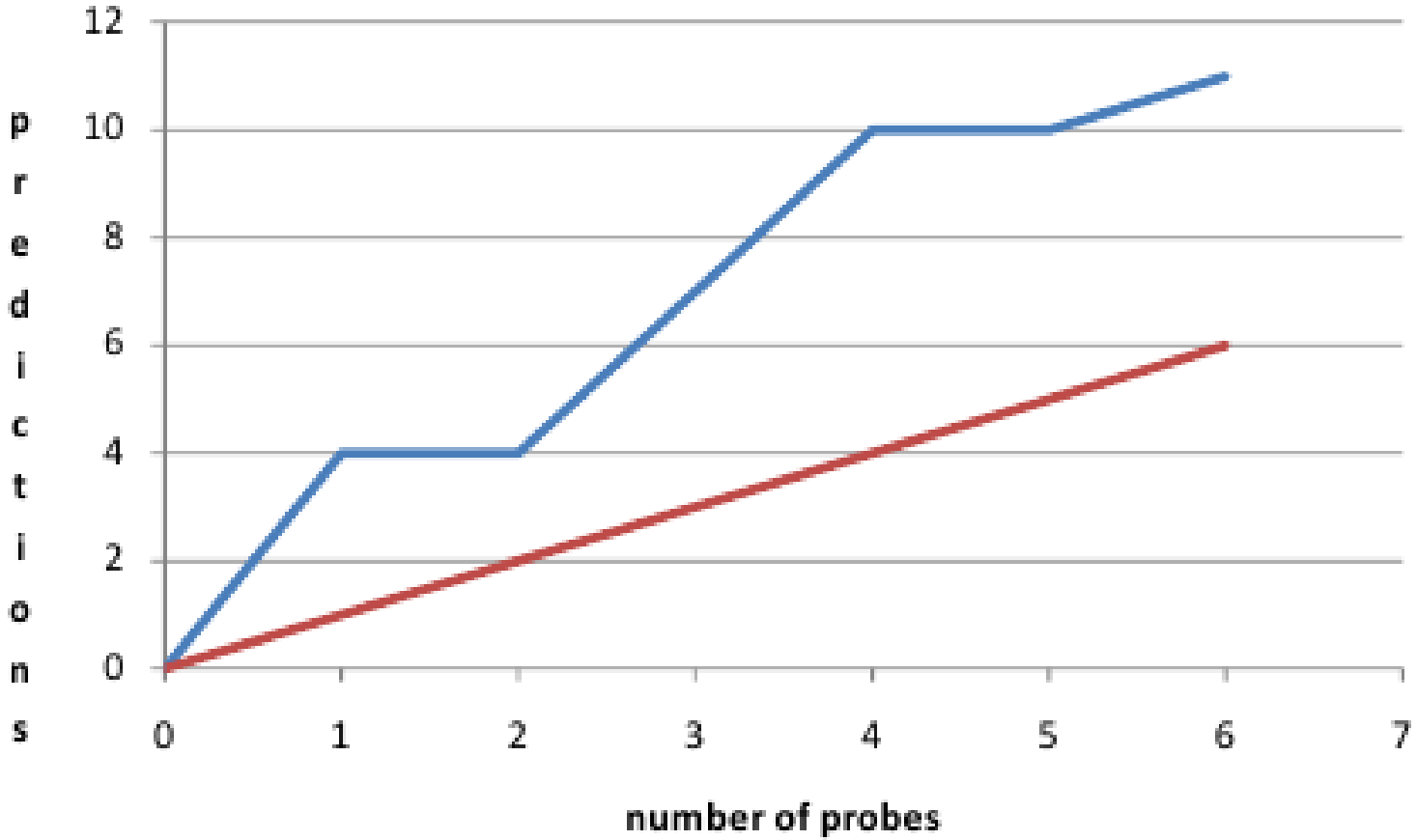
Offline set selection

- 2 structures
  1. 4 R genes: A, B, C, D
  2. 3 R genes: B, E, F
  3. 3 R genes: A, D, F
- C → B
- A → C
- B ↛ C
- AB ↛ C

$$P = \frac{O(A,B)}{O(A)}$$

	A	B	C	D	E	F
A	2	1	1	2		1
B		2	1	1	1	1
C			1	1		
D				1		1
E					1	1
F						1

Post-test results extrapolation



Results Interpretation - Example

Offline selected probes (5/270):

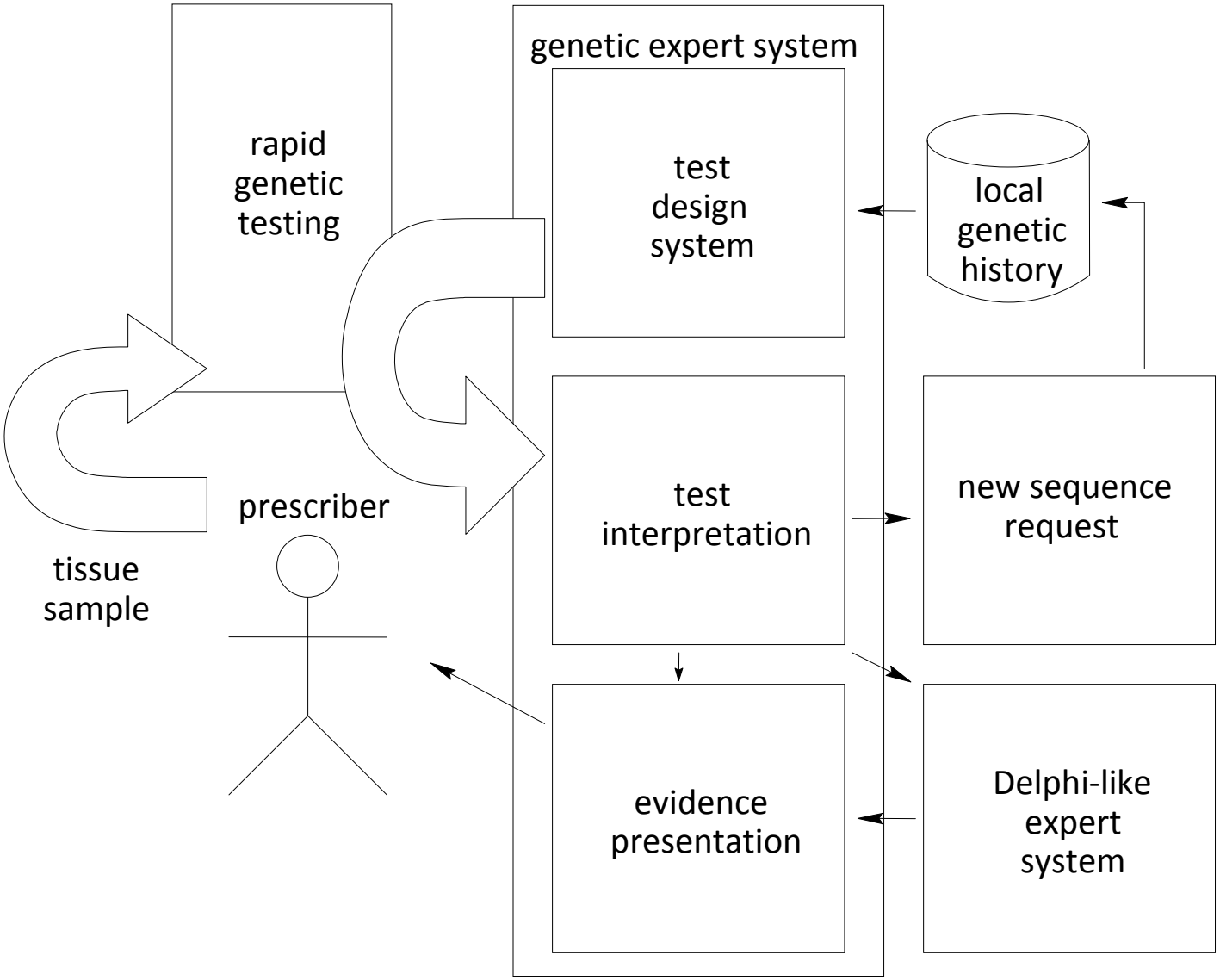
aadB1a aacA4 dfrB17 blaVIM-1 dfrA1

Rapid test returns

x x x

Interpretation adds

blaOXA-10 dfrB1 dfrB2 aadB


genetic expert system
rapid genetic testing
test design system
local genetic history
test interpretation
new sequence request
prescriber
tissue sample
evidence presentation
Delphi-like expert system

Thank You …

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