Addiction and Rehabilitation: A Non-monotonic Computational Process

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Supplementary material

In the following we present the mathematical details of calculating G and its parameters. All dynamic equations are chosen to be the simplest ones that agree with the notions and data in the field. First are describe the feedback parameters P, S and D; second the acute parameters A_P, A_S, A_D and Q; and then h, f, r and G.

Let us define the bounding function σ as:

$$\sigma(x) = \begin{cases} 0 & \text{if } x < 0 \\ x & \text{if } x \in [0, 1] \\ 1 & \text{if } x > 1 \end{cases}$$

We will note by ν_X the noise for the signal X, for any signal X. In this work all $\nu_X \in [-0.05, 0.05]$.

S **- stress**

$$S(t) = \begin{cases} \sigma\Big(1 - (1 - S_0) \cdot e^{-\beta_S \cdot d} + \nu_S\Big) & \text{if } G > 0 \\ \sigma\Big(S(t-1) + \nu_S\Big) & \text{if } G = 0 \\ \sigma\Big(S_0 \cdot e^{-\gamma_S \cdot d} + \nu_S\Big) & \text{if } G < 0 \end{cases}$$

where

t_c = time of last change of sign of G

S_0 = value of $S(t_c)$, $S_0 < 1$

β_S = exponential constant of S when $G > 0$ (e.g. 10^{-5})

γ_S = exponential constant of S when $G < 0$ (e.g. $2 \cdot 10^{-2}$)

d = number of steps after t_c, $d \in \mathbb{N}$ (positive integers)

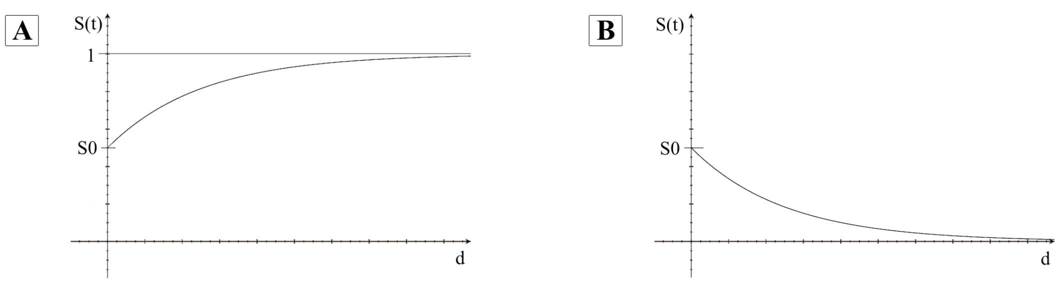

Figure 1: A) $S(t)$ when $G > 0$, B) $S(t)$ when $G < 0$.

$S \in [0, 1]$

ν_S uniform noise $\in [-0.05, 0.05]$

The signal $S(t)$ behaves as follows:

- When $G > 0$, $S(t)$ increases exponentially from the constant value S_0 to 1 by an increasing factor β_S. The noise ν_S is added, and in order to assure that $S(t)$ is bounded, the function σ is applied.
- When $G = 0$, the noise ν_S is added and the function σ is applied.
- When $G < 0$, $S(t)$ decreases exponentially from the constant value S_0 to 0 by a decreasing factor β_S. The noise ν_S is added and the function σ is applied.

P **- pain**

$$P(t) = \begin{cases} \sigma\Big(P_0 \cdot e^{-\beta_P \cdot d} + \nu_P\Big) & \text{if } G > 0 \\ \sigma\Big(P(t-1) + \nu_P\Big) & \text{if } G = 0 \\ \sigma\Big(1 - (1 - P_0) \cdot e^{-\gamma_P \cdot d} + \nu_P\Big) & \text{if } G < 0 \end{cases}$$

where

t_c = time of last change of sign of G

P_0 = value of $P(t_c)$, $P_0 < 1$

β_P = exponential constant of P when $G > 0$ (e.g. $3 \cdot 10^{-5}$)

γ_P = exponential constant of P when $G < 0$ (e.g. 10^{-3})

d = number of steps after t_c, $d \in \mathbb{N}$ (positive integers)

$P \in [0, 1]$

ν_P uniform noise $\in [-0.05, 0.05]$

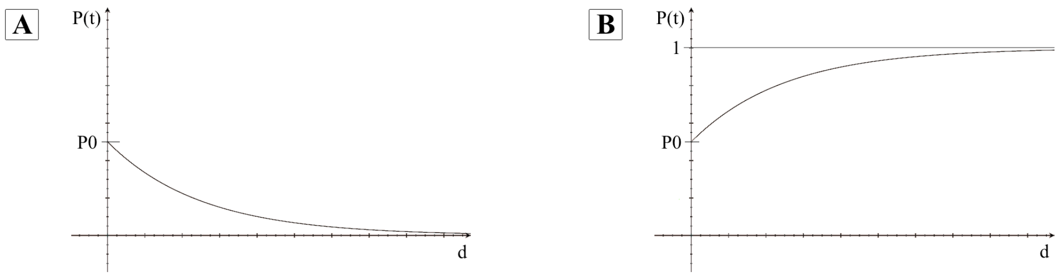

Figure 2: A) $S(t)$ when $G > 0$, B) $S(t)$ when $G < 0$.

The signal $P(t)$ behaves as follows:

- When $G > 0$, $P(t)$ decreases exponentially from the constant value P_0 to 0 by a decreasing factor β_P.
- When $G = 0$, the noise ν_P is added and σ is applied.
- When $G < 0$, P increases exponentially from the constant value P_0 to 1 by an increasing factor γ_P.

D **- dopamine related craving**

$$D(t) = \begin{cases} \sigma\Big(1 - (1 - D_0) \cdot e^{-\beta_D \cdot d} + \nu_D\Big) & \text{if } G > 0 \text{ and } d \in [1, \tau] \\ \sigma\Big(D_0' \cdot e^{-\beta_D \cdot d} + \nu_D\Big) & \text{if } G > 0 \text{ and } d > \tau \\ \sigma\Big(D(t-1) + \nu_D\Big) & \text{if } G = 0 \\ \sigma\Big(1 - (1 - D_0) \cdot e^{-\gamma_D \cdot d} + \nu_D\Big) & \text{if } G < 0 \end{cases}$$

where

t_c = time of last change of sign of G

D_0 = value of $D(t_c)$, $D_0 < 1$

τ = number of time steps in which the dopamine related craving increases after there is no drug consumption (e.g. 15)

D_0' = value of $D(t)$ at $t = \tau$

β_D = exponential constant of D when $G > 0$ (e.g. $2 \cdot 10^{-2}$)

γ_D = exponential constant of D when $G < 0$ (e.g. 10^{-5})

d = number of steps after t_c, $d \in \mathbb{N}$ (positive integers)

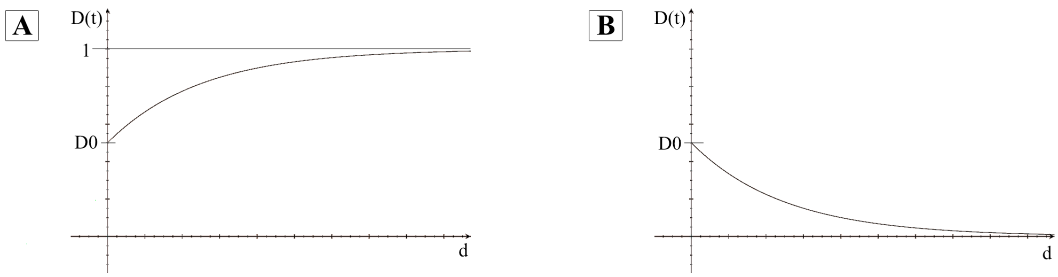

Figure 3: A) $D(t)$ when $G < 0$ or when $G > 0$ and $d \in [1, \tau]$, B) $D(t)$ when $G > 0$ and $d > \tau$.

$D \in [0, 1]$

ν_D uniform noise $\in [-0.05, 0.05]$

The signal $D(t)$ behaves as follows:

- When $G > 0$, for the first τ time steps, $D(t)$ increases exponentially from the constant value D_0 to 1 by an increasing factor β_D and after that, when $t > \tau$, $D(t)$ decreases exponentially from the constant value D_0 to 0 by a decreasing factor β_D. The noise ν_D is added and $D(t)$ is bounded in $[0, 1]$ by applying σ.
- When $G = 0$, the noise ν_D is added and σ is applied.
- When $G < 0$, $D(t)$ increases exponentially from the constant value D_0 to 1 by an increasing factor γ_D. The noise ν_D is added and σ is applied.

A_S **- acute shock**

$$A_S(t) = \begin{cases} A_{S_0} & \text{if } (G > 0 \text{ and } b_S(t) = 1) \text{ or } t_S \in [1, \tau_1] \\ \rho_S \cdot A_S(t-1) & \text{if } t_S \in [\tau_1, \tau_2] \\ 0 & \text{else} \end{cases}$$

where

$b_S(t)$ is a Boolean variable $\in \{0, 1\}$. $b_S(t) = 1$ means that a shock begins at time t.

A_{S_0} = constant (e.g. 0.85)

ρ_S = constant < 1 (e.g. 0.7)

t_0 = starting time of a shock

t_S = number of steps after t_0, $t_S \in \mathbb{N}$ (positive integers)

τ_1 = number of time steps in which the shock effect is constant (e.g. 70)

τ_2 = number of time steps in which the shock effect is decreasing (e.g. 800)

$\tau_2 > \tau_1$

$A_S \in [0, A_{S_0}]$

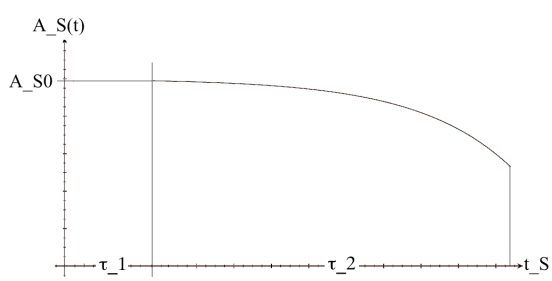

Figure 4: Behavior for $A_S(t)$.

The signal $A_S(t)$ behaves as follows:

- When an acute shock is detected, its value becomes A_{S_0} for the first τ_1 time steps, then for τ_2 steps its value decreases exponentially by a factor ρ_S. After $t = \tau_1 + \tau_2$, $A_S(t)$ becomes 0.

The signals A_S, A_P and A_D are mathematically very similar. The first difference is that an event A_P can starts only when $G < 0$, but events A_S and A_D can start only when $G > 0$. The second difference are the constants used in the definition of those signals.

A_P **- acute trauma**

$$A_P(t) = \begin{cases} A_{P_0} & \text{if } (G < 0 \text{ and } b_P(t) = 1) \text{ or } t_P \in [1, \tau_1] \\ \rho_P \cdot A_P(t-1) & \text{if } t_P \in [\tau_1, \tau_2] \\ 0 & \text{else} \end{cases}$$

where

$b_P(t)$ is a Boolean variable $\in \{0, 1\}$. $b_P(t) = 1$ means that a trauma begins at time t.

A_{P_0} = constant (e.g. 0.7)

ρ_P = constant < 1 (e.g. 0.9)

t_0 = starting time of a trauma

t_P = number of steps after t_0, $t_P \in \mathbb{N}$ (positive integers)

τ_1 = number of time steps in which the trauma effect is constant (e.g. 100)

τ_2 = number of time steps in which the trauma effect is decreasing (e.g. 1000)

$\tau_2 > \tau_1$

$A_P \in [0, A_{P_0}]$

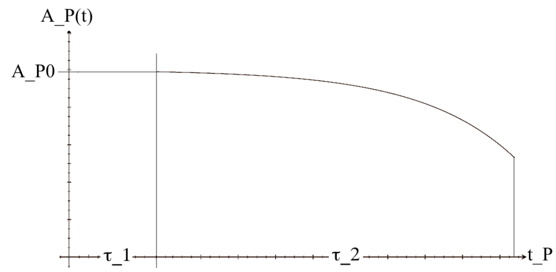

Figure 5: Behavior for $A_P(t)$.

The signal $A_P(t)$ behaves as follows:

- When an acute trauma is detected, its value becomes A_{P_0} for the first τ_1 time steps, then for τ_2 steps its value decreases by a factor ρ_P. At $t = \tau_1 + \tau_2$, $A_P(t)$ becomes 0.

A_D **- acute priming to drugs**

$$A_D(t) = \begin{cases} A_{D_0} & \text{if } (G > 0 \text{ and } b_D(t) = 1) \text{ or } t_D \in [1, \tau_1] \\ \rho_D \cdot A_D(t-1) & \text{if } t_D \in [\tau_1, \tau_2] \\ 0 & \text{else} \end{cases}$$

where

$b_D(t)$ is a Boolean variable $\in \{0, 1\}$. $b_D(t) = 1$ means that a priming effect begins at time t.

A_{D_0} = constant (e.g. 0.9)

ρ_D = constant < 1 (e.g. 0.4)

t_0 = starting time of a shock

t_D = number of steps after t_0, $t_D \in \mathbb{N}$ (positive integers)

τ_1 = number of time steps in which the priming effect is constant (e.g. 30)

τ_2 = number of time steps in which the priming effect is decreasing (e.g. 200)

$\tau_2 > \tau_1$

$A_D \in [0, A_{D_0}]$

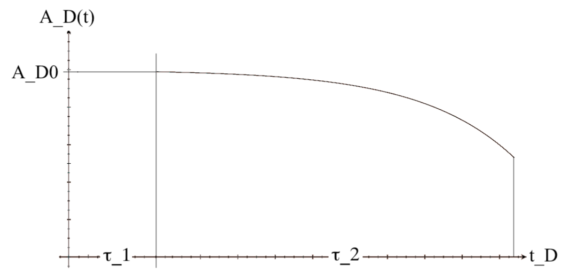

Figure 6: Behavior for $A_D(t)$.

The signal $A_D(t)$ behaves as follows:

- When an acute priming to drugs is detected, its value becomes A_{D_0} for the first τ_1 time steps, then for τ_2 steps its value decreases by a factor ρ_D. At $t = \tau_1 + \tau_2$, $A_D(t)$ becomes 0.

q **- saliency to drug cues**

$$q(t) = \begin{cases} \sigma\Big(q(t-1) + \nu_q\Big) & \text{if } (G > 0 \text{ and } d \in [1, \tau]) \text{ or if } G = 0 \\ \sigma\Big(q_0^{'} \cdot e^{-\beta_q \cdot d} + \nu_q\Big) & \text{if } G > 0 \text{ and } d > \tau \\ \sigma\Big(1 - (1 - q_0) \cdot e^{-\gamma_q \cdot d} + \nu_q\Big) & \text{if } G < 0 \end{cases}$$

where

t_c = time of last change of sign of G

q_0 = value of $q(t_c)$, $q_0 < 1$

τ = number of time steps in which saliency to drug cues saliency does not decrease even that there is no drug consumption (e.g. 20)

$q_0^{'}$ = value of $q(t)$ when $t = \tau$

β_q = exponential constant of q when $G > 0$ (e.g. 10^{-5})

γ_q = exponential constant of q when $G < 0$ (e.g. 10^{-4})

d = number of steps after t_c, $d \in \mathbb{N}$ (positive integers)

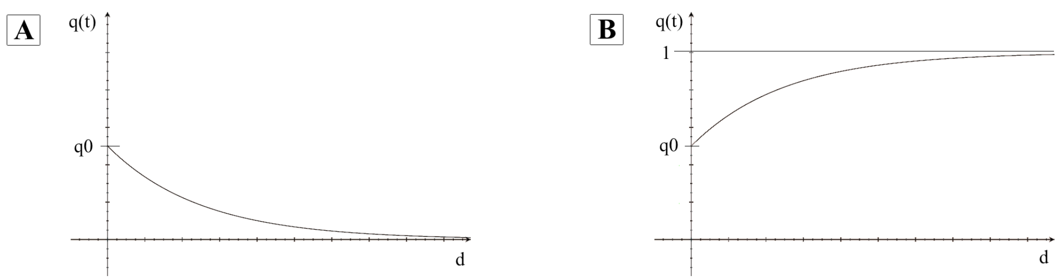

Figure 7: A) $q(t)$ when $G = 0$ or when $G > 0$ and $d > \tau$, B) $q(t)$ when $G < 0$.

$q \in [0, 1]$

ν_q uniform noise $\in [-0.05, 0.05]$

The signal $q(t)$ behaves as follows:

- When $G > 0$, for the first τ time steps, only the noise ν_q is added. After that, when $t > \tau$, $q(t)$ start to exponentially decrease from the constant value $q_0^{'}$ (the value of q when $t = \tau$) to 0 by a decreasing factor β_q.
- When $G = 0$, the noise ν_q is added and σ is applied.
- When $G < 0$, q increases exponentially from the constant value q_0 to 1 by an increasing factor γ_q. The noise ν_q is added and σ is applied.

Q **- encountering drug cues**

$$Q(t) = \begin{cases} q(t) & \text{if } b_Q(t) = 1 \\ Q(t-1) & \text{if } t_Q \in [1, \tau_1] \\ \rho_Q \cdot Q(t-1) & \text{if } t_Q \in [\tau_1, \tau_2] \\ 0 & \text{else} \end{cases}$$

where

$b_Q(t)$ is a Boolean variable $\in \{0, 1\}$. $b_Q(t) = 1$ means that a cue begins at time t.

ρ_Q = constant > 1 (e.g. 1.35)

t_0 = starting time of a cue

t_Q = number of steps after t_0, $t_Q \in \mathbb{N}$ (positive integers)

τ_1 = number of time steps in which the cue effect is constant (e.g. 20)

τ_2 = number of time steps in which the cue effect is decreasing (e.g. 400)

$\tau_2 > \tau_1$

$Q \in [0, \rho_Q]$

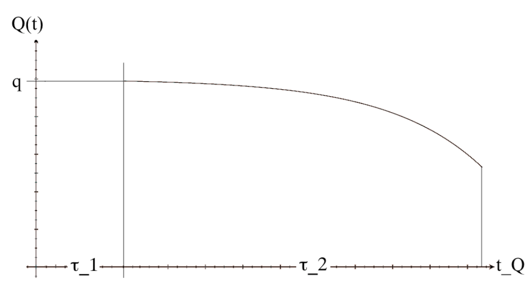

Figure 8: Behavior for $Q(t)$.

The signal $Q(t)$ behaves as follows:

- When first detected, the signal $Q(t)$ becomes the value of q at the same time step t. For the first τ_1 time steps its value remain constant, then for τ_2 steps its value decreases by a factor ρ_Q. At $t = \tau_1 + \tau_2$, $Q(t)$ becomes 0.

h **- recovery power**

$$h(t) = \begin{cases} h_0 & \text{if } b_h(t) = 1 \text{ or } t_h \in [1, \xi(h(t))] \\ 0 & \text{else} \end{cases}$$

where $\xi(h(t))$ is the memory of the recovery power, described by:

$$\xi(h(t)) = \begin{cases} \lfloor \xi(h(t-1)) + \Delta_i \rfloor & \text{if } h(t) = h_0 \text{ and } b_h(t) = 1 \\ \xi(h(t-1)) & \text{if } h(t) = h_0 \text{ and } b_h(t) = 0 \\ \max(0, \xi(h(t-1)) - \Delta_d) & \text{if } h(t) = 0 \end{cases}$$

and

$b_h(t)$ is a Boolean variable $\in \{0, 1\}$. $b_h(t) = 1$ means that an recovery power begins at time t.

h_0 = constant (e.g. 0.6)

$\xi(h(t))$ = number of time steps in which recovery power effect remain active, $\xi(h(t)) \in \mathbb{N}$ (positive integers)

t_0 = the last recovery power starting time

t_h = number of steps after t_0, $t_h \in \mathbb{N}$ (positive integers)

Δ_i = constant to increase memory of h with every new recovery power event (e.g. 10)

Δ_d = constant to decrease memory of h when no active recovery power (e.g. 0.5)

At $t = \xi(h(t))$, when the last effect of the recovery power ended, there is a stochastic decision of whether to cause a permanent effect or not.

The effect of h on the key parameter of the cognitive rationality f is described later in this document.

h takes two possible values: $h \in \{0, h_0\}$

The signal $h(t)$ behaves as follows:

- The value of $h(t)$ is the constant h_0 when it is active, within the time intervall since it last encountered as long as the memory is active.

The signal $\xi(h(t))$, representing the memory of the recovery power, behaves as follows:

- If an recovery power event is encountered, then $\xi(h(t))$ increases by the constant Δ_i. $\xi(h(t))$ doesn't change when h is active. When no recovery power is present, the memory $\xi(h(t))$ decreases by the constant Δ_d, without the possibility to reach negative values. The value of $\xi(h(t))$ is rounded to the highest integer not larger than it.

f - the key parameter of the cognitive rationality

$$\begin{aligned} f(t,h) &= \Big[\omega_P(h) \cdot P(t) - \omega_S(h) \cdot S(t) - \omega_D(h) \cdot D(t)\Big] + \\ & \Big[\omega_A \cdot \Big(A_P(t) - A_S(t) - A_D(t)\Big) - \omega_{A_Q} \cdot Q(t)\Big] + \omega_h \cdot h(t) \end{aligned}$$

where

$\omega_S(h)$, $\omega_P(h)$ and $\omega_D(h)$ weight the functions $S(t)$, $P(t)$ and $D(t)$ respectively

ω_A is the weight of $A_P(t)$, $A_S(t)$ and $A_D(t)$

ω_{A_Q} is the weight of $A_Q(t)$

ω_h is the weight of $h(t)$

The functions $\omega_i(h)$, where $i \in \{S, P, D\}$, are affected by h in a stochastic manner:

$$\omega_i(h) = \begin{cases} \kappa_i + \zeta_i & \text{if } d \in [1, \xi(h(t))] \\ \kappa_i & \text{if } d \notin [1, \xi(h(t))] \end{cases}$$

and

$$\kappa_i = \begin{cases} \kappa_i + \zeta_i & \text{if } d = \xi(h(t)) \text{ and } p > \theta_i \\ \kappa_i & \text{else} \end{cases}$$

where

κ_i = weight of i, constant (e.g. 0.91)

ζ_i = effect of h on $\kappa_i(h)$, constant (e.g. 0.03)

$\zeta_i > 0$ for P

$\zeta_i < 0$ for S and D

θ_i is the probability that the effect of h on $\omega_i(h)$ is permanent.

- The signal $f(t, h)$ is a weighted sum of many biologically relevant signals. The weights of the feedback parameters are affected by the recovery power h and present the fundamental change in the cognitive rationality as a result of the recovery power.

r **- cognitive rationality factor**

$$r(t) = \frac{1}{2}[\tanh(\alpha \cdot r(t-1) + \beta \cdot f(t, h) + \gamma)] + \frac{1}{2}$$

where

α = constant

β = constant

γ = 0.2449 (to bound r)

$r \in [0, 1]$

G **- addiction**

$$G(t) = (1 - r(t)) \cdot (-C) + r(t) \cdot I$$

where

I = inhibition constant

C = compulsion constant