A Bayesian Model for **Pediatric Chronic Pain**

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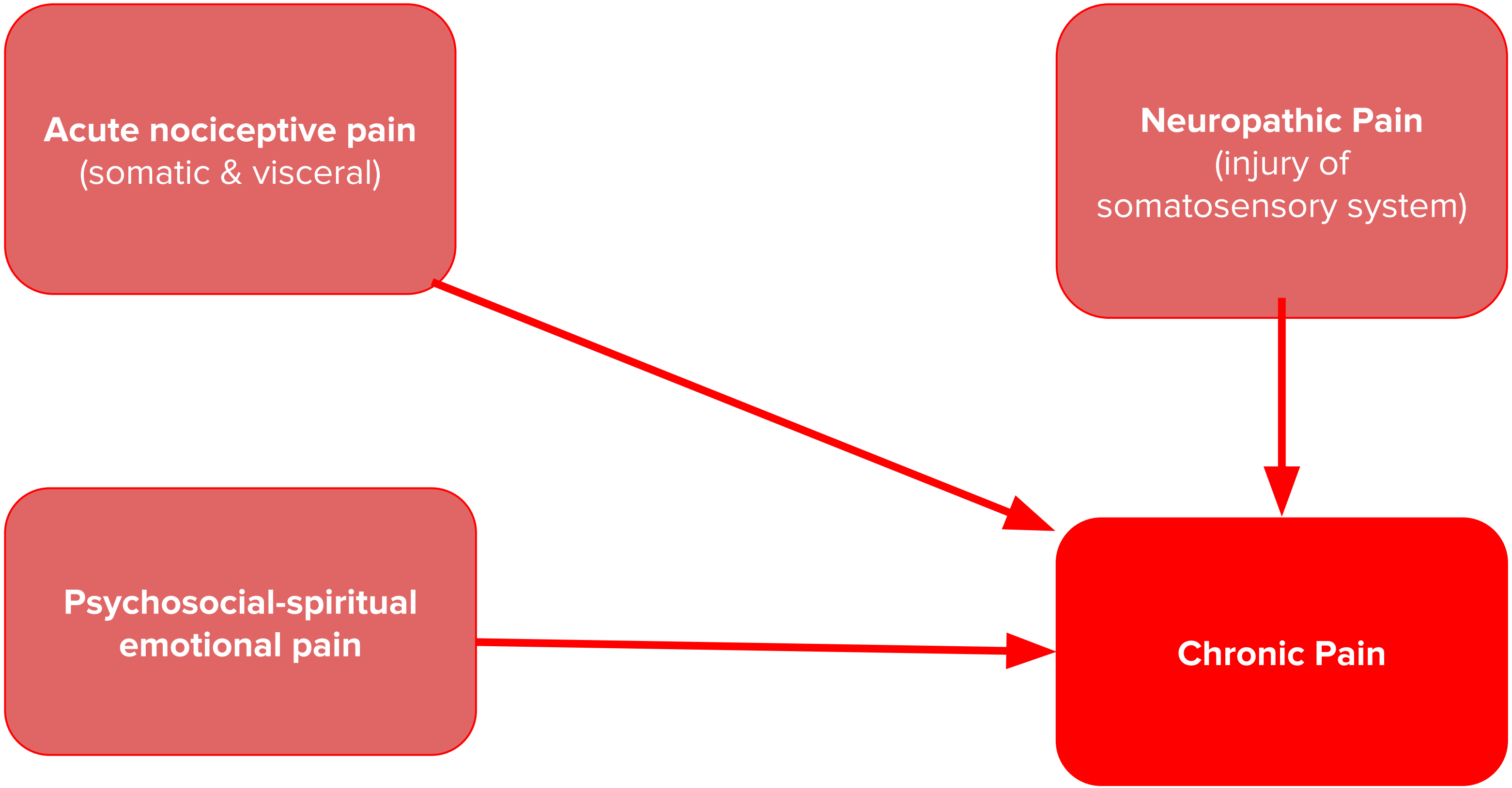


Acute nociceptive pain
(somatic & visceral)
Neuropathic Pain
(injury of somatosensory system)
Psychosocial-spiritual emotional pain
Chronic Pain

Epidemiology Pediatric chronic pain

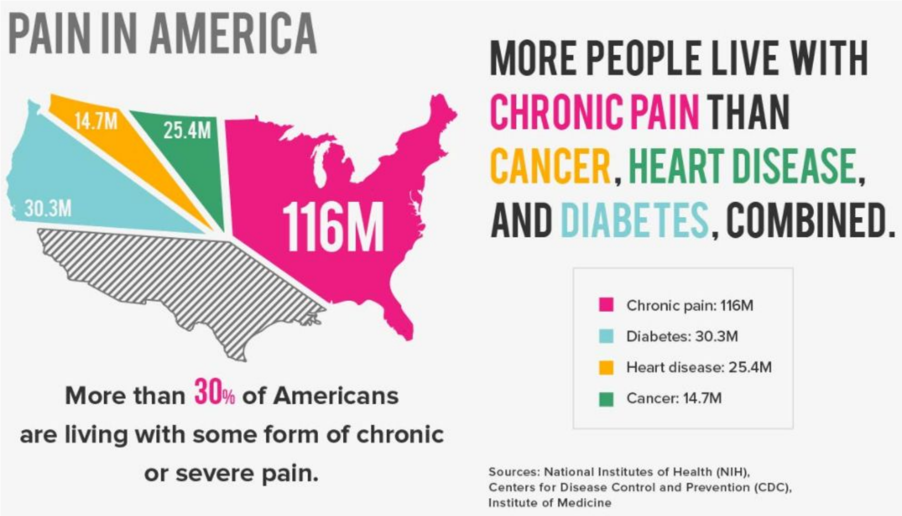
- Worldwide **3-5%** of children affected *(severely underdiagnosed)*
- 10% of hospitalized children show features of CP
- 3% disabled by pain, require **intensive treatment**

- **Time**-based definition: Pain that persists for **2** (Rome IV criteria) or **3** (ICD-10) months
- **Functional** definition:

> "Pain that extends beyond the **expected period of healing**" and
> "Hence lacks the **acute warning function** of physiological nociception. "
>
> Turk & Okifuji; 2001

Economic impact Pediatric chronic pain

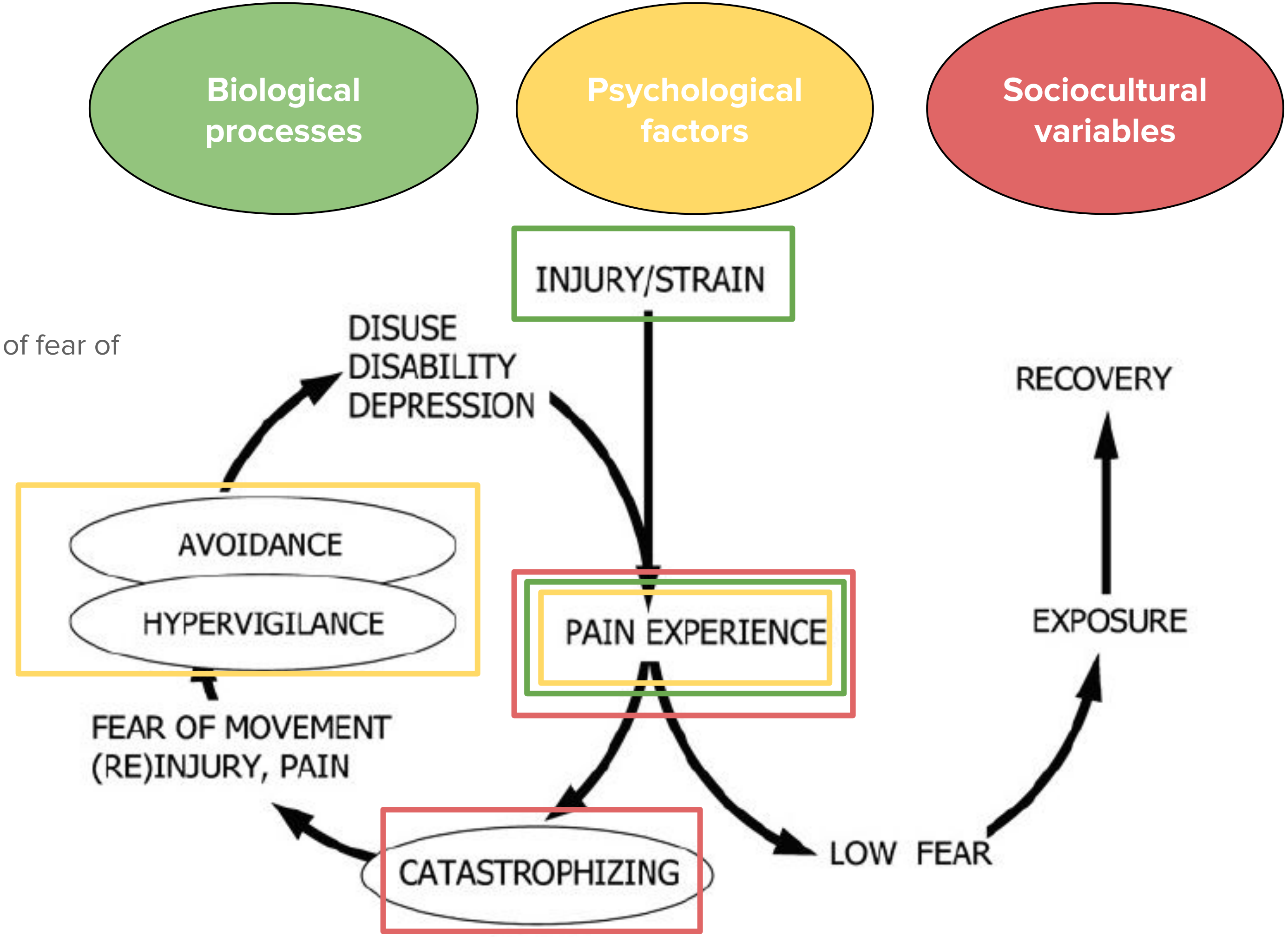
- $19.5 billion per year Groenewald et al., 2014
  - Health services; social services; informal care; productivity loss of child and parent
- High risk of persistence into adulthood
  - About ⅓, Walker et al., 2010
- $600 billion costs annually for adults with chronic pain



Etiology

Vlaeyen, 2000

Cognitive behavioral model of fear of movement injury



Case example: Liz

Biological processes

Psycho-logical factors

Socio-cultural variables

- Chronic abdominal pain for 5 years after acute inflammation
- Ever Since: fear/ avoidance of pain
- Terrible fights with single mother every morning before school
    - Missed substantial parts of grade 6-9

- Socially isolated; “outsider” among peer group
    - Aggressive behavior; narcissism

- Helplessness, frustration;
- Pressure, tension; productivity impaired (doctor visits; late for work)

- Decision to transfer Liz to private boarding school

Newer developments

The role of expectations for mental disorders
(Hechler, Endres & Thorwart, 2016; Rief et al., 2015)

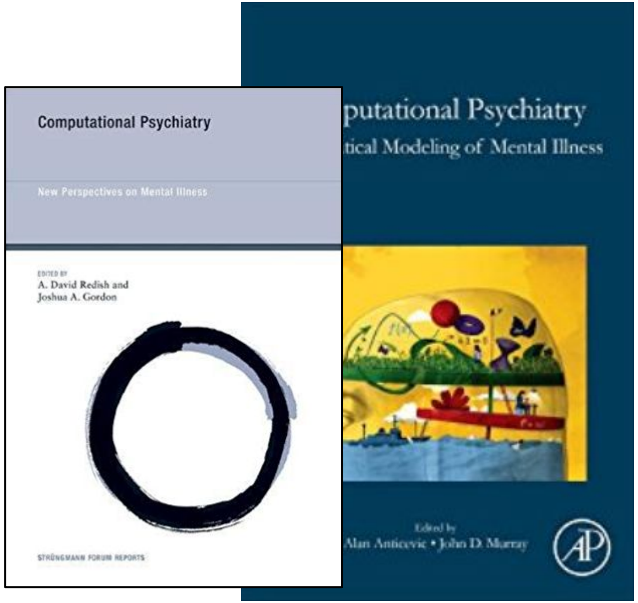
computational psychiatry

Interoceptive predictive coding theory of chronic pain

Computational psychiatry

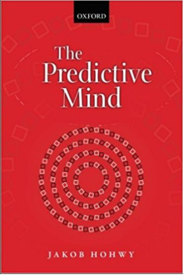
- Diagnostic categories: **empirical basis** unclear
- Treatment selection: **“educated guessing”** (Huis, Maia & Frank, 2016)
- Connects neurosciences and psychiatry/ clinical psychology
- **Data driven approach**
  - Machine-learning methods on high-dimensional data
  - Improve disease classification
  - Predict treatment outcomes
  - Improve treatment selection

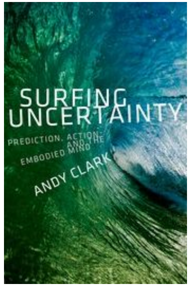
- **Theory driven approach**
  - Use models to represent underlying mechanisms
  - Rely on prior knowledge, explicit hypotheses



Expectations and predictions

- Discussed as **"core features of mental disorder"** Rief et al., 2015
  - Especially **persisting expectations**
  - No modification of expectation/ learning - despite **alternative evidence**
  - Maladaptive anticipatory responses
- Emergence of an **entire framework** focusing on the role of expectations/ predictions
- What is predictive coding?





Prediction Error framework

World represented in top-down predictions of sensory input

Brain is a prediction testing machine

Predictions query the world
→ **"Predictions + sensations influence perceptions"**

Goal: minimize prediction error
→ **Predictions determine sensations**

Ancient "representational" view

Senses form **representations** of world

Brain soaks everything up in a passive **bottom up** manner (S-R organ)

Only sensations produce perception

Top Down signals: only as feedback from the cognitive system on the signal

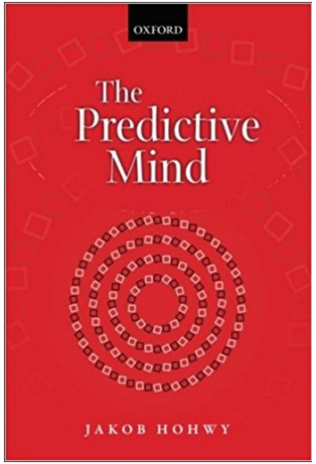
Predictive Coding...

Minimizing prediction error:

1. Change prior predictions
2. Move the body (active inference)
3. Sample sensory input differently

Both **action and perception** are active processes, serving to **minimize error**

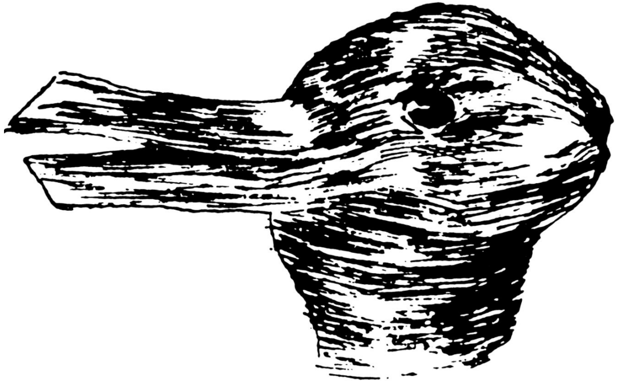
Associated: **Bayesian Brain** (eg Doya) and **Free energy** (Friston)



Hohwy, 2013

Predictive Coding...

... some examples you might already know



Interoceptive Predictive Coding

Seth, 2013; Seth & Friston, 2016; Barrett & Simmons, 2015

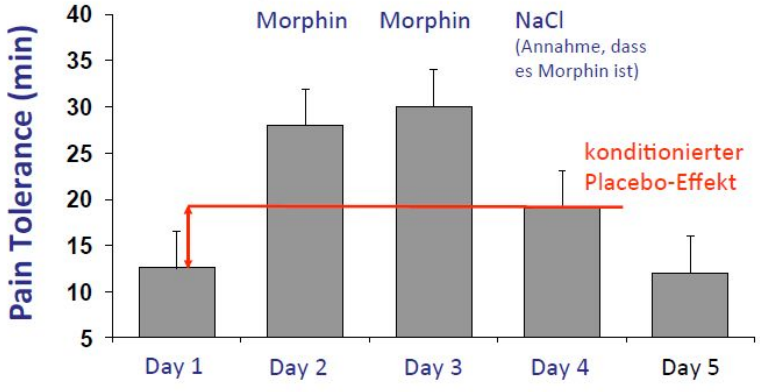
- So far: prediction drives perception of external world

- Interoceptive Predictive Coding:
    - Predictions (generated by models) also determine perception of interoceptive signals
- Interoceptive experiences are **limbic predictions** about the state of the body
    - [temperature; heart rate; glucose levels, inflammation; emotion; pain]
    - See EPIC model by Barrett & Simmons, 2015
- Visceromotor cortizes generates **hormonal and immunological predictions**
    - Body deploys autonomic, **metabolic and immunological** resources
    - Responses underlie **allostatic** and **anticipatory** principles
- What about Pain?

Chronic Pain & predictive brains

- Buchel et al.: 2014
- Brain is not waiting passively for nociceptive stimuli - it is **active**!
  - Predicting pain based on prior experiences and expectations
- **Expectations influence pain perception**

- **Well-known example:** “Placebo Analgesia” (Beh. med. lecture - Amanzio & Benedetti, 1999)
  - Placebo hypogesia
    - Decreased sensation of pain!



Quick reminder: Bayes' theorem

Conditional Probability
Likelihood of **A,** given **B** is true

"Posterior probability"

Conditional Probability
Likelihood of B, given A is true

"Likelihood"

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

Likelihood to observe **A**

Part of the *"Prior"*

Likelihood to observe **B**

Evidence for B

Bayesian Pain

- To what probability do we perceive pain **given** we experienced a sensation? (Hechler, Endres & Thorwart, 2016)

$$P(A|B) = \frac{P(B|A)\ P(A)}{P(B)}$$

- Let **A** be the **PAIN**
- Let **B** be the **SENSATION**...

Bayesian Pain

Active Inference and Learning

Represent beliefs about causal relationships between a sensation and pain

Likelihood

Pain perception

The Probability of Perceiving Pain given we have experienced a sensation

Posterior

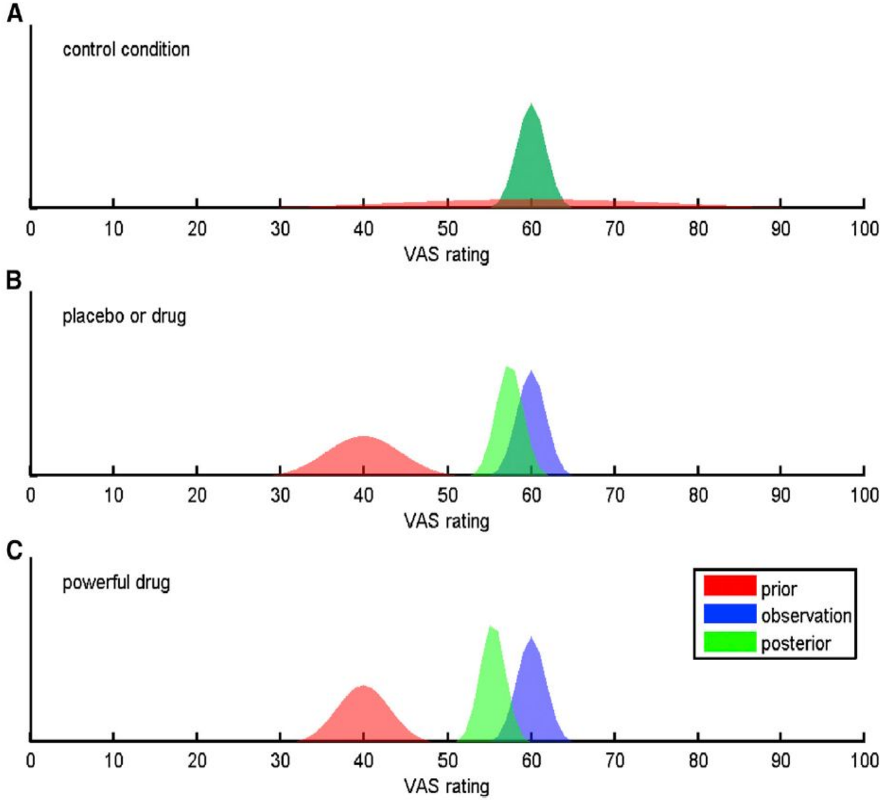
Prior probability of pain

$$p(pain \mid sensation) = \frac{p(sensation \mid pain) * p(pain)}{p(sensation)}$$

Probability of sensation

Bayesian Pain: Evidence

- Büchel et al., 2014 refering to Pollo et al, 2001
- Control Condition
  - Flat, uninformative prior
  - Perceived pain and sensual data: Match!
- B: Instruction: Either placebo or drug
  - Imprecise info → flat prior
  - Perceived pain smaller than sensual data
- C: Instruction: powerful analgesic drug
  - Narrow prior - precise information
  - Posterior distribution “moves” towards prior



What’s underlying chronic pain?

- Heightened anticipation of pain (as a cause for random sensation) $p(pain)$
- Dysfunctional longer term learning

  And active inference $p(sensation \mid pain)$

Pain perception

Active Inference and Learning

Prior probability of pain

$$p(pain \mid sensation) = \frac{p(sensation \mid pain) * p(pain)}{p(sensation)}$$

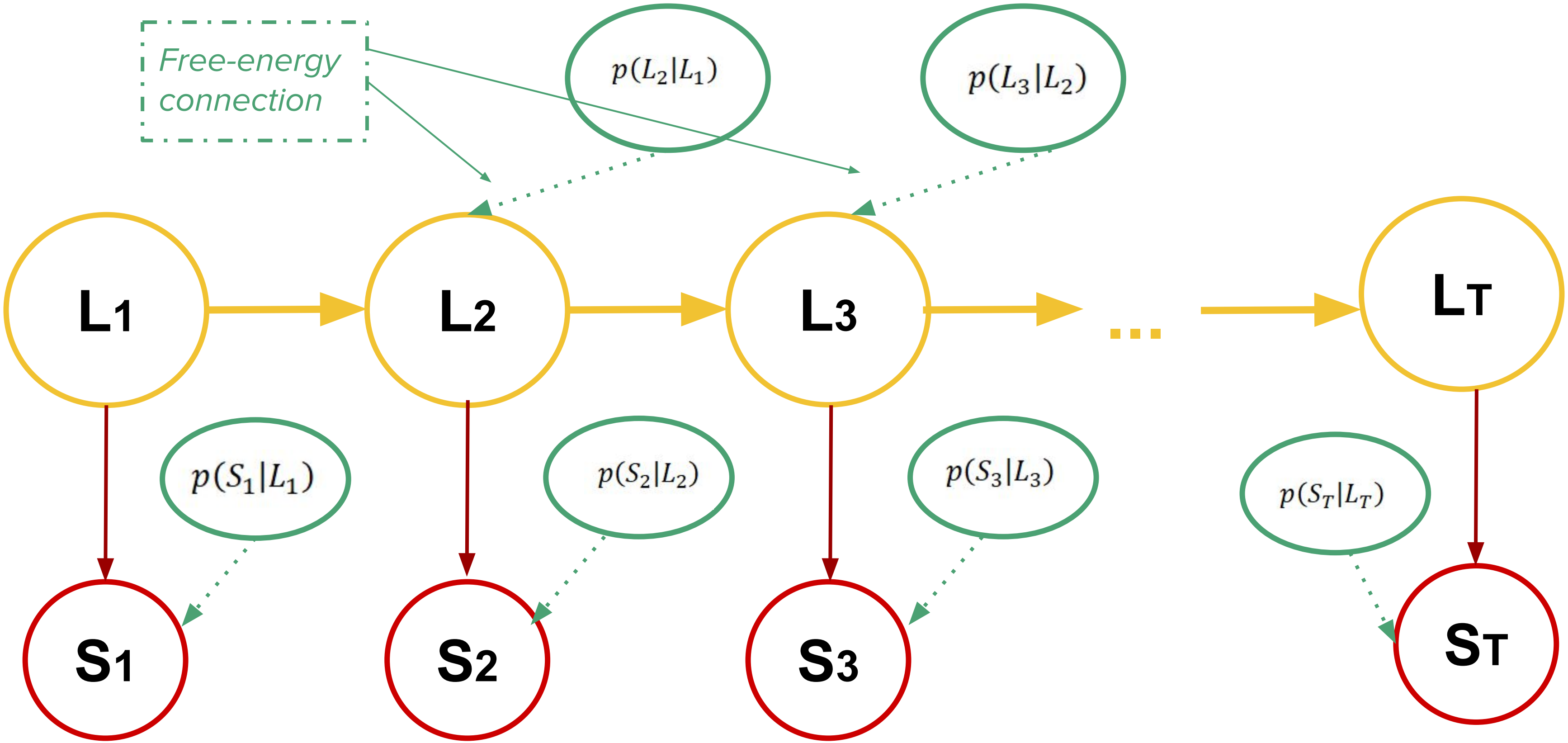
Prior probability of sensation

Hierarchical Model

- What we want to model:

- **Expectations** as a **time series** of (conditional) **probabilities**
  - Representing **increasing anticipation** of pain
    - Learning processes (conditioning)
    - Active inference ➔ actions generating pain (rubbing, muscle tension)
    - Attentional shifts
  - … even when confronted with harmless sensations

- Example of abdominal pain
  - latent conditions {hunger; stomach rumbling; pain}
  - sensations {stomach pain; pressure, bloating; nociception}
- Hierarchical Markov Model



Dysfunctional learning over time (Result of prior)/ altered learning rate?

Likelihood model messed up?

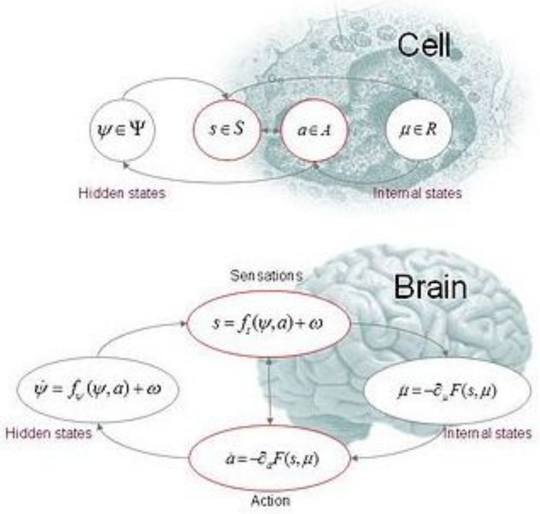
Active inference: implicitly value pain state?

L = Latent conditions
S = sensations

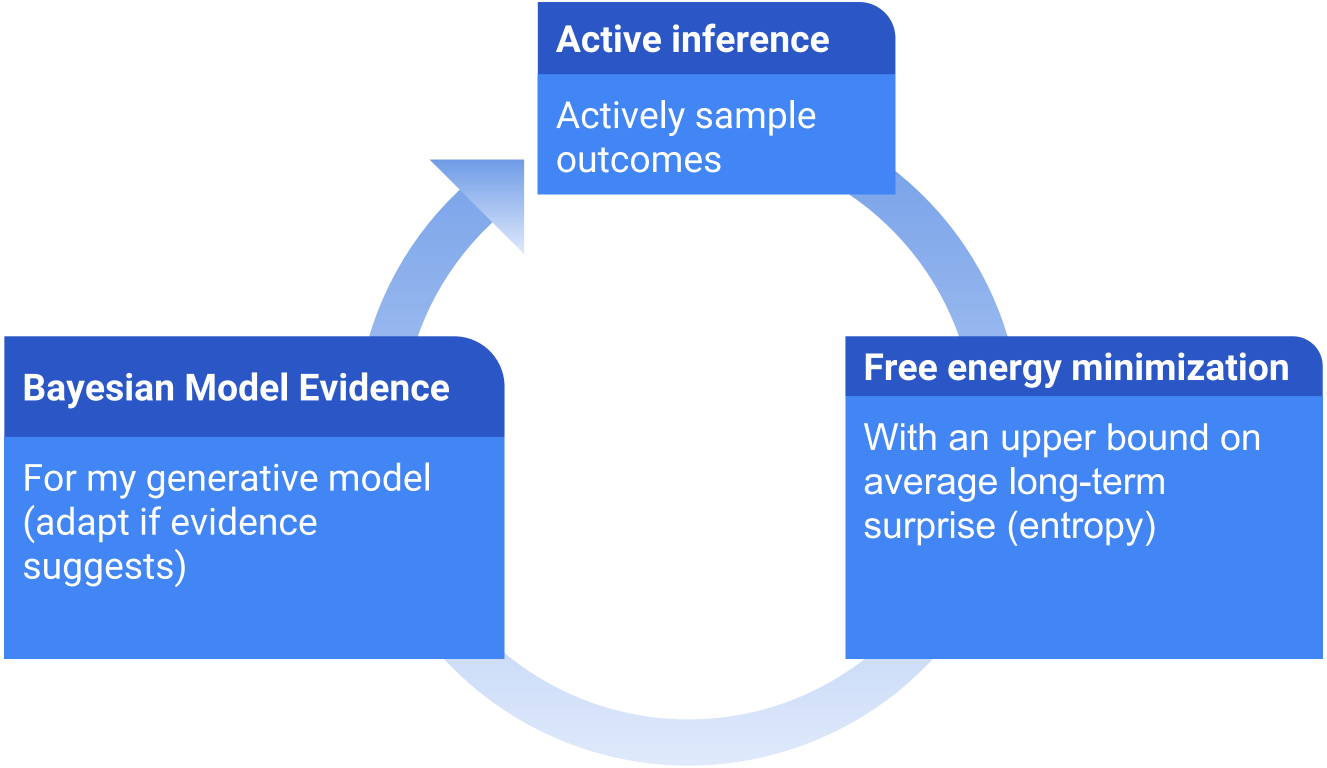
What's the Free Energy Principle?

- Karl Friston University College London
- Concept from thermodynamics

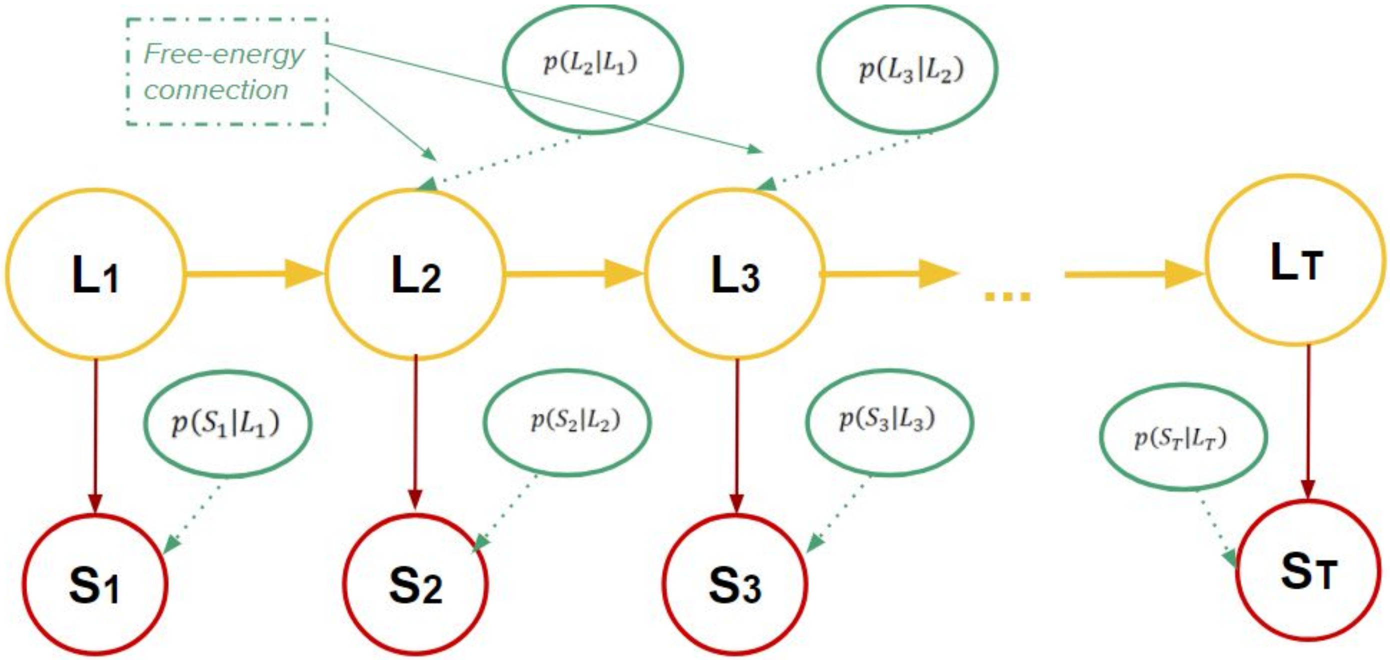
- Related to Prediction Error Framework
- Biological systems maintain their order
  - by minimizing an **internal free-energy functional**
  - Related to idea of a "**Bayesian model evidence**"
  - Goal is to minimize **entropy** (or "surprise")



What’s the Free Energy Principle?



Message passing in Bayesian Networks

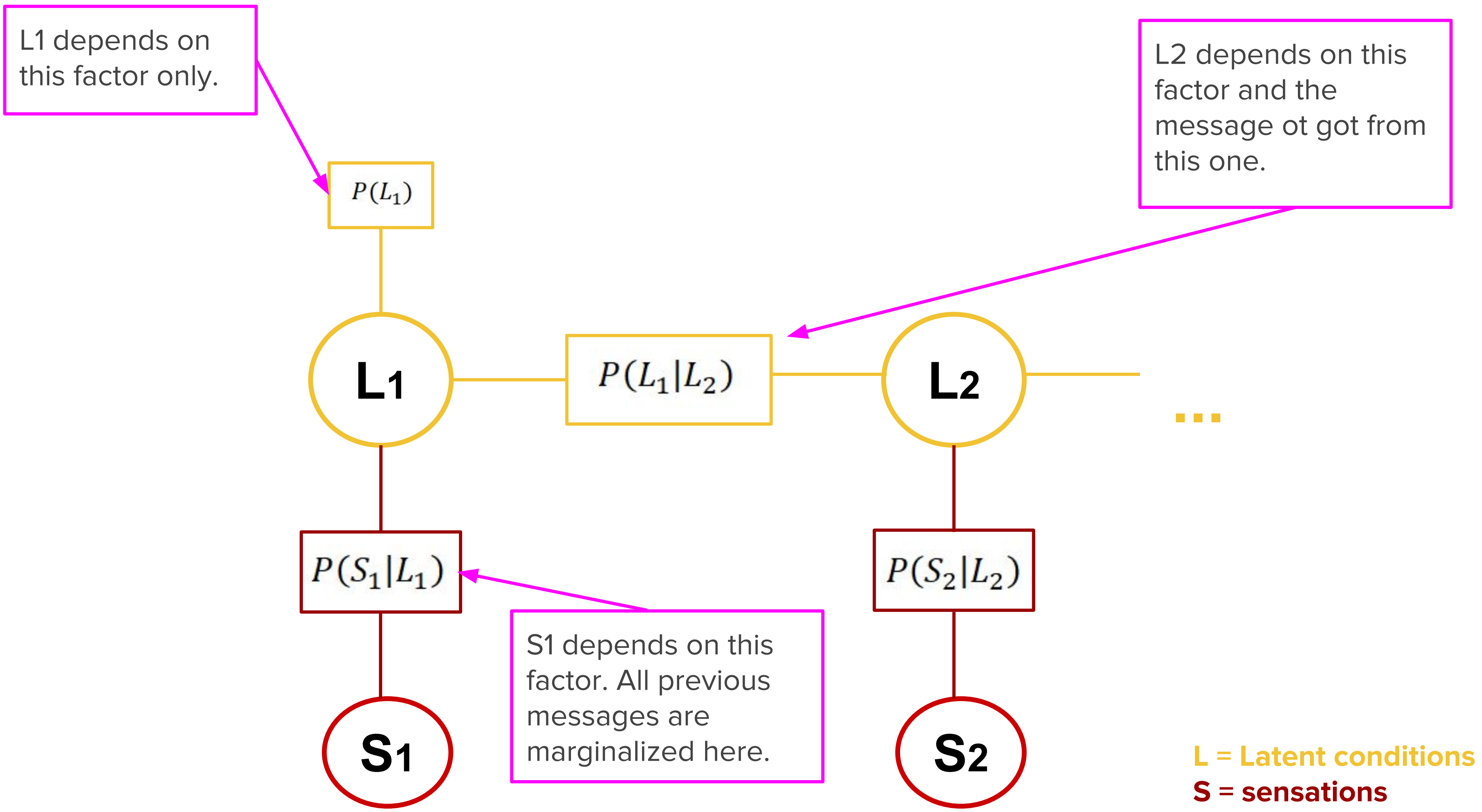


Message passing in Bayesian Networks

- **Sum product algorithm** for singly connected graphs

- Derive a factor graph from graphical model *(next slide*)

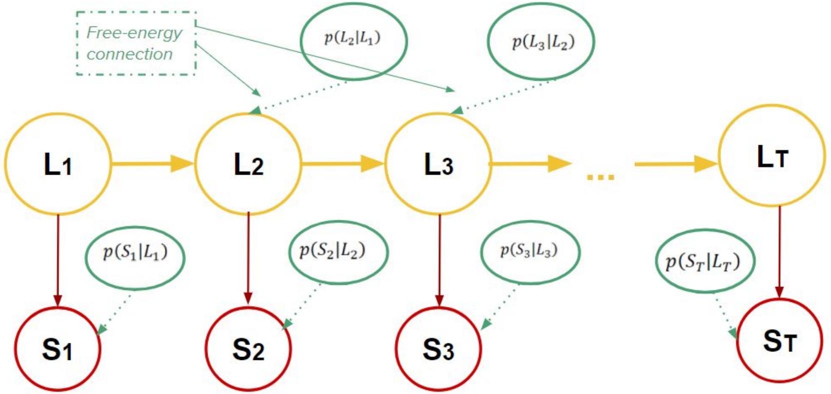
- In factors: collect all information from nodes, then send it to next node.
    - Sum over all variables...


L1 depends on this factor only.
$P(L_1)$
L2 depends on this factor and the message ot got from this one.
L1
$P(L_1|L_2)$
L2
...
$P(S_1|L_1)$
$P(S_2|L_2)$
S1 depends on this factor. All previous messages are marginalized here.
S1
S2
L = Latent conditions
S = sensations

Summary: Preliminary graphical model

- Time series model
  - Increasing anticipation leads to pain perception on a theoretical level

- Conditional probabilities (hierarchy level) represent learning processes
- Message passing between nodes via Sum-Product algorithm
- Some free-energy learning

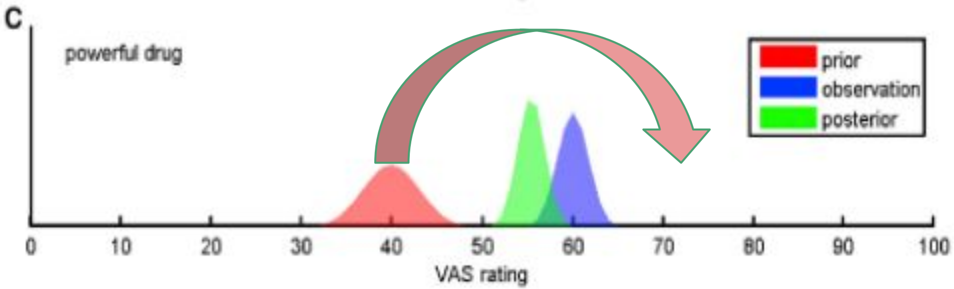


Modeling pediatric chronic pain data

- Collaboration with **Tanja Hechler**; Vestische Kinderklinik Datteln

- Questionnaire data on **pain predictions**
  - How likely do you think it is that sensation X caused by **pain?**
  - What causes sensation X? Name as many as possible.

- Maybe later: Experimental data on higher **pain prior** in children w CP



Outlook

- Next steps in my thesis project
  - Learn more about modeling, machine learning techniques & free energy learning
  - Learn more about computational psychiatry and PC framework
  - Get the modeling going somehow

- Best case:
  - Derive specific etiologic and therapeutic hypotheses
  - Identify mathematically informed therapy recommendations & simulate

Literature

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Thank you for your attention

Questions and comments?