An example of medical treatment optimization under model uncertainty

Orlane Le Quellennec  $^1$ , Alice Cleynen  $^{1,2}$ , Benoîte de Saporta  $^1$  and Régis Sabbadin  $^3$ 

<sup>1</sup>IMAG, Univ Montpellier, CNRS, Montpellier, France

<sup>2</sup> John Curtin School of Medical Research, The Australian National University, Canberra, ACT, Australia

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

June 7, 2023

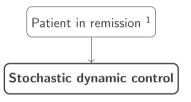






### A medical context



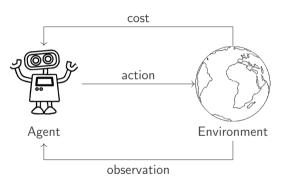


To solve this we use **reinforcement learning**.

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

## Reinforcement learning

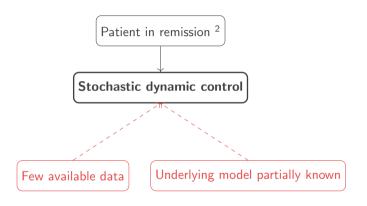




The aim is to learn how to behave based on past experience and perceived costs.

### A medical context



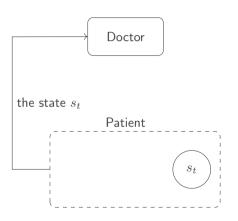


How can these issues be addressed in a simplified problem?

<sup>&</sup>lt;sup>2</sup>Data from IUC Oncopole, Toulouse, and CRCT, Toulouse, France

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

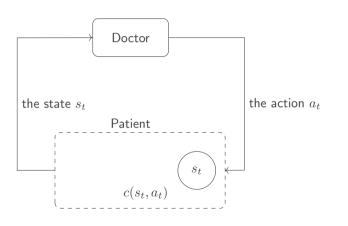




- $s \in \mathcal{S}$  the state space
- $a \in \mathcal{A}$  the action space
- ullet  ${\cal P}$  the transition matrix
- ullet  $c(s_t,a_t)$  the cost function

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

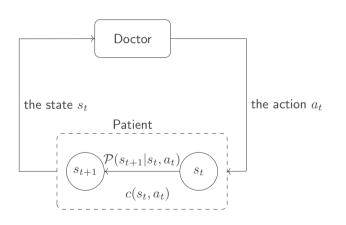




- $s \in \mathcal{S}$  the state space
- $a \in \mathcal{A}$  the action space
- ullet  ${\cal P}$  the transition matrix
- ullet  $c(s_t,a_t)$  the cost function

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





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

<sup>&</sup>lt;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**





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	1	0	0	0	0	0	0
(1, 0, 2)	0	0	0	0	0	0	1	0	0	0
(1, 1, 1)	0	0	0	0	0	1	0	0	0	0
(1, 1, 2)	0	0	0	0	0	0	0	0	1	0
(1, 2, 1)	0	0	0	0	0	0	0	1	0	0
(1, 2, 2)	0	0	0	0	0	0	0	0	0	1
(1, 3, 1)	0	0	0	0	0	0	0	0	0	1
(1, 3, 2)	0	0	0	0	0	0	0	0	0	1
(2, 4, 0)	0	0	0	0	0	0	0	0	0	1

### **State transition**

The transition matrix is partially known



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

$s_t \setminus s_{t+1}$	(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)	$p^{ ho}_{(0,0,0)}$	$p^{ ho}_{({ extbf{1}},{ extbf{0}},1)}$	$p^{ ho}_{({ extbf{1}},{ extbf{0}},2)}$	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



#### The list of costs:

• Treatment: 300

• Disease 1: 200

• Disease 2: 300

• Death: 1000

#### Policy $\pi$

Let  $f: \mathcal{S} \to \mathcal{A}$  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

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



#### The list of costs:

• Treatment: 300

• Disease 1: 200

• Disease 2: 300

• Death: 1000

#### Policy $\pi$

Let  $f: \mathcal{S} \to \mathcal{A}$  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

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

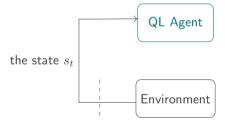
#### Optimization criterion

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

## A model-free method

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

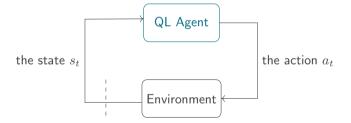




## A model-free method

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



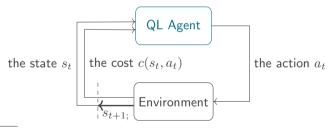


### A model-free method

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>&</sup>lt;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.

<sup>&</sup>lt;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. eprint: 2110.15093v3.

# A bayesian approach



#### Remark:

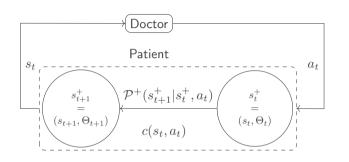
• 
$$P(.|s=(0,0,0),a=\emptyset) \sim \mathcal{M}(p_{(\mathbf{0},\mathbf{0},0)}^{\emptyset},p_{(\mathbf{1},\mathbf{0},1)}^{\emptyset},p_{(\mathbf{1},\mathbf{0},2)}^{\emptyset})$$

$$\bullet \ \ \mathsf{Conjugate \ distribution}: \ f(p^\emptyset|\Theta^\emptyset) \sim \mathcal{D}(\theta^\emptyset_{({\color{red}0,0,0})}^\emptyset,\theta^\emptyset_{({\color{red}1,0,1})},\theta^\emptyset_{({\color{red}1,0,2})})$$

• 
$$f(p^{\emptyset}|\Theta^{\emptyset}) \propto \prod_{s_{t+1} \in \mathcal{S}} p_{s_{t+1}}^{\emptyset, \theta_{s_{t+1}}^{\emptyset} - 1}$$

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





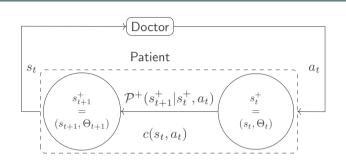
- $s^+ \in \mathcal{S}^+$  the hyper-state space
- ullet  $\mathcal{P}^+$  the transition matrix
- $\bullet \ \Theta_{t+1} = \Theta_t + \Delta^{a_t}_{s_{t+1}} \text{, with}$

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

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

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





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

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

#### Optimization criterion

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

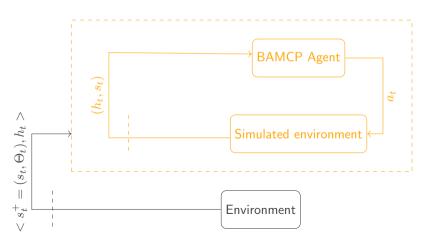
<sup>&</sup>lt;sup>6</sup>Michael O'Gordon Duff (2002). "Optimal learning: Computational procedures for Bayes -adaptive Markov decision processes". PhD thesis. University of Massachusetts Amherst.

## A model-based method

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



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

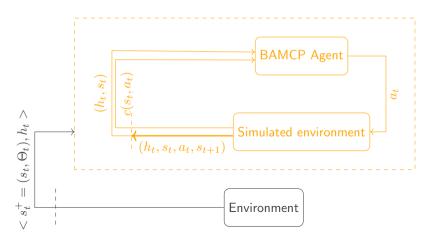


## A model-based method

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



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

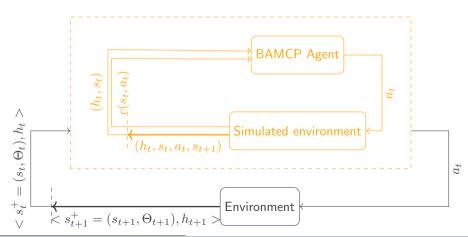


## A model-based method

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



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



## Results

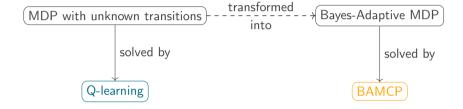


The optimal policy exact cost: 888.89

Simulated patients	Q-learn	ing	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



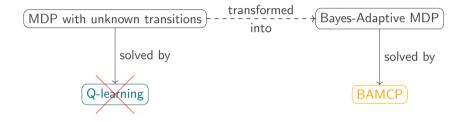


- Mathemathical framework
- Model-free method
- Model-based method

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

### Conclusion





Mathemathical framework

Model-free method

Model-based method

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

## Perspectives



 $\mathsf{MDP} \; \mathsf{model} \qquad \qquad \to \quad \mathsf{PDMP^8} \; \mathsf{model}$ 

Finite state space  $\rightarrow$  Continuous state space

 $\mathsf{Markovian} \qquad \qquad \to \quad \mathsf{Semi\text{-}Markovian}$ 

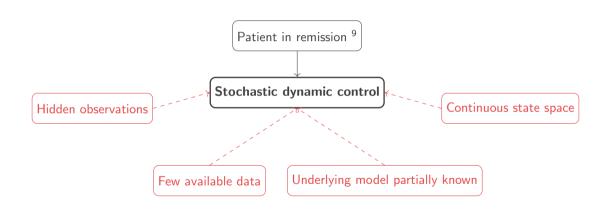
 ${\sf Complete \ observations} \quad \to \quad {\sf Hidden \ observations}$ 

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

<sup>&</sup>lt;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.

## Perspectives





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