LATENT INHIBITION AND ITS NEURAL SUBSTRATES

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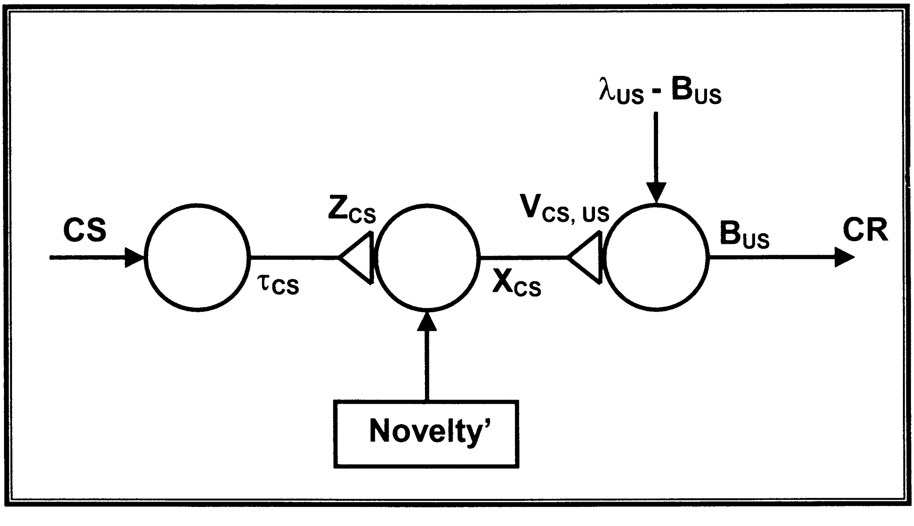
A Neural Network Model Of Latent Inhibition: From Animal Experiments to Schizophrenia



To Mabel, Gabriela, and Mariana

Contents

Preface

For a long time, psychological theories were simply presented in verbal form and the complexity and intricacies of some cognitive behaviors prevented these theories from providing a precise account of the data. With the advent of mathematical models, theoretical psychology entered a realm so far reserved for the more mature natural sciences.

Today, complex behavioral interactions and complex brain mechanisms can be described in terms of the non-linear dynamics of neural networks. The systems of differential equations that formalize the neural networks, although difficult to solve by hand, are easily solved by computers. In addition, we can rapidly experiment with computer models and predict the behavior of animals in different experimental situations. Furthermore, neural network models allow us to simultaneously develop psychological theories and models of the brain.

In a previous book (Schmajuk, 1997), I described several connectionist theories of animal learning and cognition. Starting with the simple assumption that psychological associations are represented by the strength of synaptic connections, I offered mechanistic descriptions of complex behaviors. The present book applies a neural network model of classical conditioning to the description of the behavioral aspects of latent inhibition (LI) and the specification of the effects of brain manipulations on this phenomenon.

Chapter 1 presents a taxonomy of different models of LI. Chapter 2 presents a real-time, neural network model that describes LI. Chapter 3 shows that, by combining storage and retrieval processes, the model describes many of the properties of LI. Chapter 4 maps nodes and connections in the model onto different brain regions. Critically, a variable called Novelty' is mapped onto the dopaminergic projection to the nucleus accumbens.

Based on the mapping offered in Chapter 4, Chapter 5 shows how the model describes the effect of dopaminergic agonists and antagonists in combination with different behavioral parameters. Chapter 6 shows that, under the mapping described in Chapter 4, the model describes the apparently conflicting data base related to the effect of hippocampal lesions on LI. Again, by applying the mapping described in Chapter 4, Chapter 7shows how the model describes the effect of lesions of different regions of the nucleus accumbens in combination with dopaminergic antagonists. Finally, Chapter 8 proposes that the relevance of animal research on the neural bases of LI is underscored by the fact that LI is absent in acute schizophrenia, a psychopathological disorder in which hippocampal dysfunction is suspected.

A version of the program used to run the computer simulations presented in this book is available on request.

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This book is the result of a long collaboration with Professor Jeffrey Gray of the Institute of Psychiatry in London. My interaction with Jeffrey started when we discovered that, although different in the details, our views of schizophrenia were centered on the hippocampus. During a short visit to London, we decided to collaborate in building a model of LI and using the model to show how LI is impaired in schizophrenic patients. First through a Fellowship from the Royal Society and then with support from NATO, Jeffrey and I worked together for several years on the model. My memories of this collaboration are among the best of my scientific career.

Some of my students at Northwestern and Duke also participated of the enterprise. Beth Christiansen, with whom we studied the effect of hippocampal lesions on LI. Patrick Lam, who wrote the computer programs and ran the simulations of the behavioral properties of the model. Catalin Buhusi, who ran the simulations of the effect of dopaminergic manipulations and hippocampal lesions on LI. Landon Cox, who ran the simulations of the effect of lesions of the nucleus accumbens. John Tye and Chris Lai who worked on the preliminary results in some of our projects. Finally, Lynn Talton who proofread this book. To all of them my most sincere tanks.

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Buhusi, C.V., Gray, J.A, and Schmajuk, N.A. (1996). The perplexing effects of hippocampal lesions on latent inhibition: A neural network solution. *Behavioral Neuroscience, 112*, 316-351.

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Schmajuk, N.A. (2001) Hippocampal dysfunction in schizophrenia. *Hippocampus, 11*, 599-613.

Glossary

$B_{i,k}$: Prediction of CS_k by CS_i
$B_{i,US}$: Prediction of the US by CS_i
B_k: Aggregate prediction of event k by all CSs with τ_i's active at a given time
$\bar{B}_k$: Average prediction of event k
BS: Between-subject procedure
B_{US}: Aggregate prediction of the US by all CSs with τ_i's active at a given time
$\bar{B}_{US}$: Average prediction of the US
BW: Between-subject procedure with interspersed water presentations
CN: Compound stimulus
CR: Conditioned Response
CS: Conditioned Stimulus
CX: Contextual stimuli
DA: Dopamine
EC: Entorhinal cortex
GABA: γ -aminobutiric acid.
GLU: Glutamate
HAL: Haloperidol
HF: Hippocampal Formation
HFL:Hippocampal Formation lesion
HP: Hippocampus Proper
HPL: Hippocampus Proper lesion
ITI: Intertrial interval
LI: Latent Inhibition
NAC: Nucleus Accumbens
NCX: Neocortex
$Novelty_i$: Novelty of stimulus CS_i
$Novelty = \Sigma_k |\bar{\lambda}_k - \bar{B}_k|$
Novelty': Normalized value of Novelty
NPE: Nonpreexposed
PPT: Pendunculopontine tegmental nucleus
PRE: Preexposed
SAL : Saline
SL: Sham lesion
SN: Substantia nigra
THAL: Thalamic areas
UR: Unconditioned Response
US: Unconditioned Stimulus
$V_{i,j}$: Association of CS_i with CS_j
$V_{i,US}$: Association of CS_i with the US
VP: Ventral Pallidus
VTA: Ventral Tegmental Area
WS: Within-subject procedure,
WX: Within-subject procedure with context change
WW: Within-subject procedure with interspersed water presentations
X_i : Internal representation of CS_j
z_i : Association of X_i with Novelty'
λ_j: Observed value of CS_j
$\bar{\lambda}_j$: Average observed value of CS_j
λ_{US}: Observed value of the US
$\bar{\lambda}_{US}$: Average observed value of the US
τ_i: Trace of stimulus CS_i