

# An example of medical treatment optimization under model uncertainty

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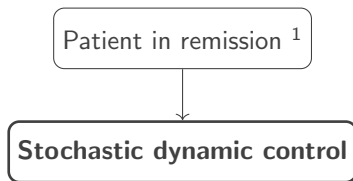
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<sup>3</sup>Univ Toulouse, INRAE-MIAT, Toulouse, France

June 7, 2023



# A medical context

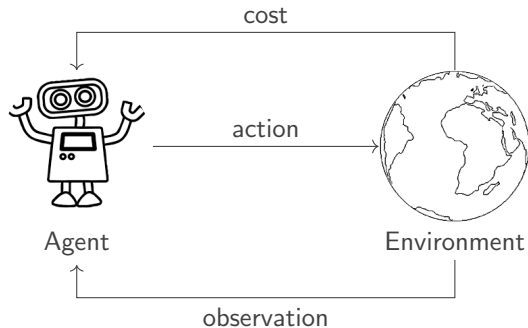


To solve this we use **reinforcement learning**.

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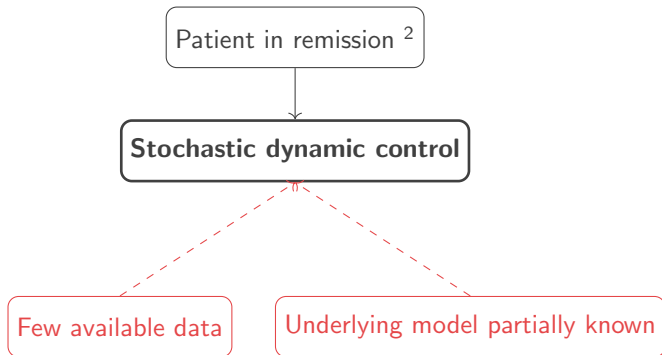
<sup>1</sup>Data from IUC Oncopole, Toulouse, and CRCT, Toulouse, France

# Reinforcement learning



The aim is to learn how to behave based on past experience and perceived costs.

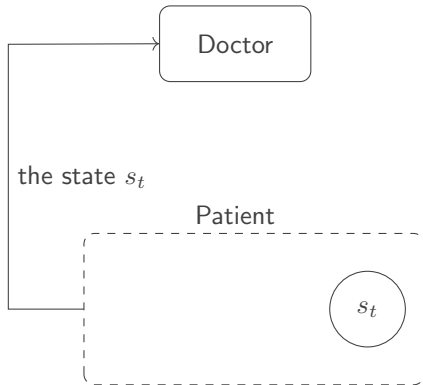
# A medical context



**How can these issues be addressed in a simplified problem ?**

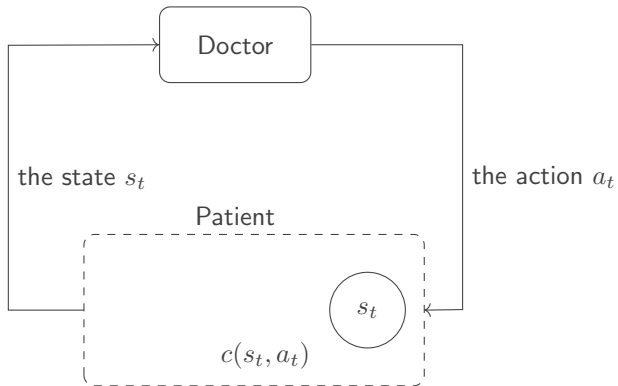
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# Markov Decision Process (MDP<sup>3</sup> )



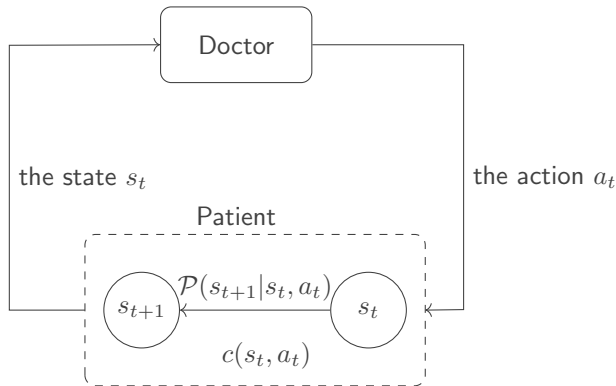
- $s \in \mathcal{S}$  the state space
- $a \in \mathcal{A}$  the action space
- $\mathcal{P}$  the transition matrix
- $c(s_t, a_t)$  the cost function

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<sup>3</sup>ML Puterman (1994). "Finite-horizon Markov decision processes". In: *Markov Decision Processes: Discrete Stochastic Dynamic Programming*. New York: Wiley-Interscience, pp. 78–9.

# State transition

The transition matrix is partially known



Table: Transition matrix when patient has no treatment ( $a = \emptyset$ ).

$s_t \backslash s_{t+1}$	(0,0,0)	(1,0,1)	(1,0,2)	(1,1,1)	(1,1,2)	(1,2,1)	(1,2,2)	(1,3,1)	(1,3,2)	(2,4,0)
(0,0,0)	$p_{(0,0,0)}^\emptyset$	$p_{(1,0,1)}^\emptyset$	$p_{(1,0,2)}^\emptyset$	0	0	0	0	0	0	0
(1,0,1)	0	0	0	<b>1</b>	0	0	0	0	0	0
(1,0,2)	0	0	0	0	0	0	<b>1</b>	0	0	0
(1,1,1)	0	0	0	0	0	<b>1</b>	0	0	0	0
(1,1,2)	0	0	0	0	0	0	0	0	<b>1</b>	0
(1,2,1)	0	0	0	0	0	0	0	<b>1</b>	0	0
(1,2,2)	0	0	0	0	0	0	0	0	0	<b>1</b>
(1,3,1)	0	0	0	0	0	0	0	0	0	<b>1</b>
(1,3,2)	0	0	0	0	0	0	0	0	0	<b>1</b>
(2,4,0)	0	0	0	0	0	0	0	0	0	<b>1</b>



# State transition

The transition matrix is partially known



Table: Transition matrix when patient has treatment ( $a = \rho$ ).

$s_t \backslash s_{t+1}$	(0,0,0)	(1,0,1)	(1,0,2)	(1,1,1)	(1,1,2)	(1,2,1)	(1,2,2)	(1,3,1)	(1,3,2)	(2,4,0)
(0,0,0)	$p_{(0,0,0)}^\rho$	$p_{(1,0,1)}^\rho$	$p_{(1,0,2)}^\rho$	0	0	0	0	0	0	0
(1,0,1)	1	0	0	0	0	0	0	0	0	0
(1,0,2)	1	0	0	0	0	0	0	0	0	0
(1,1,1)	1	0	0	0	0	0	0	0	0	0
(1,1,2)	1	0	0	0	0	0	0	0	0	0
(1,2,1)	0	0	0	1	0	0	0	0	0	0
(1,2,2)	0	0	0	0	1	0	0	0	0	0
(1,3,1)	0	0	0	0	0	0	0	1	0	0
(1,3,2)	0	0	0	0	0	0	0	0	1	0
(2,4,0)	0	0	0	0	0	0	0	0	0	1

# Solving a MDP

Minimizing a cost



The list of costs:

- Treatment: 300
- Disease 1: 200
- Disease 2: 300
- Death: 1000

## Policy $\pi$

Let  $f : \mathcal{S} \rightarrow \mathcal{A}$  for all  $s \in \mathcal{S}$  is a decision rule.

A sequence of decision rules  $\pi = (f_0, f_1, \dots, f_{H-1})$  is a policy.

## Policy cost

$$J_H(\pi, s) = \mathbb{E}\left[\sum_{t=0}^{H-1} c(s_t, a_t) | \pi, s\right]$$

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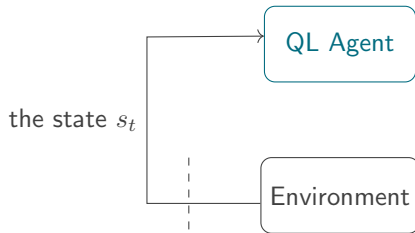
$$J_H(\pi, s) = \mathbb{E}\left[\sum_{t=0}^{H-1} c(s_t, a_t) \mid \pi, s\right]$$

## Optimization criterion

$$V^*(s_t) = \min_{a \in \mathcal{A}} [c(s_t, a) + \sum_{s_{t+1} \in \mathcal{S}} \mathcal{P}(s_{t+1} \mid s_t, a) V^*(s_{t+1})]$$

# A model-free method

Q-learning<sup>4,5</sup> algorithm

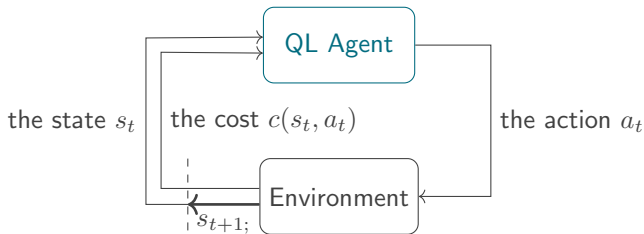


# A model-free method

Q-learning<sup>4,5</sup> algorithm



$$Q'(s_t, a_t) = (1 - \alpha) * Q(s_t, a_t) + \alpha [c(s_t, a_t) + \min_{a_{t+1} \in \mathcal{A}} Q(s_{t+1}, a_{t+1})]$$



<sup>4</sup>Christopher J. C. H. Watkins and Peter Dayan (May 1992). “Q-learning”. In: *Mach. Learn.* 8.3, pp. 279–292. ISSN: 1573-0565. DOI: [10.1007/BF00992698](https://doi.org/10.1007/BF00992698).

<sup>5</sup>VP Vivek and Dr. Shalabh Bhatnagar (Aug. 2022). “Finite Horizon Q-learning: Stability, Convergence, Simulations and an application on Smart Grids”. In: *arXiv:2110.15093v3*. DOI: [10.48550/arXiv.2110.15093](https://doi.org/10.48550/arXiv.2110.15093). eprint: [2110.15093v3](https://arxiv.org/abs/2110.15093v3).

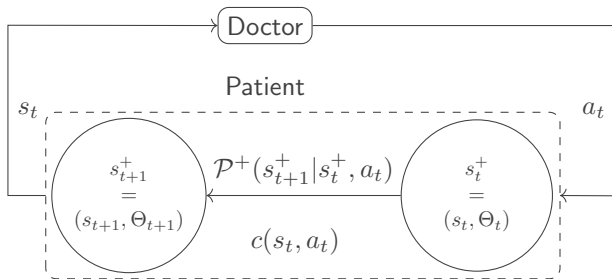
# A bayesian approach

$s_t \backslash s_{t+1}$	(0, 0, 0)	(1, 0, 1)	(1, 0, 2)	(1, 1, 1)	(1, 1, 2)	(1, 2, 1)	(1, 2, 2)	(1, 3, 1)	(1, 3, 2)	(2, 4, 0)
(0, 0, 0)	$p_{(0,0,0)}^\emptyset$	$p_{(1,0,1)}^\emptyset$	$p_{(1,0,2)}^\emptyset$	0	0	0	0	0	0	0

Remark:

- $P(\cdot | s = (0, 0, 0), a = \emptyset) \sim \mathcal{M}(p_{(0,0,0)}^\emptyset, p_{(1,0,1)}^\emptyset, p_{(1,0,2)}^\emptyset)$
- Conjugate distribution :  $f(p^\emptyset | \Theta^\emptyset) \sim \mathcal{D}(\theta_{(0,0,0)}^\emptyset, \theta_{(1,0,1)}^\emptyset, \theta_{(1,0,2)}^\emptyset)$
- $f(p^\emptyset | \Theta^\emptyset) \propto \prod_{s_{t+1} \in \mathcal{S}} p_{s_{t+1}}^{\emptyset, \theta_{s_{t+1}}^\emptyset - 1}$

# Bayes-Adaptive Markov Decision Process (BAMDP<sup>6</sup>)

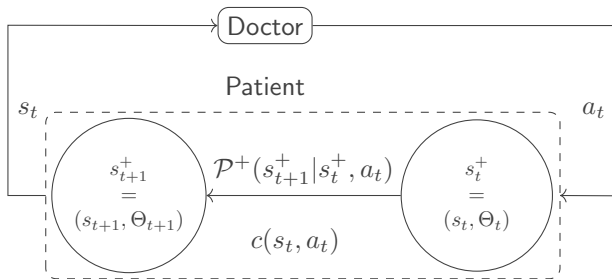


- $s^+ \in \mathcal{S}^+$  the hyper-state space
- $\mathcal{P}^+$  the transition matrix
- $\Theta_{t+1} = \Theta_t + \Delta_{s_{t+1}}^{a_t}$ , with

$$\Delta_{s_{t+1}}^{a_t} = \begin{cases} 1 & \text{if } (s = (\text{0}, \text{0}, \text{0}), a_t, s_{t+1}), \\ 0 & \text{else.} \end{cases}$$

<sup>6</sup>Michael O'Gordon Duff (2002). "Optimal learning: Computational procedures for Bayes -adaptive Markov decision processes". PhD thesis. University of Massachusetts Amherst.

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Optimization criterion

$$V^*(s_t, \Theta_t) = \min_{a \in \mathcal{A}} [c(s_t, a_t) + \sum_{s_{t+1}^+ \in \mathcal{S}^+} \mathcal{P}^+(s_{t+1}^+ | s_t^+, a_t) V^*(s_{t+1}, \Theta_{t+1})]$$

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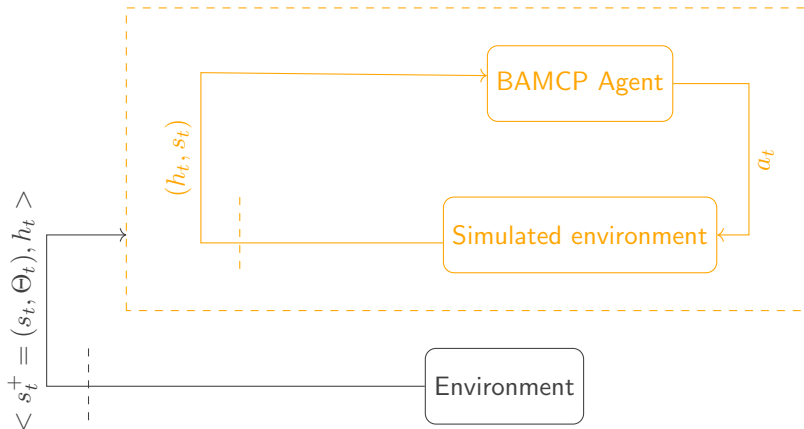


# A model-based method

Bayes-Adaptive Monte-Carlo Planning (BAMCP<sup>7</sup>)



with  $h_t = (s_0, a_0, s_1, \dots, s_{t-1}, a_{t-1})$ ,

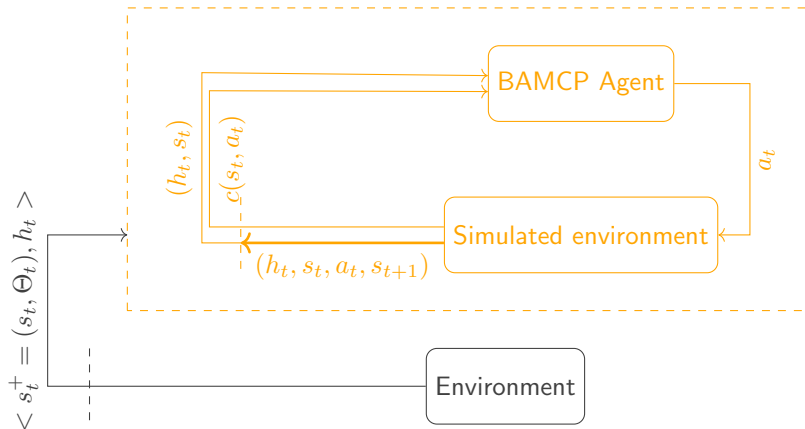


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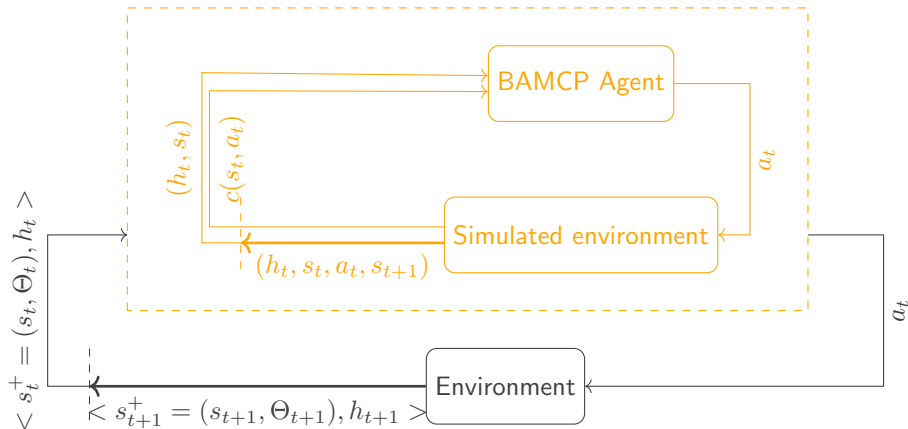


# A model-based method

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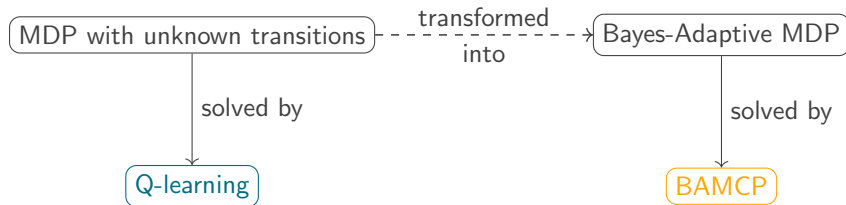
with  $h_t = (s_0, a_0, s_1, \dots, s_{t-1}, a_{t-1})$ ,



The optimal policy exact cost: 888.89

Simulated patients	Q-learning		BAMCP	
	Cost	Time	Cost	Time
$10^2$	$1427.06 \pm 1.05$	0.07 sec	$1377.62 \pm 1.21$	15.41 min
$10^3$	$936.96 \pm 0.70$	2.48 min	$1340.92 \pm 1.04$	17.86 min
$10^4$	$936.93 \pm 0.70$	4.17 min	NC	4 days
$10^6$	$891.6 \pm 0.68$	10.21 min	NC	1.5 years

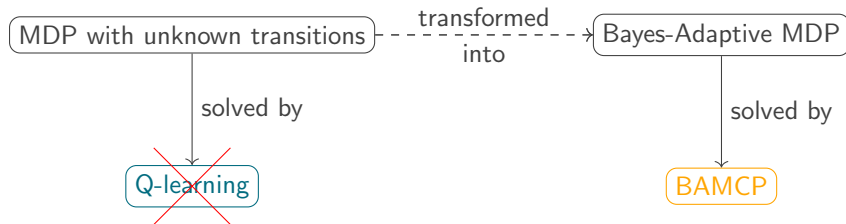
# Conclusion



◆ Mathematical framework      ◆ Model-free method      ◆ Model-based method

Model-free methods don't work because we don't have enough to interact with.

# Conclusion



◆ Mathematical framework

◆ Model-free method

◆ Model-based method

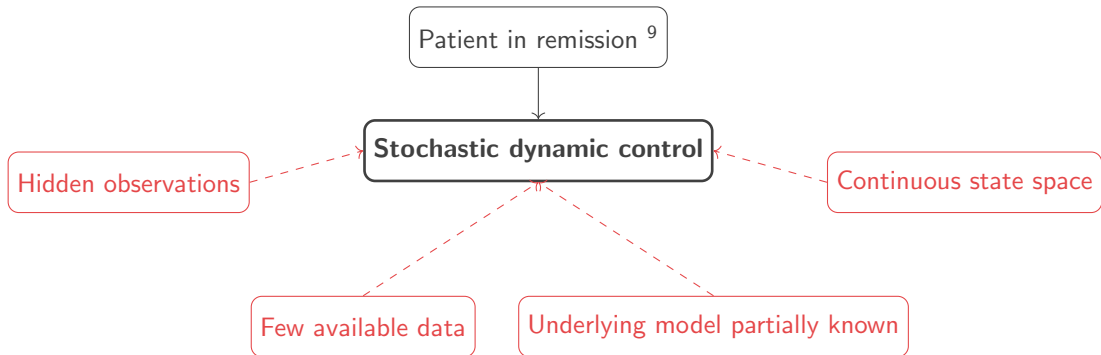
Model-free methods don't work because we don't have enough to interact with.

MDP model	→	PDMP <sup>8</sup> model
Finite state space	→	Continuous state space
Markovian	→	Semi-Markovian
Complete observations	→	Hidden observations

Unlike model-free methods and deep reinforcement learning, **bayesian approaches** do not require as much interaction with the environment.

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<sup>8</sup>Mark H. A. Davis (1984). “Piecewise-Deterministic Markov Processes: A General Class of Non-Diffusion Stochastic Models”. In: *Journal of the Royal Statistical Society Series B (Methodological)* 46, pp. 353–376.



<sup>9</sup>Data from IUC Oncopole, Toulouse, and CRCT, Toulouse, France