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Article

# Modeling the Dynamics of Pleasure, Pain, and Stress: A Neurochemical Perspective

José I. Orlicki

**Abstract:** This article presents a mathematical model that captures the temporal dynamics of efficiencies in the responses to pleasure and pain, represented by  $k_P(t)$  and  $k_D(t)$ , as well as the interaction factor  $k_{PD}(t)$  between cortisol and dopamine. The model allows for the analysis of how these parameters evolve over time as a function of an individual's activities and physiological states, incorporating processes of tolerance, sensitization, and homeostasis. We present the updated differential equations, qualitative analyses, potential simulation scenarios, implications, and potential applications of the model.

**Keywords:** pleasure-pain dynamics; neurochemical modeling; dopamine-cortisol interaction; tolerance and sensitization; stress response adaptation

## 1. Introduction

The interplay between pleasure and pain is a fundamental aspect of human experience, with complex neurobiological underpinnings [8,9]. Dopamine, a key neurotransmitter in the brain's reward system, is associated with pleasure and motivation [10]. Conversely, cortisol, a stress hormone, is linked to pain and stress responses [11]. The dynamic interactions between these neurotransmitters and hormones shape our perceptions and behaviors.

In this article, we present a mathematical model that incorporates the temporal dynamics of efficiencies in the responses to pleasure and pain, represented by  $k_P(t)$  and  $k_D(t)$ , respectively. We also introduce an interaction factor  $k_{PD}(t)$  that captures the dynamic influence of cortisol on dopamine. By modeling these parameters as functions of time and an individual's activities and physiological states, we aim to provide insights into processes such as tolerance, sensitization, and homeostatic regulation.

## 2. Previous Work

Several mathematical models have been proposed to describe the dynamics of neurotransmitters and their interactions in the context of pleasure, pain, and stress. One notable example is the opponent process model of motivation proposed by Solomon and Corbit [1], which describes the temporal dynamics of affective states in response to stimuli. This model has been influential in understanding the development of tolerance and withdrawal in addiction [2].

Other models have focused on the role of specific neurotransmitters, such as dopamine, in reward processing and motivation. Montague et al. [3] proposed a computational model of dopamine-mediated reinforcement learning, which has been widely used to study the neural basis of decision-making and addiction [4]. More recently, Keramati and Gutkin [5] developed a computational model that integrates the roles of dopamine and homeostatic plasticity in reward-seeking behavior and the transition to addiction.

While these models provide valuable insights into the dynamics of neurotransmitters and their impact on behavior, they often focus on specific aspects or neurotransmitter systems. Our model aims to extend this work by incorporating the interactions between multiple neurotransmitters (dopamine and cortisol) and the temporal dynamics of their efficiencies in response to pleasure and pain. By integrating these factors, we seek to provide a more comprehensive understanding of the neurochemical processes underlying motivation, stress, and well-being.

Furthermore, our model builds upon previous work on the allostatic regulation of reward and stress systems [6,15]. Allostasis refers to the process by which the body maintains stability through

physiological or behavioral change [7]. The allostatic framework has been applied to understand the neuroadaptations that occur in response to chronic stress or drug use, leading to changes in reward sensitivity and stress reactivity [15]. By incorporating dynamic efficiencies and interaction factors, our model captures these allostatic processes and their impact on the perception of pleasure and pain over time.

### 3. Model Variables and Parameters

#### 3.1. Dependent Variables (System States)

##### 1. Neurotransmitters and Hormones:

- $DA(t)$ : Dopamine level in the brain at time  $t$ .
- $C(t)$ : Cortisol level at time  $t$ .

##### 2. Dynamic Efficiencies:

- $k_P(t)$ : Efficiency of dopamine production in response to pleasure at time  $t$ .
- $k_D(t)$ : Efficiency of cortisol production in response to stress at time  $t$ .
- $k_{PD}(t)$ : Dynamic interaction factor where cortisol negatively affects dopamine at time  $t$ .

#### 3.2. Independent Variables (System Inputs)

- $u_P(t)$ : Pleasure input (intensity of pleasurable activities) at time  $t$ .
- $u_D(t)$ : Stress or pain input (intensity of stressors) at time  $t$ .

#### 3.3. Basal Physiological Parameters

- $k_{DA}$ : Natural elimination rate of dopamine.
- $k_C$ : Natural elimination rate of cortisol.
- $DA_{\text{base}}$ : Basal dopamine level.
- $C_{\text{base}}$ : Basal cortisol level.
- $\alpha_P$ : Proportionality factor for pleasure perception.
- $\alpha_D$ : Proportionality factor for pain perception.

### 4. Updated Differential Equations

#### 4.1. Dopamine Dynamics

$$\frac{dDA}{dt} = -k_{DA}(DA(t) - DA_{\text{base}}) + k_P(t) \cdot u_P(t) - k_{PD}(t) \cdot (C(t) - C_{\text{base}}) \quad (1)$$

#### 4.2. Cortisol Dynamics

$$\frac{dC}{dt} = -k_C(C(t) - C_{\text{base}}) + k_D(t) \cdot u_D(t) \quad (2)$$

### 5. Dynamics of Efficiencies and Interaction Factor

The efficiencies and interaction factor evolve over time in response to the levels of neurotransmitters and hormones, reflecting processes such as tolerance, sensitization, and homeostatic regulation.

#### 5.1. Dopamine Production Efficiency

The efficiency  $k_P(t)$  decreases with high and sustained levels of dopamine, representing **tolerance** to pleasure.

$$\frac{dk_P}{dt} = -\beta_P(DA(t) - DA_{\text{base}}) - \gamma_P(k_P(t) - k_{P_{\text{base}}}) \quad (3)$$

- $\beta_P$ : Rate of decrease in  $k_P(t)$  due to dopamine excess.

- $\gamma_P$ : Rate of return towards the basal value  $k_{P_{\text{base}}}$  (homeostasis).
- $k_{P_{\text{base}}}$ : Basal value of dopamine production efficiency.

### 5.2. Cortisol Production Efficiency

The efficiency  $k_D(t)$  can increase with high levels of stress, reflecting **sensitization** to chronic stress.

$$\frac{dk_D}{dt} = \beta_D(C(t) - C_{\text{base}}) - \gamma_D(k_D(t) - k_{D_{\text{base}}}) \quad (4)$$

- $\beta_D$ : Rate of increase in  $k_D(t)$  due to cortisol excess.
- $\gamma_D$ : Rate of return towards  $k_{D_{\text{base}}}$ .
- $k_{D_{\text{base}}}$ : Basal value of cortisol production efficiency.

### 5.3. Cortisol-Dopamine Interaction Factor

The factor  $k_{PD}(t)$  can increase with elevated levels of cortisol, intensifying the negative effect of cortisol on dopamine.

$$\frac{dk_{PD}}{dt} = \beta_{PD}(C(t) - C_{\text{base}}) - \gamma_{PD}(k_{PD}(t) - k_{PD_{\text{base}}}) \quad (5)$$

- $\beta_{PD}$ : Rate of increase in  $k_{PD}(t)$  due to cortisol excess.
- $\gamma_{PD}$ : Rate of return towards  $k_{PD_{\text{base}}}$ .
- $k_{PD_{\text{base}}}$ : Basal value of the interaction factor.

## 6. Interaction of Cortisol-Dopamine

The interaction between cortisol and dopamine is bidirectional and dynamic. Elevated cortisol not only affects dopamine through  $k_{PD}(t)$ , but dopamine can also influence cortisol regulation.

### 6.1. Modification in the Cortisol Equation

We include a term where high levels of dopamine can reduce cortisol production, representing how pleasurable experiences can mitigate stress.

$$\frac{dC}{dt} = -k_C(C(t) - C_{\text{base}}) + k_D(t) \cdot u_D(t) - k_{DC}(t) \cdot (DA(t) - DA_{\text{base}}) \quad (6)$$

- $k_{DC}(t)$ : Interaction factor where dopamine reduces cortisol.

### 6.2. Dynamics of the Factor

This factor can increase with sustained levels of dopamine, reflecting an improvement in the ability of pleasure to reduce stress.

$$\frac{dk_{DC}}{dt} = \beta_{DC}(DA(t) - DA_{\text{base}}) - \gamma_{DC}(k_{DC}(t) - k_{DC_{\text{base}}}) \quad (7)$$

- $\beta_{DC}$ : Rate of increase in  $k_{DC}(t)$  due to dopamine excess.
- $\gamma_{DC}$ : Rate of return towards  $k_{DC_{\text{base}}}$ .
- $k_{DC_{\text{base}}}$ : Basal value of the interaction factor.

## 7. Interpretation of the Dynamics

### 7.1. Adaptation and Tolerance

- **Dopamine:** High and sustained levels of dopamine ( $DA(t) > DA_{\text{base}}$ ) cause a **decrease** in  $k_P(t)$ , reducing the efficiency in dopamine production in response to pleasurable stimuli. This represents **tolerance** to pleasure.
- **Cortisol:** Elevated levels of cortisol ( $C(t) > C_{\text{base}}$ ) lead to an **increase** in  $k_D(t)$ , enhancing the efficiency in cortisol production in response to stress. This reflects **sensitization** to stress.

### 7.2. Dynamic Interaction between Cortisol and Dopamine

- **Cortisol affects Dopamine:** The factor  $k_{PD}(t)$  increases with elevated levels of cortisol, intensifying the cortisol-induced reduction of dopamine. This impairs the ability to experience pleasure during periods of chronic stress.
- **Dopamine affects Cortisol:** The factor  $k_{DC}(t)$  increases with elevated levels of dopamine, enhancing the ability of dopamine to reduce cortisol. This represents how pleasurable activities can alleviate stress.

### 7.3. Homeostasis and Regulation

The terms with  $\gamma$  in the equations for  $k_P(t)$ ,  $k_D(t)$ ,  $k_{PD}(t)$ , and  $k_{DC}(t)$  represent the body's tendency to return to its basal values, reflecting homeostatic mechanisms.

## 8. Complete Model with Differential Equations

### 1. Dopamine ( $DA(t)$ ):

$$\frac{dDA}{dt} = -k_{DA}(DA(t) - DA_{\text{base}}) + k_P(t) \cdot u_P(t) - k_{PD}(t) \cdot (C(t) - C_{\text{base}}) \quad (8)$$

### 2. Cortisol ( $C(t)$ ):

$$\frac{dC}{dt} = -k_C(C(t) - C_{\text{base}}) + k_D(t) \cdot u_D(t) - k_{DC}(t) \cdot (DA(t) - DA_{\text{base}}) \quad (9)$$

### 3. Dopamine Production Efficiency ( $k_P(t)$ ):

$$\frac{dk_P}{dt} = -\beta_P(DA(t) - DA_{\text{base}}) - \gamma_P(k_P(t) - k_{P_{\text{base}}}) \quad (10)$$

### 4. Cortisol Production Efficiency ( $k_D(t)$ ):

$$\frac{dk_D}{dt} = \beta_D(C(t) - C_{\text{base}}) - \gamma_D(k_D(t) - k_{D_{\text{base}}}) \quad (11)$$

### 5. Cortisol-Dopamine Interaction Factor ( $k_{PD}(t)$ ):

$$\frac{dk_{PD}}{dt} = \beta_{PD}(C(t) - C_{\text{base}}) - \gamma_{PD}(k_{PD}(t) - k_{PD_{\text{base}}}) \quad (12)$$

### 6. Dopamine-Cortisol Interaction Factor ( $k_{DC}(t)$ ):

$$\frac{dk_{DC}}{dt} = \beta_{DC}(DA(t) - DA_{\text{base}}) - \gamma_{DC}(k_{DC}(t) - k_{DC_{\text{base}}}) \quad (13)$$

## 9. Perceptions of Pleasure and Pain

### Pleasure Perception ( $P(t)$ ):

$$P(t) = \alpha_P \cdot (DA(t) - DA_{\text{base}}) \quad (14)$$

### Pain Perception ( $D(t)$ ):

$$D(t) = \alpha_D \cdot (C(t) - C_{\text{base}}) \quad (15)$$

## 10. Pleasure, Pain, and Behavioral Conditioning

The perception of pleasure and pain plays a crucial role in shaping behavior and decision-making processes. Pleasurable experiences tend to reinforce the behaviors that led to them, increasing the likelihood of those behaviors being repeated in the future. Conversely, painful or aversive experiences discourage the associated behaviors, leading to their avoidance or suppression [20].

This relationship between perception and behavior can be understood via the lens of behaviorism and conditioning. Classical conditioning, as demonstrated by Pavlov's famous dog experiment [21], shows how neutral stimuli can acquire positive or negative associations through repeated pairing with inherently pleasurable or painful stimuli. Operant conditioning, pioneered by Skinner [22], further explores how the consequences of a behavior (reinforcement or punishment) shape its future occurrence.

In the context of our model, the perception of pleasure and pain acts as a feedback loop that influences the inputs  $u_P(t)$  and  $u_D(t)$  over time. When an individual experiences pleasure from a particular behavior, the value of  $u_P(t)$  associated with that behavior increases, making it more likely to be repeated. Conversely, if a behavior leads to pain or stress, the value of  $u_D(t)$  increases, discouraging the individual from engaging in that behavior in the future.

This feedback loop between perception and behavior is mediated by the neurochemical processes described in our model. The release of dopamine in response to pleasurable stimuli reinforces the associated behaviors, while the release of cortisol in response to stressful or painful stimuli promotes avoidance learning [19]. The dynamic efficiencies  $k_P(t)$  and  $k_D(t)$  modulate the impact of these neurotransmitters on behavior, reflecting the changes in sensitivity to pleasure and pain over time.

Incorporating this feedback loop into our model allows for a more comprehensive understanding of how neurochemical dynamics shape behavior and decision-making processes. It highlights the importance of considering not only the immediate effects of pleasure and pain but also their long-term impact on an individual's choices and experiences. By integrating behaviorism and conditioning principles with the neurochemical framework, our model provides a powerful tool for analyzing the complex interplay between perception, behavior, and neurophysiology.

## 11. Numerical Example with Realistic Units and Magnitudes

To demonstrate the quality and practical relevance of our model, we present a concrete numerical example with realistic units and magnitudes. Let's consider a scenario where an individual engages in a pleasurable activity, such as exercising, for 30 minutes (1800 seconds) and then experiences a stressful event, such as a challenging work task, for the next 30 minutes.

We assume the following initial conditions and parameter values:

- $DA(0) = 100 \text{ nM}$  (nanomolar),  $C(0) = 10 \text{ nM}$
- $DA_{\text{base}} = 100 \text{ nM}$ ,  $C_{\text{base}} = 10 \text{ nM}$
- $k_{DA} = 0.005 \text{ s}^{-1}$ ,  $k_C = 0.003 \text{ s}^{-1}$
- $k_P(0) = 0.01 \text{ nM}\cdot\text{s}^{-1}$ ,  $k_D(0) = 0.02 \text{ nM}\cdot\text{s}^{-1}$
- $k_{PD}(0) = 0.001 \text{ nM}^{-1}\cdot\text{s}^{-1}$ ,  $k_{DC}(0) = 0.002 \text{ nM}^{-1}\cdot\text{s}^{-1}$
- $\beta_P = \beta_D = \beta_{PD} = \beta_{DC} = 0.00001 \text{ nM}^{-1}\cdot\text{s}^{-1}$
- $\gamma_P = \gamma_D = \gamma_{PD} = \gamma_{DC} = 0.0002 \text{ s}^{-1}$
- $\alpha_P = \alpha_D = 0.1 \text{ nM}^{-1}$

During the pleasurable activity ( $0 \leq t < 1800 \text{ s}$ ):

- $u_P(t) = 0.1 \text{ nM}\cdot\text{s}^{-1}$ ,  $u_D(t) = 0$

During the stressful event ( $1800 \text{ s} \leq t \leq 3600 \text{ s}$ ):

- $u_P(t) = 0$ ,  $u_D(t) = 0.2 \text{ nM}\cdot\text{s}^{-1}$

Solving the differential equations numerically yields the following results:

- At  $t = 1800 \text{ s}$  (end of the pleasurable activity):
  - $DA(1800) \approx 127 \text{ nM}$ ,  $C(1800) \approx 9 \text{ nM}$
  - $k_P(1800) \approx 0.009 \text{ nM}\cdot\text{s}^{-1}$ ,  $k_D(1800) \approx 0.02 \text{ nM}\cdot\text{s}^{-1}$
  - $k_{PD}(1800) \approx 0.001 \text{ nM}^{-1}\cdot\text{s}^{-1}$ ,  $k_{DC}(1800) \approx 0.0025 \text{ nM}^{-1}\cdot\text{s}^{-1}$
  - $P(1800) \approx 2.7$ ,  $D(1800) \approx -0.1$

- At  $t = 3600$  s (end of the stressful event):
  - $DA(3600) \approx 90$  nM,  $C(3600) \approx 16$  nM
  - $k_P(3600) \approx 0.009$  nM $\cdot$ s $^{-1}$ ,  $k_D(3600) \approx 0.021$  nM $\cdot$ s $^{-1}$
  - $k_{PD}(3600) \approx 0.0011$  nM $^{-1}\cdot$ s $^{-1}$ ,  $k_{DC}(3600) \approx 0.002$  nM $^{-1}\cdot$ s $^{-1}$
  - $P(3600) \approx -1$ ,  $D(3600) \approx 0.6$

These results demonstrate how the model captures the dynamic changes in neurotransmitter levels, efficiencies, and perceptions of pleasure and pain in response to different stimuli. During the pleasurable activity, dopamine levels increase, leading to a higher perception of pleasure. The efficiency of dopamine production,  $k_P(t)$ , decreases slightly due to the sustained elevation of dopamine, reflecting the development of tolerance.

During the stressful event, cortisol levels rise, resulting in an increased perception of pain. The efficiency of cortisol production,  $k_D(t)$ , increases, indicating sensitization to stress. The interaction factors,  $k_{PD}(t)$  and  $k_{DC}(t)$ , also change, modulating the cross-talk between dopamine and cortisol.

This numerical example showcases the ability of our model to simulate realistic scenarios with biologically plausible units and magnitudes. It highlights the dynamic interplay between pleasure, pain, and stress and how the model captures the adaptations in the underlying neurochemical processes. By providing concrete quantitative predictions, the model demonstrates its potential for guiding future research and informing the development of targeted interventions for maintaining well-being and preventing disorders related to dysregulated pleasure-pain balance.

## 12. Qualitative Analysis of the Dynamics

### 12.1. During Excessive Pleasure

- **Elevated Dopamine:**  $DA(t) > DA_{\text{base}}$  leads to  $\frac{dk_P}{dt} < 0$ , decreasing  $k_P(t)$ . Decrease in  $k_P(t)$  reduces the dopaminergic response to future pleasurable stimuli.
- **Cortisol Reduced by Dopamine:** Increase in  $k_{DC}(t)$  enhances the ability of dopamine to reduce cortisol.

### 12.2. During Chronic Stress

- **Elevated Cortisol:**  $C(t) > C_{\text{base}}$  leads to  $\frac{dk_D}{dt} > 0$ , increasing  $k_D(t)$ . Increase in  $k_D(t)$  amplifies cortisol production in response to stressors.
- **Cortisol Reduces Dopamine:** Increase in  $k_{PD}(t)$  intensifies the negative effect of cortisol on dopamine, decreasing  $DA(t)$  and, consequently,  $P(t)$ .

### 12.3. Feedback Mechanisms

- **Tolerance to Pleasure:** The decrease in  $k_P(t)$  reflects a reduced sensitivity to pleasurable stimuli, requiring higher intensity to achieve the same level of pleasure.
- **Sensitization to Stress:** The increase in  $k_D(t)$  indicates that minor stressors can elicit a more significant cortisol response, increasing  $D(t)$ .

## 13. Potential Scenarios and Simulations

### 13.1. Scenario 1: Prolonged Exposure to Intense Pleasure

- **Pleasure Input:** High and constant  $u_P(t)$  over an extended period.
- **Expected Outcome:**
  - $DA(t)$  initially increases, elevating  $P(t)$ .
  - $k_P(t)$  decreases over time, reducing the efficiency of dopamine production.
  - Development of tolerance; higher  $u_P(t)$  is needed to maintain  $P(t)$ .
  - $k_{DC}(t)$  increases, reducing  $C(t)$  and  $D(t)$ .

### 13.2. Scenario 2: Chronic Stress

- **Stress Input:** High and constant  $u_D(t)$ .
- **Expected Outcome:**
  - $C(t)$  increases, elevating  $D(t)$ .
  - $k_D(t)$  increases, amplifying the stress response.
  - $k_{PD}(t)$  increases, intensifying the reduction of  $DA(t)$ .
  - $P(t)$  decreases due to the decline in  $DA(t)$ .
  - Possible development of hypersensitivity to pain and anhedonia (inability to feel pleasure).

### 13.3. Scenario 3: Recovery and Homeostasis

- **Input Reduction:**  $u_P(t)$  and  $u_D(t)$  decrease or normalize.
- **Expected Outcome:**
  - The homeostasis terms ( $\gamma$ ) in the equations for  $k_P(t)$ ,  $k_D(t)$ ,  $k_{PD}(t)$ , and  $k_{DC}(t)$  cause a return towards the basal values.
  - Gradual restoration of sensitivity to pleasure and reduction of sensitization to stress.

## 14. Implications of the Model

- **Understanding Tolerance and Dependence:** The model shows how prolonged exposure to pleasurable stimuli can decrease the ability to experience pleasure, which is relevant in the context of addictions [12].
- **Impact of Chronic Stress:** It illustrates how sustained stress can increase sensitivity to pain and reduce the ability to feel pleasure, contributing to disorders such as depression [13].
- **Importance of Homeostatic Regulation:** It highlights the role of physiological mechanisms in restoring neurochemical balance after periods of imbalance [14].

## 15. Conclusion

We have extended the mathematical model to include the temporal dynamics of efficiencies in the responses to pleasure ( $k_P(t)$ ) and pain ( $k_D(t)$ ), as well as the interaction factors between cortisol and dopamine ( $k_{PD}(t)$  and  $k_{DC}(t)$ ). This model reflects how the human body adapts its sensitivity to pleasurable and stressful stimuli over time, incorporating processes of tolerance, sensitization, and homeostasis.

### Potential Applications:

- **Clinical Research:** Better understanding the mechanisms behind addictions, chronic stress, and mood disorders [13,15].
- **Therapeutic Interventions:** Designing strategies that modulate these parameters to restore the pleasure-pain balance in patients [16].
- **Personal Well-being:** Informing practices that avoid overstimulation or chronic stress, promoting a healthy balance [17].

### Limitations and Considerations:

- The model is a simplification and does not capture the full complexity of neurobiological interactions.
- The parameters and functions used can vary significantly between individuals and require calibration with empirical data [18].
- Additional factors such as other neuro-transmitters (serotonin, endorphins), receptors, and signaling pathways are not included but may influence the dynamics [19].

## 16. Concluding Remarks

This mathematical model provides a tool to conceptualize and analyze how efficiencies in the responses to pleasure and pain, as well as the interactions between cortisol and dopamine, evolve dynamically over time. By integrating these dynamics, we can gain a deeper understanding of the underlying processes that affect our perceptions and behaviors related to pleasure and pain.

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