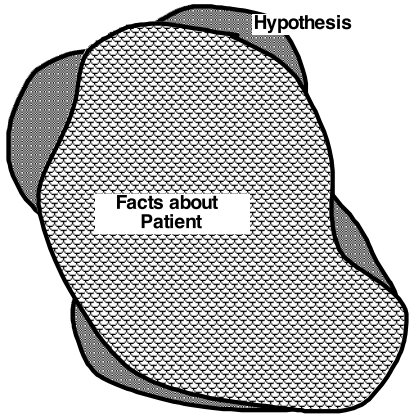
Decision Support via Expert Systems

6.872/HST950

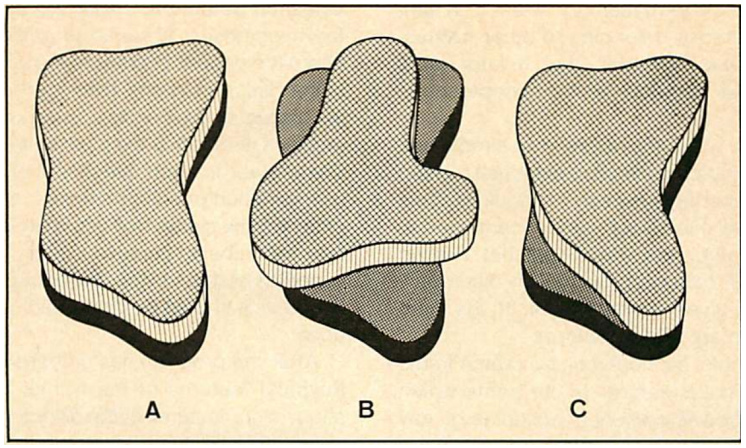
Peter Szolovits

Taking the Present Illness—Diagnosis by Pattern Directed Matching



Matching as Basis for Reasoning

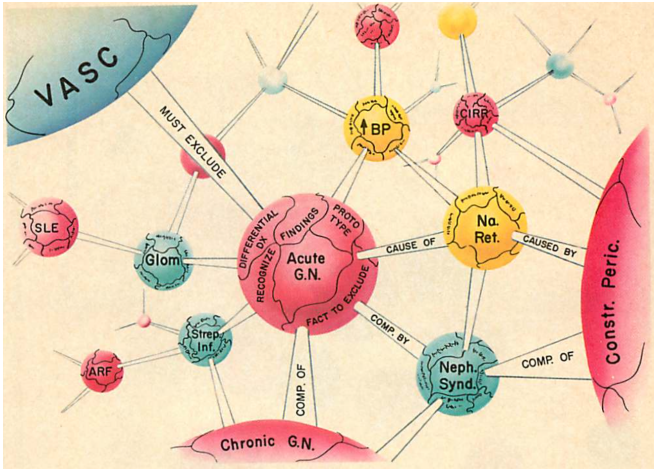
Pauker, S. G., Gorry, G. A., Kassirer, J. P., & Schwartz, W. B. (1976). Towards the simulation of clinical cognition. Taking a present illness by computer. The American Journal of Medicine, 60(7), 981–996.



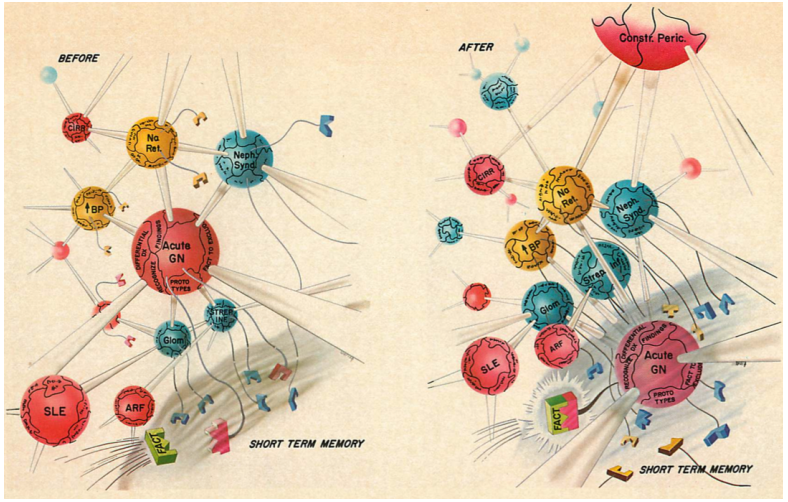
PIP's Theory of Diagnosis

- **From initial complaints, *guess* suitable hypothesis.**
- **Use current active hypotheses to guide questioning**
- **Failure to satisfy expectations is the strongest clue to a better hypothesis; *differential diagnosis***
- **Hypotheses are *activated, de-activated, confirmed* or *rejected* based on**
  (1) logical criteria
  (2) probabilities based on:
  findings local to hypothesis
  causal relations to other hypotheses

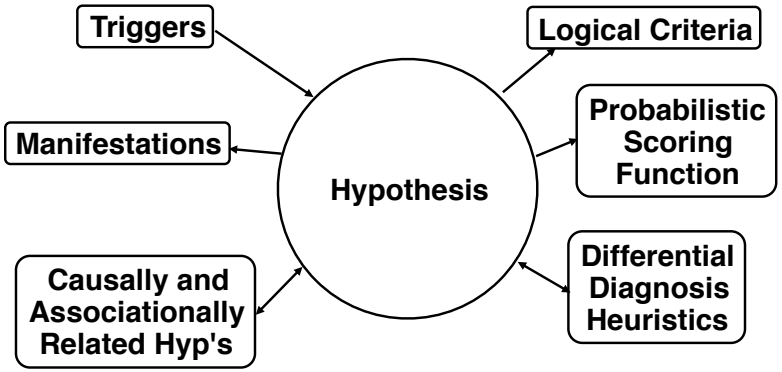
Present Illness Program (PIP) Model of Memory



Active Pattern Matching in PIP



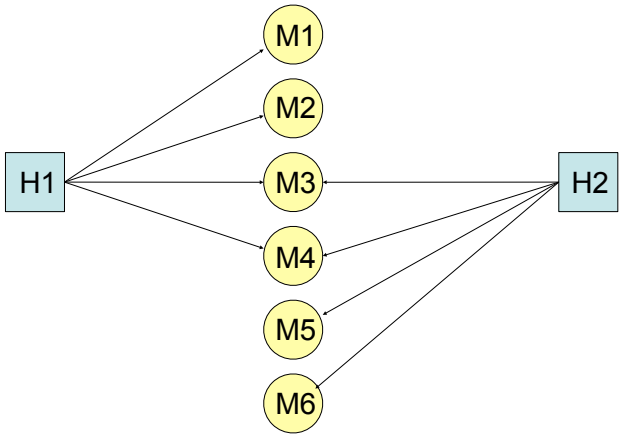
Memory Structure in PIP



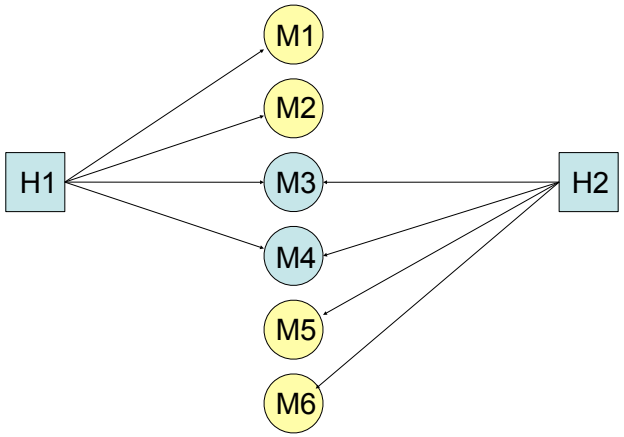
PIP's Model of Nephrotic Syndrome

NEPHROTIC SYNDROME, *a clinical state*
FINDINGS:
1* Low serum albumin concentration
2. Heavy proteinuria
3* >5 gm/day proteinuria
4* Massive symmetrical edema
5* Facial or peri-orbital symmetric edema
6. High serum cholesterol
7. Urine lipids present
IS-SUFFICIENT: Massive pedal edema & >5 gm/day proteinuria
MUST-NOT-HAVE: Proteinuria absent
SCORING . . .
MAY-BE-CAUSED-BY: AGN, CGN, nephrotoxic drugs, insect bite, idiopathic nephrotic syndrome, lupus, diabetes mellitus
MAY-BE-COMPLICATED-BY: hypovolemia, cellulitis
MAY-BE-CAUSE-OF: sodium retention
DIFFERENTIAL DIAGNOSIS:
neck veins elevated ➠ constrictive pericarditis
ascites present ➠ cirrhosis
pulmonary emboli present ➠ renal vein thrombosis

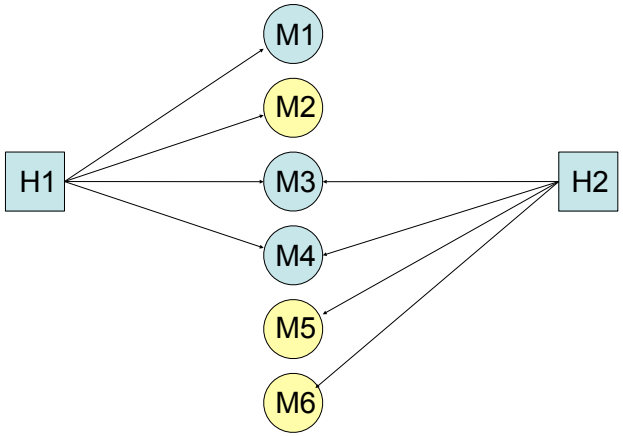
QMR Partitioning



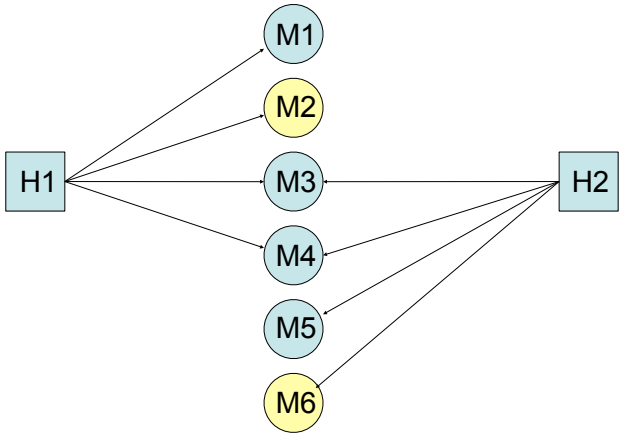
Competitors



Still Competitors



Probably Complementary



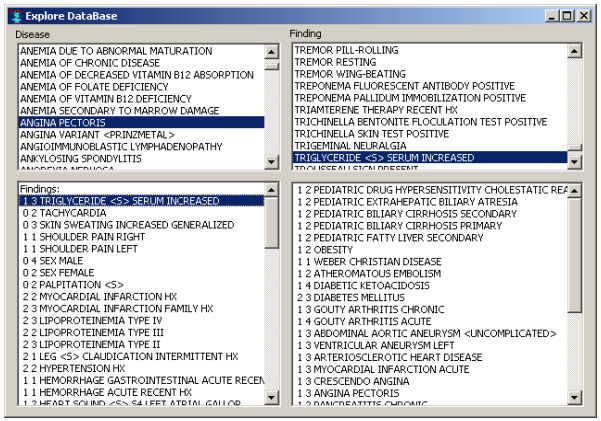
Multi-Hypothesis Diagnosis

- Set aside complementary hypotheses
- … and manifestations predicted by them
- Solve diagnostic problem among competitors
- Eliminate confirmed hypotheses and manifestations explained by them
- Repeat as long as there are coherent problems among the remaining data

Internist/QMR

- Knowledge Base:
  - 956 hypotheses
  - 4090 manifestations (about 75/hypothesis)
  - *Evocation* like P(H|M)
  - *Frequency* like P(M|H)
  - *Importance* of each M
  - *Causal relations* between H's
- Diagnostic Strategy:
  - Scoring function
  - Partitioning
  - Several questioning strategies

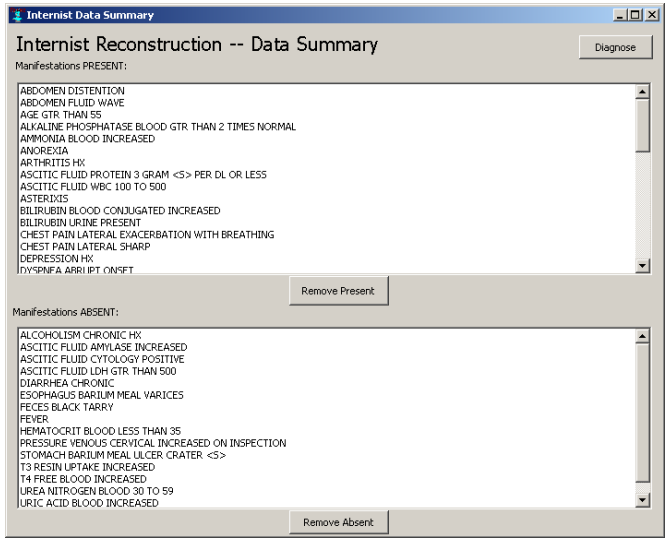
QMR Database



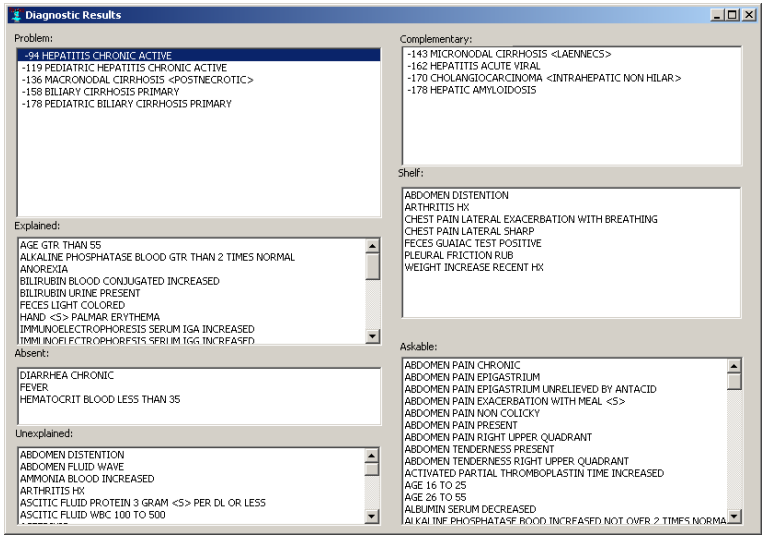
QMR Scoring

- Positive Factors
  - Evoking strength of observed Manifestations
  - Scaled Frequency of causal links from confirmed Hypotheses
- Negative Factors
  - Frequency of predicted but absent Manifestations
  - Importance of unexplained Manifestations
- Various scaling parameters (roughly exponential)

Example Case

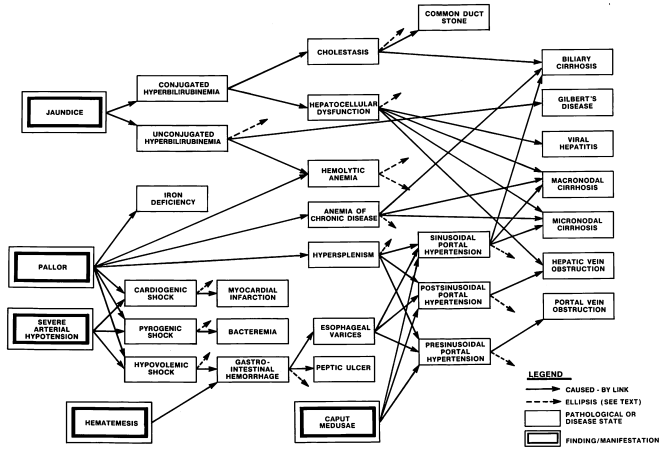


Initial Solution

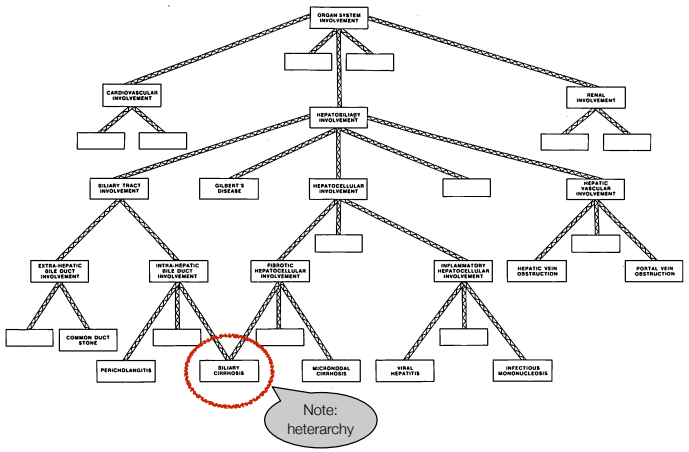


Pople's Caduceus
(proposed successor to Internist)

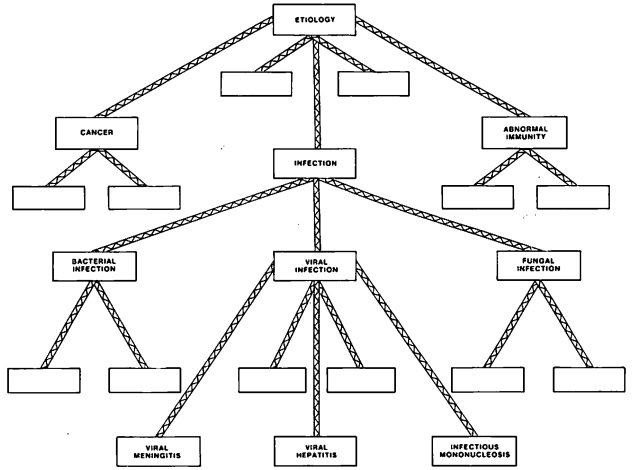
Causal Network has disease states and findings



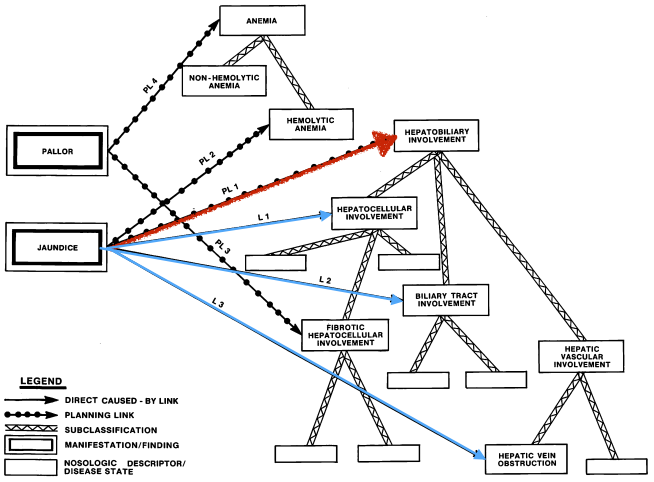
Diseases may be organized by **organ system** or etiology (cause)



Diseases may be organized by organ system or **etiology** (cause)



"Planning Links" abstract over ambiguous causal relations

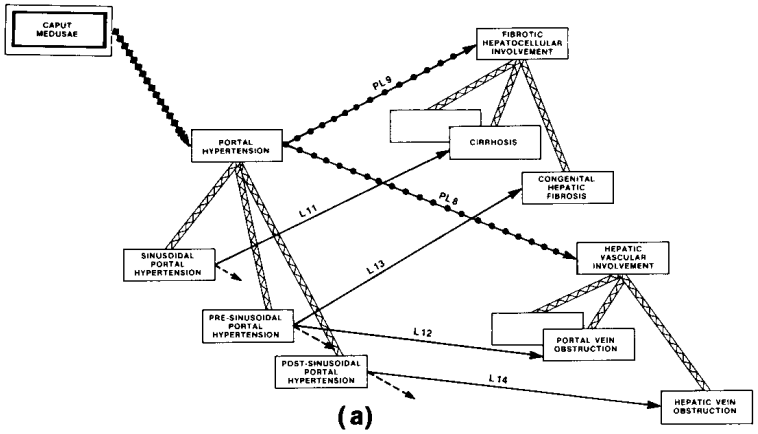


Diagnostic Tasks

- Determine which sub-categories or individual diseases in a nosology is the correct classification
- Determine which disease or disease category is the most appropriate cause of a symptom

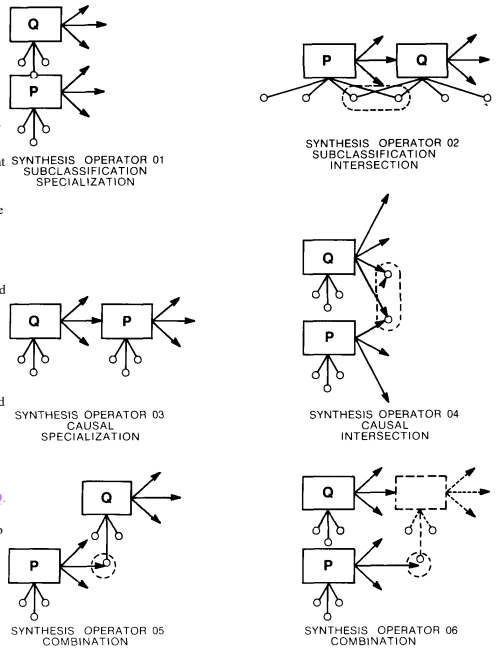
- Insight: *Possible to combine/interleave both tasks*

Explaining Caput Medusae involves both finding subtype of portal hypertension and its cause



Synthesis Operators

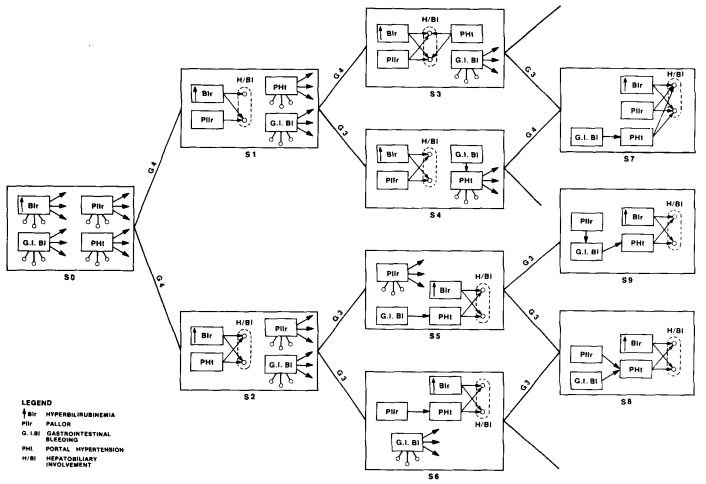
a) Descriptors P and Q might define sub-classification tasks that are related via some nosological structure; e.g.:
O1) P might be a sub-classifier of Q, in which case we say that P is a specialization of Q. In this case, the result of applying the intersection operator to P and Q is just the descriptor P.
O2) If neither P nor Q is a specialization of the other, but their differential diagnosis lists have sub-nodes in common[2a] then the result of intersection is just the list of common sub- nodes.
b) Descriptors P and Q might define causal tasks that are related via the pathophysiological network structure; e.g.:
O3) P might describe a state that is a cause of Q. As in O1 above, the result of applying the intersection operator to these two descriptors would he just the descriptor P.
O4) P and Q might not be causally related to one another, but have common causes among elements of their differential diagnosis lists. The synthesized differential diagnosis list would contain all and only these common elements.
c) Descriptors P and Q might be related through some combination of causal and subclassification tasks; e.g.,
O5) P might be causally linked to one or more sub-classifier nodes of Q. The resulting synthesized differential diagnostic task would be to decide among the selected sub-classifiers of Q. There would also be a reduced causal task associated with P.
O6) P and Q or their sub-classifiers might be causally related to identical nodes, or to nodes that are specializations of one another in some nosology. The causal tasks associated with P and Q resulting from application of the intersection operator would be the most specialized set of common causes.



Operators Formulate a Search Space

- Diagnosis is a search through the space of all hypotheses reachable by applying operators to the initial formulation
- Vast space, hence greedy search
- Driven by some measure of merit, similar to Internist's scoring:
  - How well important symptoms are explained
  - How likely are combinations of causes
  - How specific are hypotheses
  - "Okham's Razor"
  - *details were not well worked out*

Exploring the Search Space



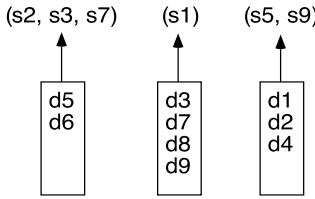
Symptom Clustering for Multi-Disorder Diagnosis

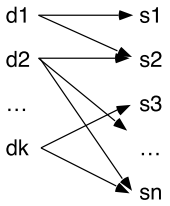
— Tom Wu, Ph.D. 1991

Assume a bipartite graph representation of diseases/ symptoms

Given a set of symptoms, how to proceed?

If we could "guess" an appropriate clustering of the symptoms so that each cluster has a single cause …





… then the solution is (d5, d6) x (d3, d7, d8, d9) x (d1, d2, d4)

Clustering Alternatives

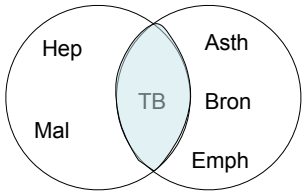
Symptom	Possible Causes
Fever	TB, Hepatitis, Malaria
Cough	TB, Asthma, Bronchitis, Emphysema

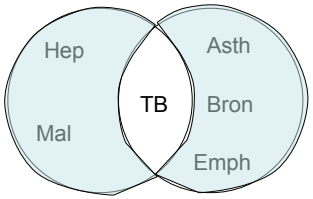
H1

Fever, Cough
TB

H2

Fever	Cough
Hep Mal	Asth Bron Emph





Synopsis in Renal Disease

- Diseases
  - Hypertension (HTN)
  - Acute glomerulonephritis (AGN)
  - IgA nephropathy (IgA)
  - Prerenal azotemia (PRA)
  - Hepatorenal syndrome (HRS)
  - Renal vasculitis (RV)
  - Congestive heart failure (CHF)
  - Aldosteronism (Aldo)
  - Constrictive pericarditis (Peri)
  - Diabetic ketoacidosis (DKA)
  - Analgesic nephropathy (AN)
  - Hypokalemic nephropathy (HKN)
  - Chronic renal failure (CRF)
- Symptoms
  - High urine osmolality (Osm↑)
  - High urine specific gravity (Sg↑)
  - Low urine sodium (Na↓)
  - Low urine pH (pH↓)

	HTN	AGN	IgA	PRA	HRS	RV	CHF	Aldo	Peri	DKA	AN	HKN	CRF	RTA
Osm↑	X	X	X	X	X	X								
Sg↑	X	X	X	X	X	X	X							
Na↓				X	X		X	X	X					
pH↓		X		X						X	X	X	X	X

After Osm↑

Osm↑
HTN AGN IgA PRA HRS RV

	HTN	AGN	IgA	PRA	HRS	RV	CHF	Aldo	Peri	DKA	AN	HKN	CRF	RTA
Osm↑	X	X	X	X	X	X								
Sg↑	X	X	X	X	X	X	X							
Na↓				X	X		X	X	X					
pH↓		X		X						X	X	X	X	X

Osm↑, Sg↑
HTN AGN IgA PRA HRS RV

Add Sg↑

Cover

	HTN	AGN	IgA	PRA	HRS	RV	CHF	Aldo	Peri	DKA	AN	HKN	CRF	RTA
Osm	X	X	X	X	X	X								
Sg↑	X	X	X	X	X	X	X							
Na↓				X	X		X	X	X					
pH↓		X		X						X	X	X	X	X

Add Na↓

Restrict

Osm↑, Sg↑, Na↓
PRA HRS

or

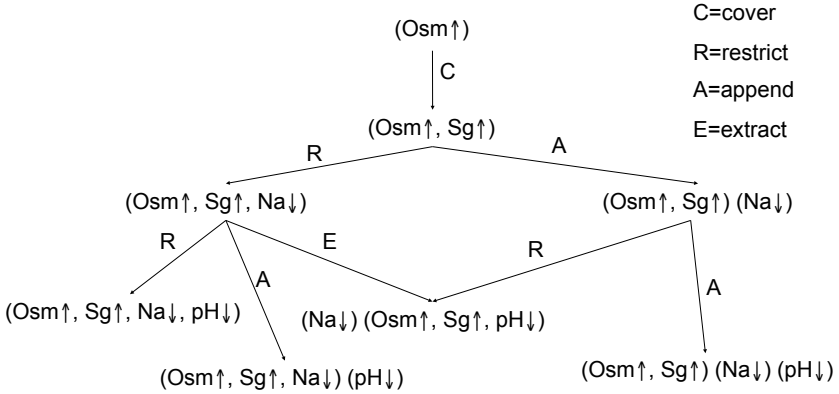
Append

Osm↑, Sg↑
HTN AGN IgA RV

Na↓
Aldo CHF Peri

	HTN	AGN	IgA	PRA	HRS	RV	CHF	Aldo	Peri	DKA	AN	HKN	CRF	RTA
Osm	X	X	X	X	X	X								
Sg↑	X	X	X	X	X	X	X							
Na↓				X	X		X	X	X					
pH↓		X		X						X	X	X	X	X

Search Space



C=cover
R=restrict
A=append
E=extract

	HTN	AGN	IgA	PRA	HRS	RV	CHF	Aldo	Peri	DKA	AN	HKN	CRF	RTA
Osm	X	X	X	X	X	X								
Sg↑	X	X	X	X	X	X	X							
Na↓				X	X		X	X	X					
pH↓		X		X						X	X	X	X	X

Symptom Clustering is Efficient

- **Like in any "planning island" approach, reducing an exponential problem to several smaller exponential problems vastly improves efficiency, *if it captures some insight into the problem.***
- **Wu's algorithm (SYNOPSIS) will keep a compact encoding even if it overgenerates slightly.**
  - **E.g., suppose that of the set of diseases represented by (d5, d6) x (d3, d7, d8, d9) x (d1, d2, d4), d6 x d8 x d1 is not a candidate. To represent this precisely would require enumerating the 23 valid candidates. Instead, the factored representation is kept.**

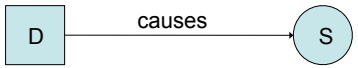
In a diagnostic problem drawn from a small subset of the Internist database, it is a *power of 3* faster and a *power of 5* more compact than standard symptom clustering.

Guide search via probabilities, if we have a reasonable model(!)

More Expert Systems

- Causality?
- What's in a Link?
- Temporal reasoning
- Quantitative reasoning
- Model-based reasoning
- Workflow

Meaning of Representation?

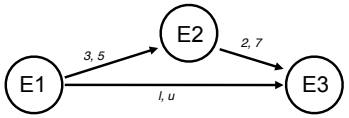


- Always? →probability
- Magnitude? →severity; bad cold → worse fever?
- Delay? →temporality
- Where? →spatial dependency
- Under what conditions? →context
- Interaction of multiple causes →physical laws
- Cross-terms →high-dimensional descriptions

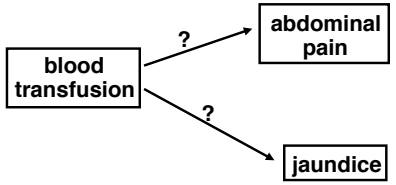
Temporal Reasoning

- **Keeping track of multiple forms of temporal relations (Kahn '75)**
  - **The time line**
    - **"On Dec. 12 last year . . ."**
  - **Special reference events**
    - **"Three days after I was hospitalized in 1965 . . ."**
  - **Temporal Ordering Chains**
    - **"It must have been before I graduated from high school."**
- **Constraint propagation (Kohane '87)**
  - **Primitive relation: e1, e2, *l*ower, *u*pper bounds**
  - **Heuristics for propagation based on semantic grouping**

$3 \le T(E2)-T(E1) \le 5$
$2 \le T(E3)-T(E2) \le 7$
Therefore
$l=5 \le T(E3)-T(E1) \le 12=u$

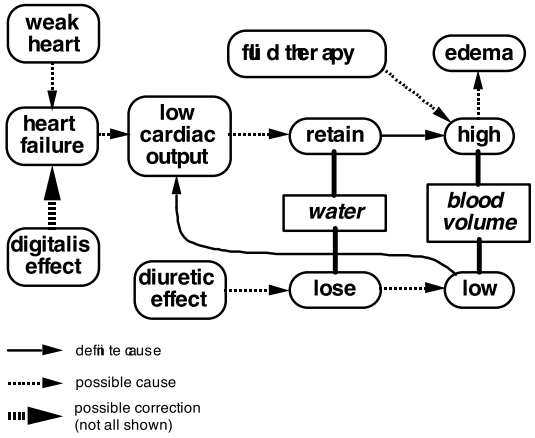


Exploiting Temporal Relations

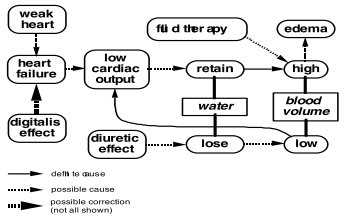


- transfusion precedes both abdominal pain and jaundice *implies* transfusion-borne acute hepatitis B
- as in 1, but only by one day
- jaundice occurred 20 years ago, transfusion and pain recent
- Can be very efficient at filtering out nonsense hypotheses.

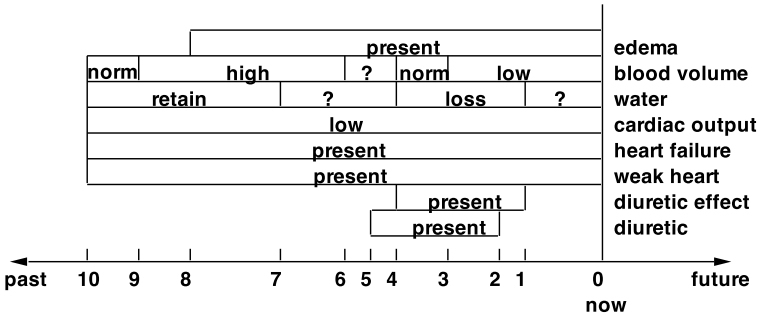
Interpreting the Past with a Causal/Temporal Model



Postdiction



Long, Reasoning about State from Causation and Time in a Medical Domain, *AAAI 83*



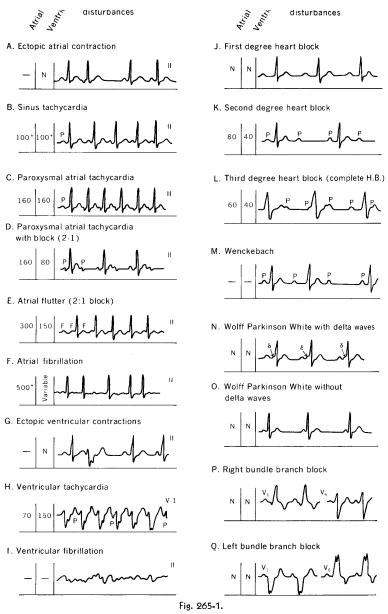


Fig. 265-1.

Temporal Representation can be Complex

Signal-to-symbol problem

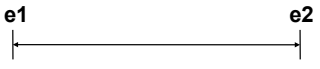
E.g., Zeeshan Syed's PhD:

1. Time-align signals via dynamic time warping
2. Cluster patterns
3. Assign symbolic name to each cluster

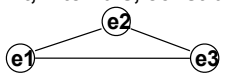
Time

The usual:

- **point, intervals, constraints**



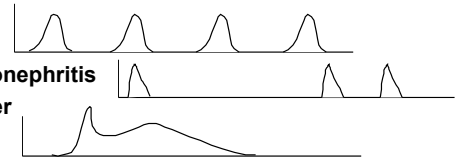
min ≤ duration ≤ max



- **timelines, reference events, fuzz, …**

The unusual

- **cyclic edema**
- **focal glomerulonephritis**
- **patterns of fever**



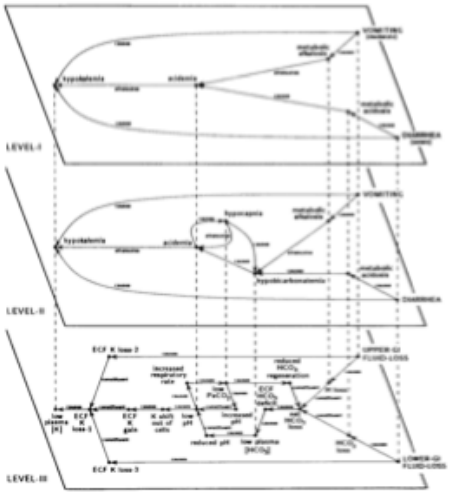
Systems issues

- **flow of "now"**
- **supporting the illusion of "instantaneous" decision-making within a temporal reasoner**
  - **correcting the past**
  - **reasoning by hindsight**

The Surprisingly Normal pH

- Diarrhea causes bicarbonate (alkali) loss
- Vomiting causes acid loss
- Therefore, normal pH is a manifestation of {diarrhea + vomiting}!

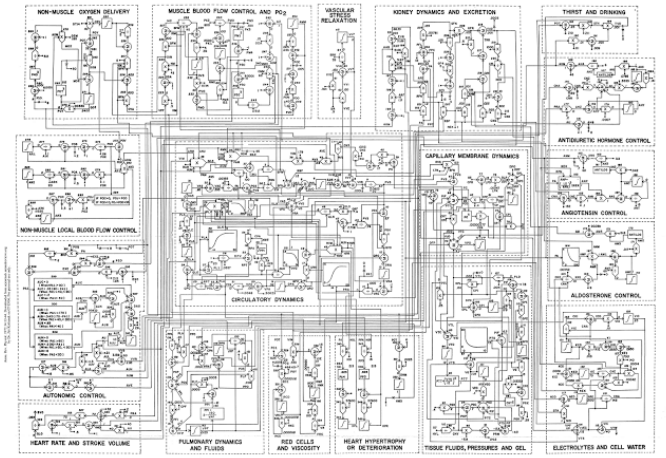
Multi-Level Causal Model



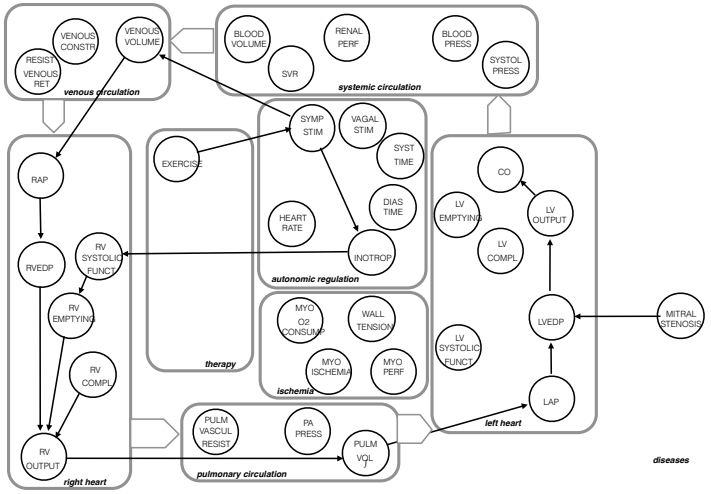
Reasoning from Models

- Model handles all possible interactions, without having explicitly to anticipate them all
- Reasoning: Fit parameters to a physiological model, then predict consequences to suggest
  - other expected findings
  - reasonable interventions
- Qualitative models
- Combining associational and model-based reasoning

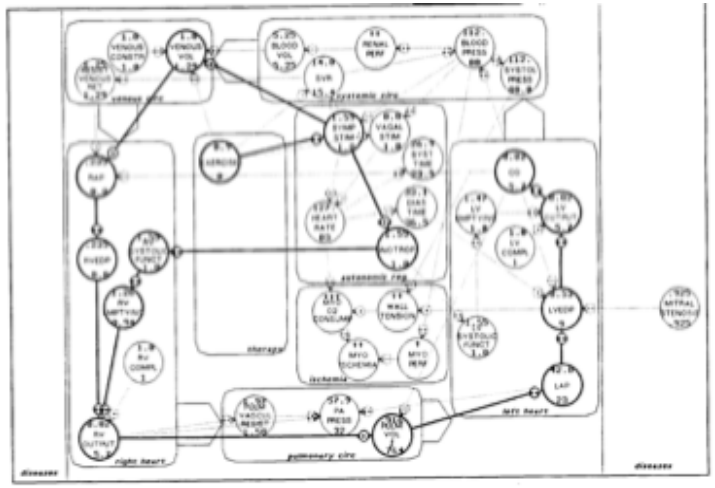
Guyton's Model of Cardio-vascular Dynamics



Heart Disease Model



Long's Clinical Model of Heart Failure
Predictions for Mitral Stenosis with Exercise



Physiological

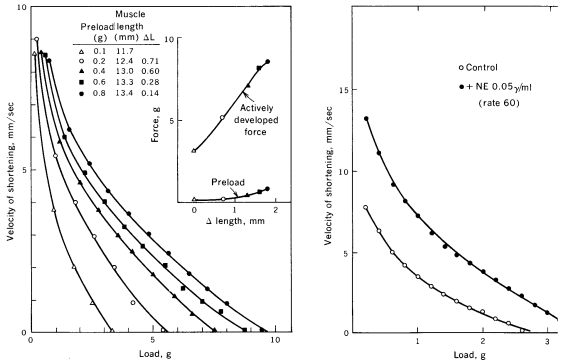
"All variations in myocardial contractile activity can be expressed as displacements of the force-velocity curve. However, there are two fundamental ways in which the force-velocity curve can be shifted. Figure {left} shows a family of force-velocity curves obtained from an isolated cardiac muscle; each curve was obtained at a different preload, i.e., with a different degree of stretch on the muscle. Note that changing the preload has altered the intercept of the force-velocity curve on the horizontal axis; i.e., it has increased the isometric force developed by the muscle. However, these alterations in preload have not altered the intrinsic velocity of shortening, since all the curves extrapolate to the same intercept on the vertical axis. Thus, a change in initial length of heart muscle shifts the force-velocity curve by altering the total force which can be developed by the muscle.

This type of shift in the force-velocity curve may be contrasted with that obtained when a positive inotropic agent, such as norepinephrine or digitalis, is added to the muscle while the initial length is held constant (Fig. {right}). These agents not only increase the force which the muscle is capable of lifting, i.e., the intercept of the force-veolocity curve on the horizontal axis, but also increase the velocity of shortening of the unloaded muscle, i.e., the extrapolated intercept on the vertical axis."

— Harrison's (6th ed.)

Figures

Normal cat-muscle **Inotropic Agent**



Clinical Knowledge

"… from the clinical point of view, heart failure may be considered to be a disease state in which an abnormality of myocardial function is responsible for the inability of the heart to pump blood at a rate commensurate with the requirements of the metabolizing tissues. Though a defect in myocardial contraction always exists in heart failure, this disorder may result from a *primary abnormality* in the heart muscle or it may be secondary to a *chronic excessive work load*. It is important to distinguish heart failure from (1) states of *circulatory insufficiency* in which myocardial function is not primarily impaired, such as cardiac tamponade, hemorrhagic shock, or tricuspid stenosis, (2) conditions in which there is *circulatory congestion* because of abnormal salt and water retention but in which there is no serious disturbance of myocardial function, and (3) conditions in which the normal heart is suddenly presented with a load which *exceeds its capacity*, e.g., accelerated hypertension."