Addiction and Rehabilitation: A Non-monotonic Computational Process

Hava T. Siegelmann,1* Dino Levy,2 Yariv Z. Levy1

1Laboratory of Biologically Inspired Neural and Dynamical Systems
University of Massachusetts Amherst, Amherst MA 01003, USA
2Department of Neurobiology, The Weizmann Institute of Science, Rehovot, Israel.

*To whom correspondence should be addressed; E-mail: hava@cs.umass.edu.

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 \( \sigma \) 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 \( \nu_X \) the noise for the signal \( X \), for any signal \( X \). In this work all \( \nu_X \in [-0.05, 0.05] \).
\[ S(t) = \begin{cases} 
\sigma \left( 1 - (1 - S_0) \cdot e^{-\beta_S \cdot d} + \nu_S \right) & \text{if } G > 0 \\
\sigma \left( S(t - 1) + \nu_S \right) & \text{if } G = 0 \\
\sigma \left( S_0 \cdot e^{-\gamma_S \cdot d} + \nu_S \right) & \text{if } G < 0
\end{cases} \]

where

\( t_c = \) time of last change of sign of \( G \)

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

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

\( \gamma_S = \) 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)

\( S \in [0, 1] \)

\( \nu_S \) 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 $\beta_S$. The noise $\nu_S$ is added, and in order to assure that $S(t)$ is bounded, the function $\sigma$ is applied.

- When $G = 0$, the noise $\nu_S$ is added and the function $\sigma$ is applied.

- When $G < 0$, $S(t)$ decreases exponentially from the constant value $S_0$ to 0 by a decreasing factor $\beta_S$. The noise $\nu_S$ is added and the function $\sigma$ is applied.

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

where

$t_c$ = time of last change of sign of $G$

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

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

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

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

$P \in [0, 1]$

$\nu_P$ uniform noise $\in [-0.05, 0.05]$
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 $\beta_P$.
- When $G = 0$, the noise $\nu_P$ is added and $\sigma$ is applied.
- When $G < 0$, $P$ increases exponentially from the constant value $P_0$ to 1 by an increasing factor $\gamma_P$.

**D - dopamine related craving**

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

where

$t_c =$ time of last change of sign of $G$

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

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

\( \gamma_D \) = 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 \( d > \tau \).

\( D \in [0, 1] \)

\( \nu_D \) uniform noise \( \in [-0.05, 0.05] \)

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

- When \( G > 0 \), for the first \( \tau \) time steps, \( D(t) \) increases exponentially from the constant value \( D_0 \) to 1 by an increasing factor \( \beta_D \) and after that, when \( t > \tau \), \( D(t) \) decreases exponentially from the constant value \( D_0 \) to 0 by a decreasing factor \( \beta_D \). The noise \( \nu_D \) is added and \( D(t) \) is bounded in \([0, 1]\) by applying \( \sigma \).

- When \( G = 0 \), the noise \( \nu_D \) is added and \( \sigma \) is applied.

- When \( G < 0 \), \( D(t) \) increases exponentially from the constant value \( D_0 \) to 1 by an increasing factor \( \gamma_D \). The noise \( \nu_D \) is added and \( \sigma \) is applied.
The signal $A_S(t)$ behaves as follows:

\begin{equation}
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}
\end{equation}

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)

$\rho_S =$ 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)

$\tau_1 =$ number of time steps in which the shock effect is constant (e.g. 70)

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

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

$\rho_P = \text{constant < 1 (e.g. 0.9)}$

$t_0 = \text{starting time of a trauma}$

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

$\tau_1 = \text{number of time steps in which the trauma effect is constant (e.g. 100)}$

$\tau_2 = \text{number of time steps in which the trauma effect is decreasing (e.g. 1000)}$

$\tau_2 > \tau_1$

$A_P \in [0, A_{P_0}]$
The signal $A_P(t)$ behaves as follows:

- When an acute trauma is detected, its value becomes $A_{P0}$ for the first $\tau_1$ time steps, then for $\tau_2$ steps its value decreases by a factor $\rho_P$. At $t = \tau_1 + \tau_2$, $A_P(t)$ becomes 0.

$A_D$ - acute priming to drugs

$$A_D(t) = \begin{cases} 
  A_{D0} & \text{if } (G > 0 \text{ and } b_D(t) = 1) \text{ or } t_D \in [1, \tau_1] \\
  \rho_D \cdot A_D(t-1) & \text{if } t_D \in [\tau_1, \tau_2] \\
  0 & \text{else} 
\end{cases}$$

where

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

$A_{D0} = \text{constant (e.g. 0.9)}$

$\rho_D = \text{constant < 1 (e.g. 0.4)}$

$t_0 = \text{starting time of a shock}$

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

$\tau_1 = \text{number of time steps in which the priming effect is constant (e.g. 30)}$

$\tau_2 = \text{number of time steps in which the priming effect is decreasing (e.g. 200)}$
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 $\tau_1$ time steps, then for $\tau_2$ steps its value decreases by a factor $\rho_D$. At $t = \tau_1 + \tau_2$, $A_D(t)$ becomes 0.

$q$ - saliency to drug cues

$$q(t) = \begin{cases} 
\sigma(q(t-1) + \nu_q) & \text{if } (G > 0 \text{ and } d \in [1, \tau]) \text{ or if } G = 0 \\
\sigma(q'_0 \cdot e^{-\beta_q d} + \nu_q) & \text{if } G > 0 \text{ and } d > \tau \\
\sigma(1 - (1 - q_0) \cdot e^{-\gamma_q d} + \nu_q) & \text{if } G < 0 
\end{cases}$$

where

$t_c = \text{time of last change of sign of } G$

$q_0 = \text{value of } q(t_c), q_0 < 1$

$\tau = \text{number of time steps in which saliency to drug cues saliency does not decrease even that there is no drug consumption (e.g. 20)}$
\[ q_0' = \text{value of } q(t) \text{ when } t = \tau \]

\[ \beta_q = \text{exponential constant of } q \text{ when } G > 0 \text{ (e.g. } 10^{-5}) \]

\[ \gamma_q = \text{exponential constant of } q \text{ when } G < 0 \text{ (e.g. } 10^{-4}) \]

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

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

\( q \in [0, 1] \)

\( \nu_q \) uniform noise \( \in [-0.05, 0.05] \)

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

- When \( G > 0 \), for the first \( \tau \) time steps, only the noise \( \nu_q \) 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 \( \beta_q \).

- When \( G = 0 \), the noise \( \nu_q \) is added and \( \sigma \) is applied.

- When \( G < 0 \), \( q \) increases exponentially from the constant value \( q_0 \) to 1 by an increasing factor \( \gamma_q \). The noise \( \nu_q \) is added and \( \sigma \) is applied.
\( Q - \text{encountering drug cues} \)

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

where

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

\( \rho_Q = \text{constant} > 1 \) (e.g. 1.35)

\( t_0 = \text{starting time of a cue} \)

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

\( \tau_1 = \text{number of time steps in which the cue effect is constant} \) (e.g. 20)

\( \tau_2 = \text{number of time steps in which the cue effect is decreasing} \) (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 $\tau_1$ time steps its value remain constant, then for $\tau_2$ steps its value decreases by a factor $\rho_Q$. 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

$h_h(t)$ 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)

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

$\Delta_d =$ 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 interval 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 $\Delta_i$.
  $\xi(h(t))$ doesn’t change when $h$ is active. When no recovery power is present, the memory $\xi(h(t))$ decreases by the constant $\Delta_d$, without the possibility to reach negative values.
  The value of $\xi(h(t))$ is rounded to the highest integer not larger than it.

\textit{f - the key parameter of the cognitive rationality}

\[ f(t, h) = \left[ \omega_P(h) \cdot P(t) - \omega_S(h) \cdot S(t) - \omega_D(h) \cdot D(t) \right] + \left[ \omega_A \cdot \left( A_P(t) - A_S(t) - A_D(t) \right) - \omega_{AQ} \cdot Q(t) \right] + \omega_h \cdot h(t) \]

where

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

$\omega_A$ is the weight of $A_P(t), A_S(t)$ and $A_D(t)$
ω_{AQ} is the weight of A_{Q}(t)

ω_h is the weight of h(t)

The functions ω_i(h), where i ∈ {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

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

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

\( \zeta_i > 0 \) for P

\( \zeta_i < 0 \) for S and D

\( \theta_i \) 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**

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

where
\[\alpha = \text{constant}\]

\[\beta = \text{constant}\]

\[\gamma = 0.2449 \text{ (to bound } r\text{)}\]

\[r \in [0, 1]\]

**G - addiction**

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

where

\[I = \text{inhibition constant}\]

\[C = \text{compulsion constant}\]