

# ***Session 2:*** **Translating discoveries of epileptogenic mechanisms into cures**

***Chair:*** Frances Jensen, MD

***Speakers:*** Shlomo Shinnar, MD, PhD

Asla Pitkanen, MD, PhD

Helen Scharfman, PhD

Nico Moshe, MD

***Discussants:*** David Van Essen, PhD

Barry Connors, PhD

Rick Huganir, PhD

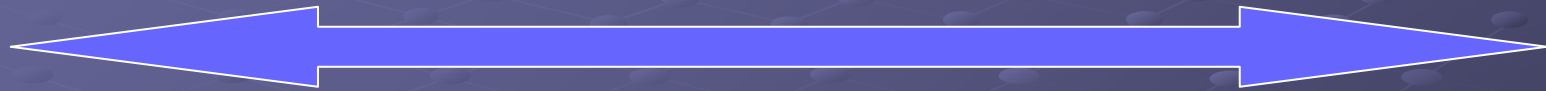
# Epileptogenesis

- Development of an epileptic condition
- *Development and extension* of tissue capable of generating chronic, recurrent, spontaneous behavioral and/or electrographic seizures
- *Progression* after the condition is established

# Seizure-induced changes in brain

“mild”

“severe”



Metabolic  
Perturbation

Altered protein  
synthesis of  
transient nature

Subtle structural  
change

Altered protein  
synthesis with  
enduring effects

Major structural  
changes

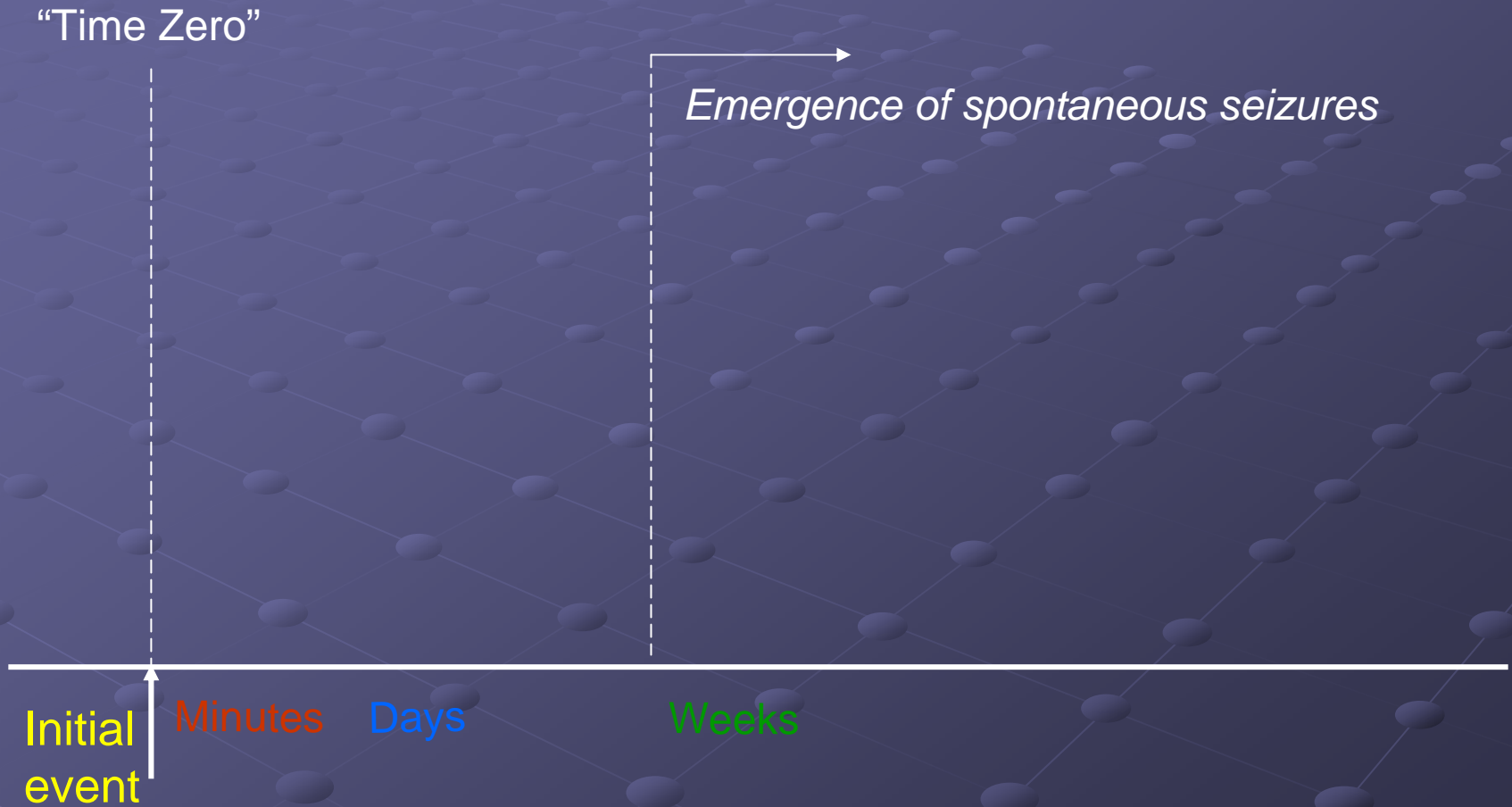
Axonal sprouting  
Dendritic  
reorganization

Neuronal death  
Gliosis



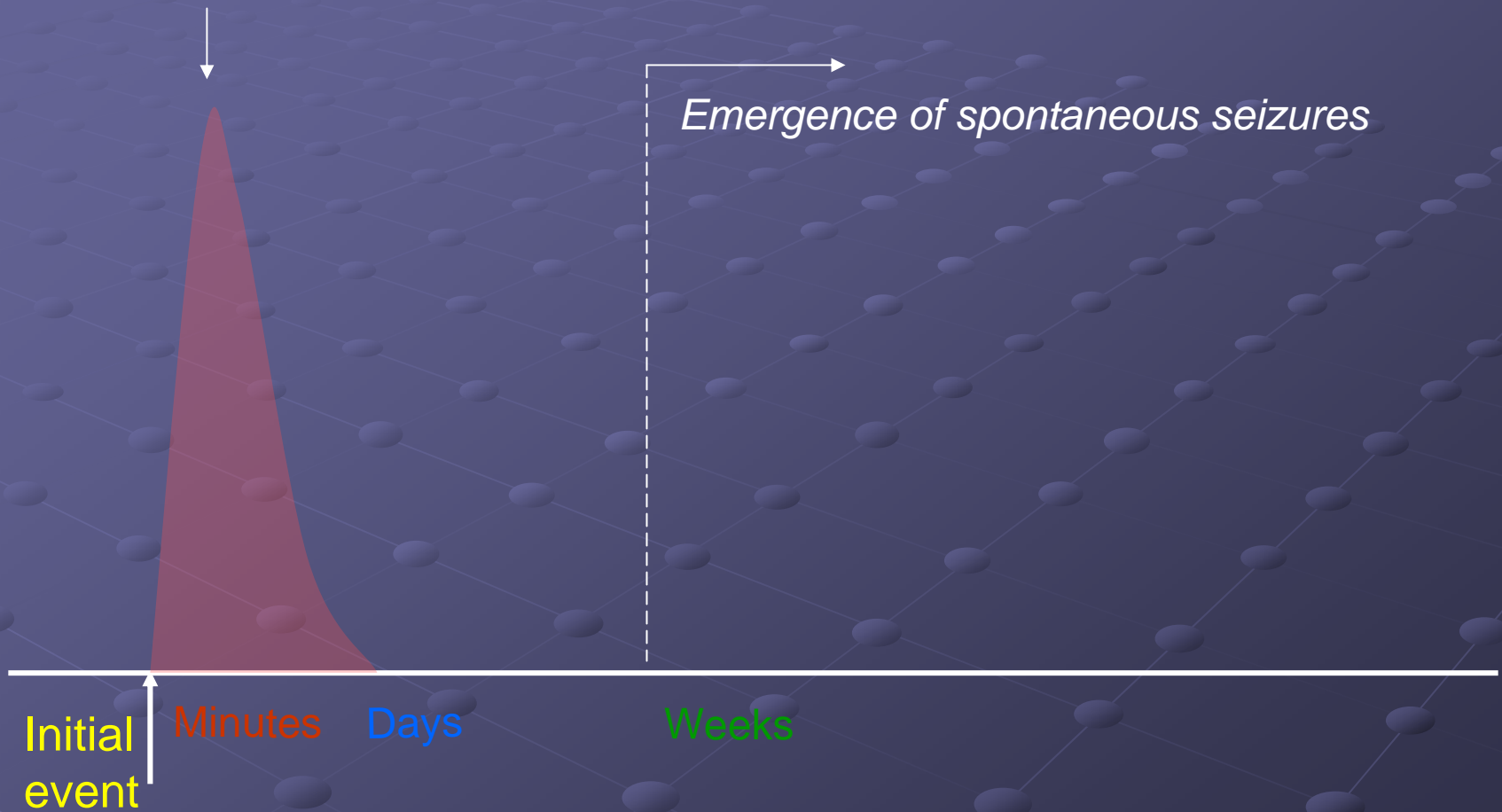
**EPILEPTOGENESIS  
COMORBIDITIES**

# Temporal Profile of Epileptogenesis



# Temporal Profile of Epileptogenesis

Ion channel activation  
Post-translational changes  
Immediate early genes



*Emergence of spontaneous seizures*

Initial  
event

Minutes

Days

Weeks

# Temporal Profile of Epileptogenesis

Transcriptional events  
Neuronal death  
inflammation



*Emergence of spontaneous seizures*

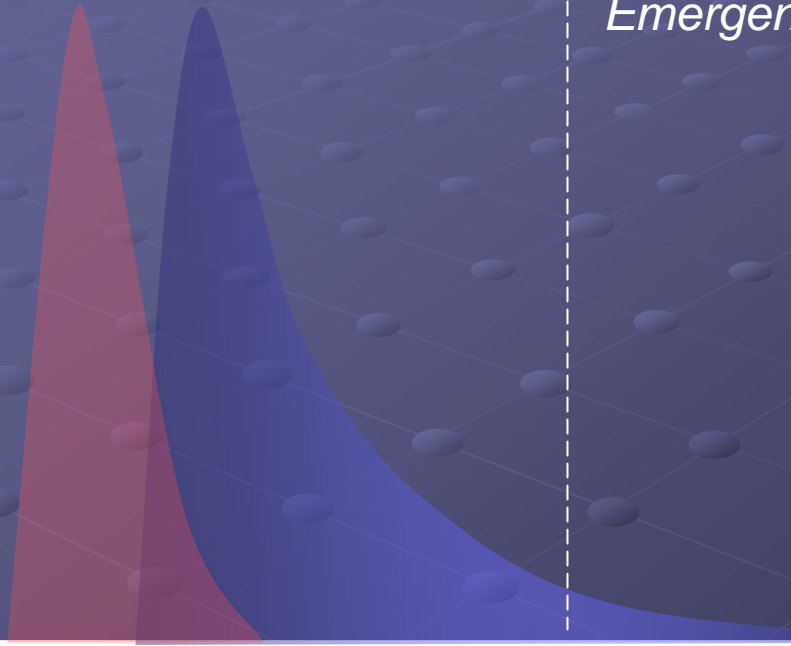


Initial event

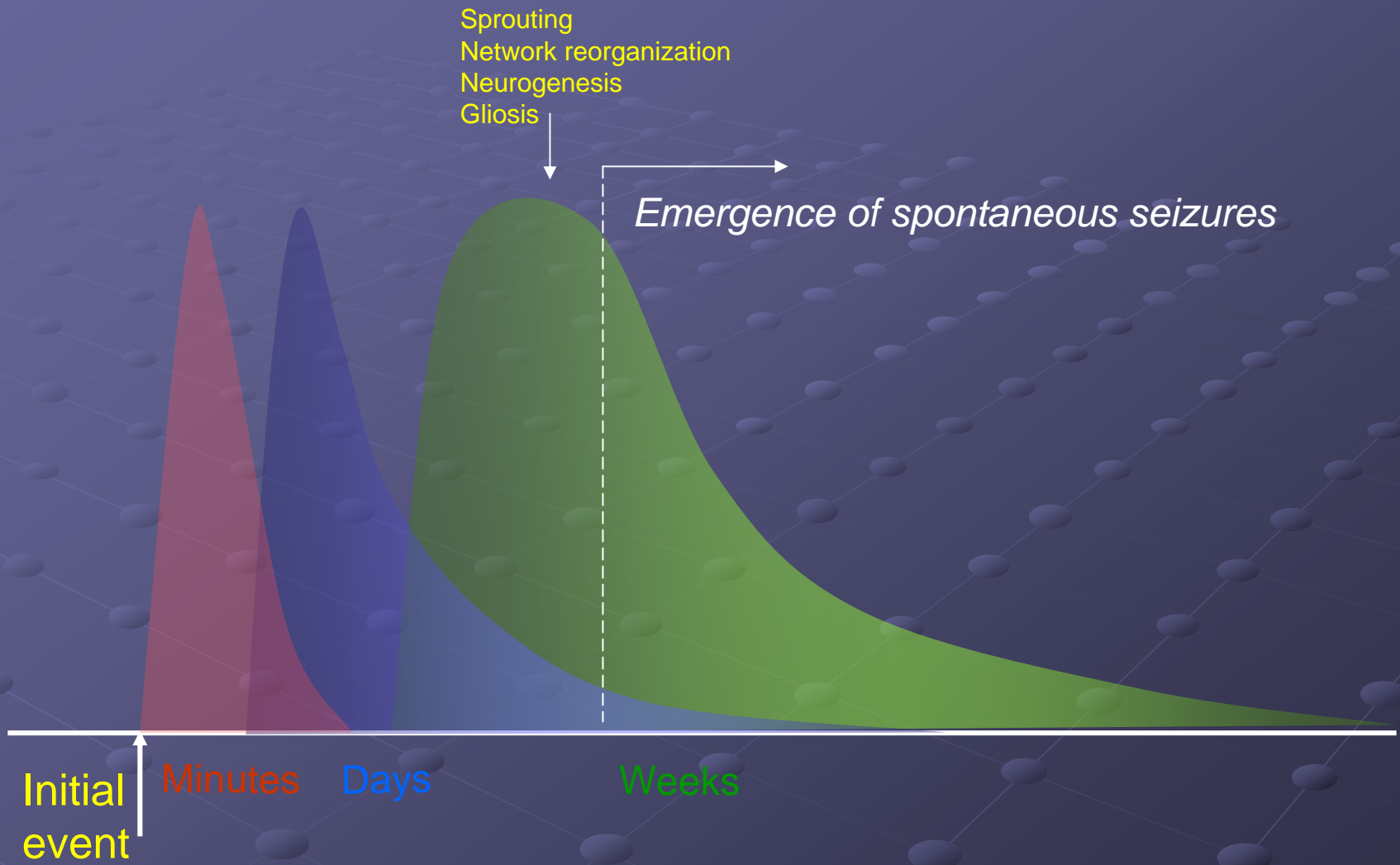
Minutes

Days

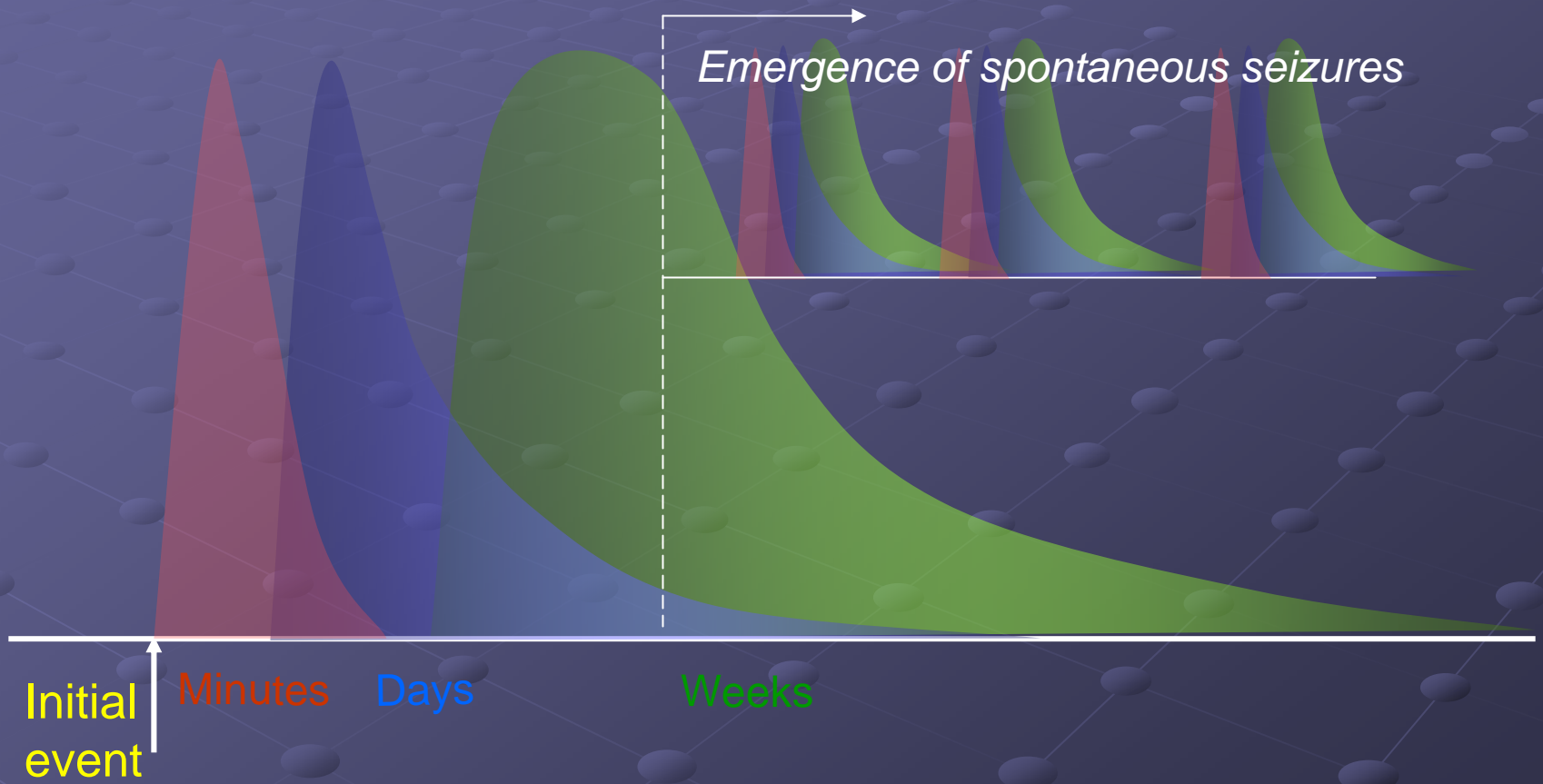
Weeks



# Temporal Profile of Epileptogenesis



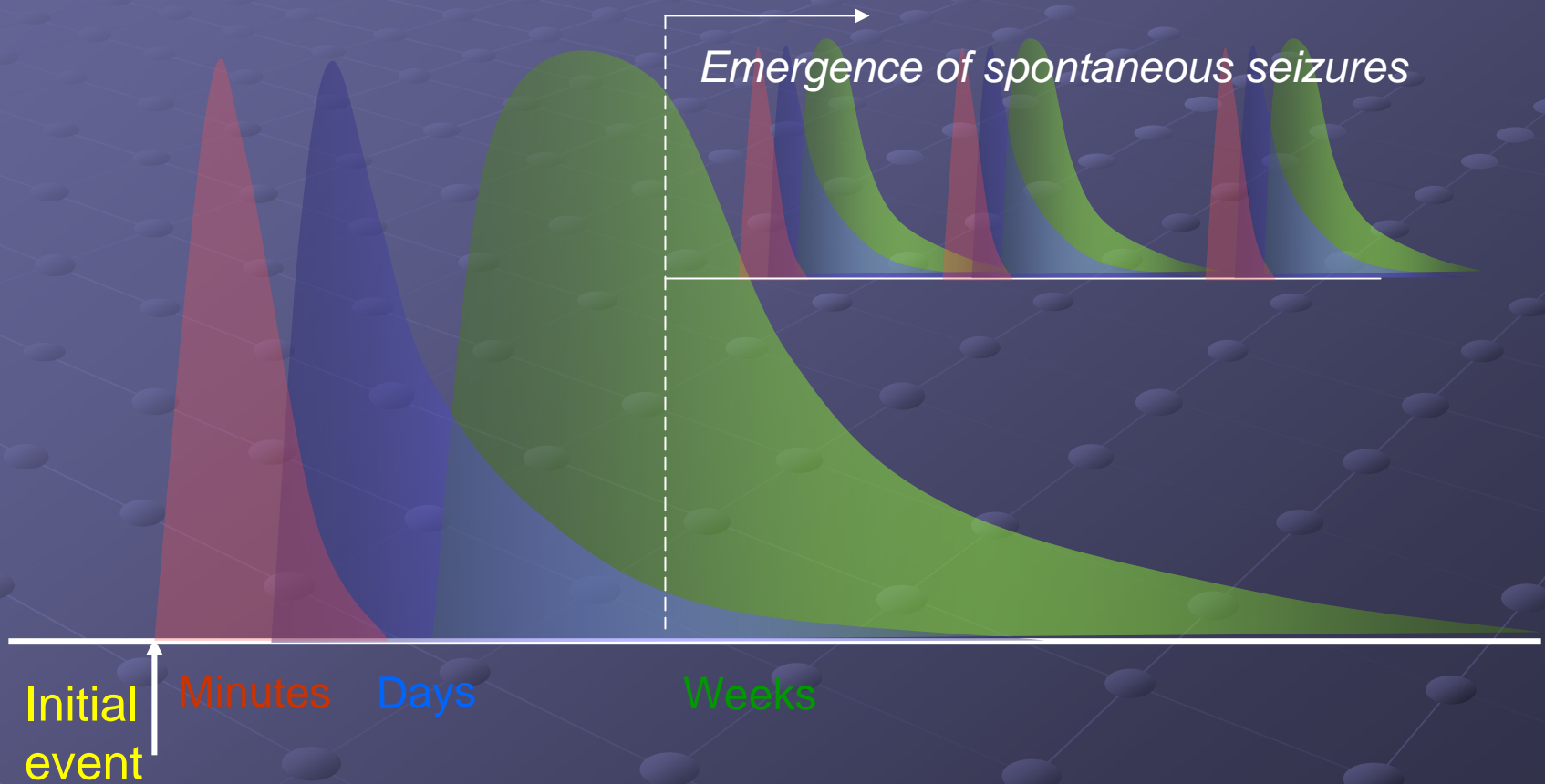
# Temporal Profile of Epileptogenesis





# Talk 1: Shinnar

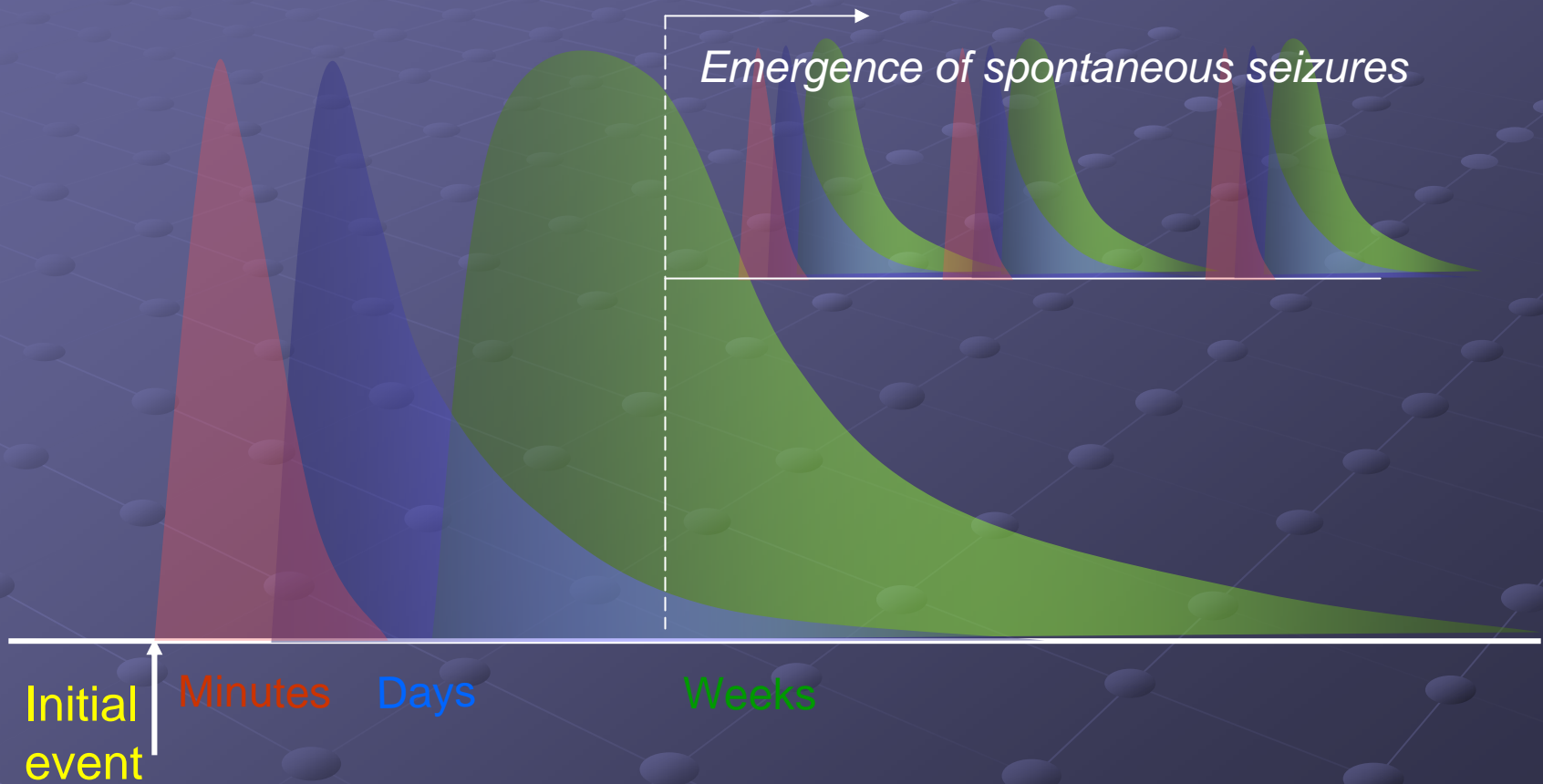
What clear examples of epileptogenesis are there?  
What is temporal profile in the human?



## Talk 2: Pitkanen

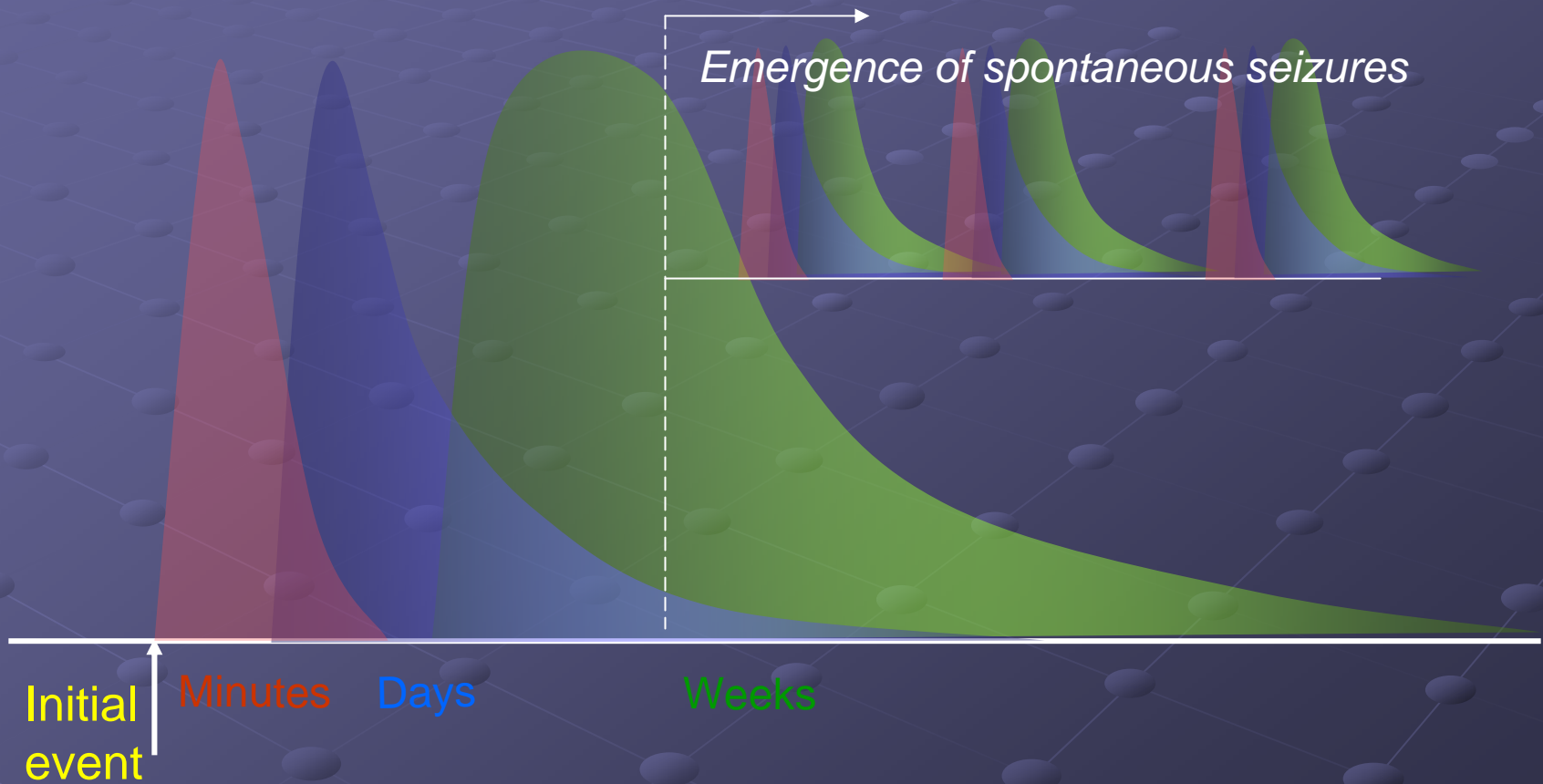
What animal models show this profile?

How can they be used for predictive studies and therapeutic trials?



## Talk 3: Scharfman

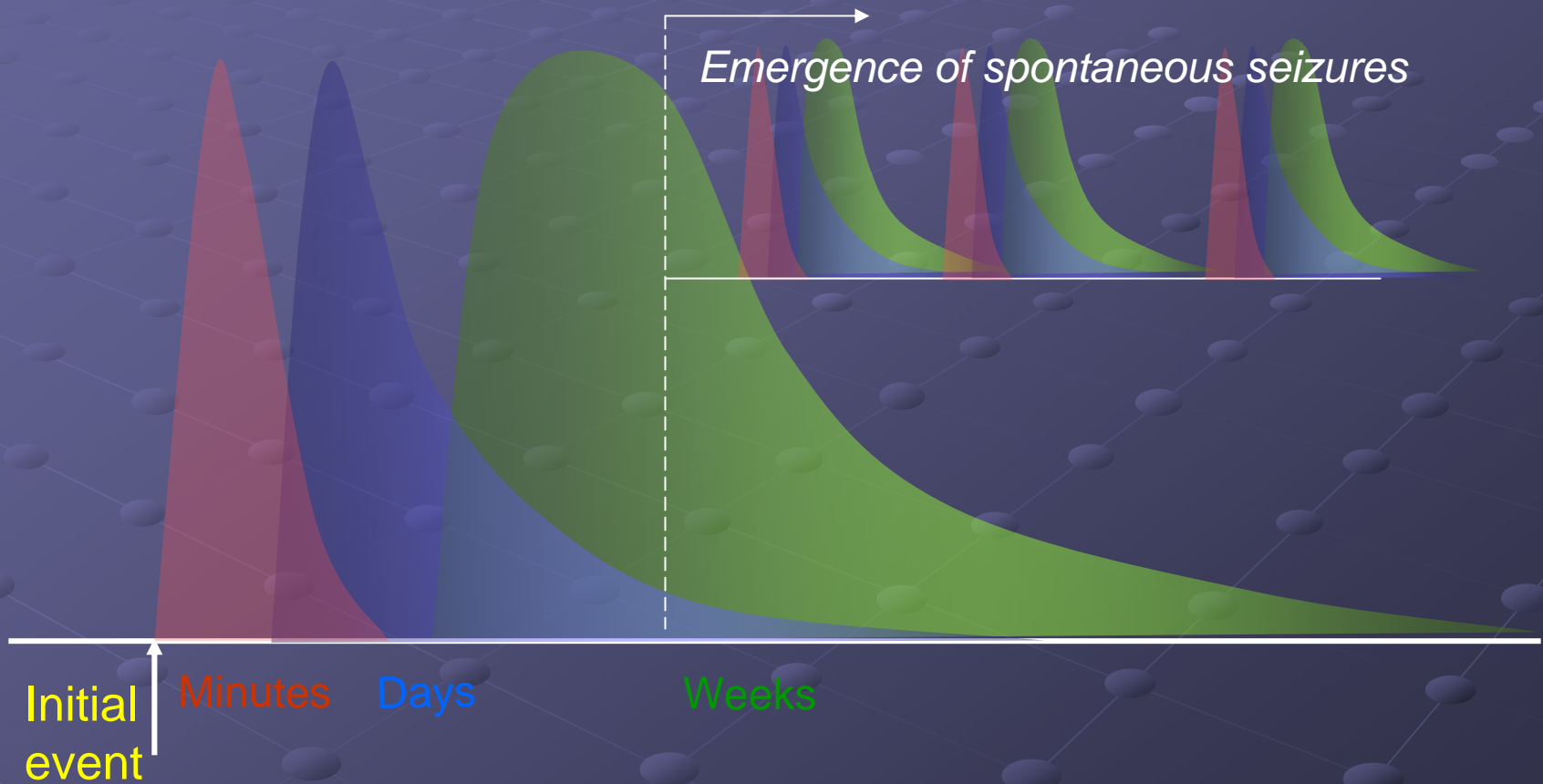
What specific mechanisms have been elucidated?  
What new classes of therapeutic targets have been identified?



## Talk 4: Moshe/Engel

How do we detect and measure epileptogenesis in the human?

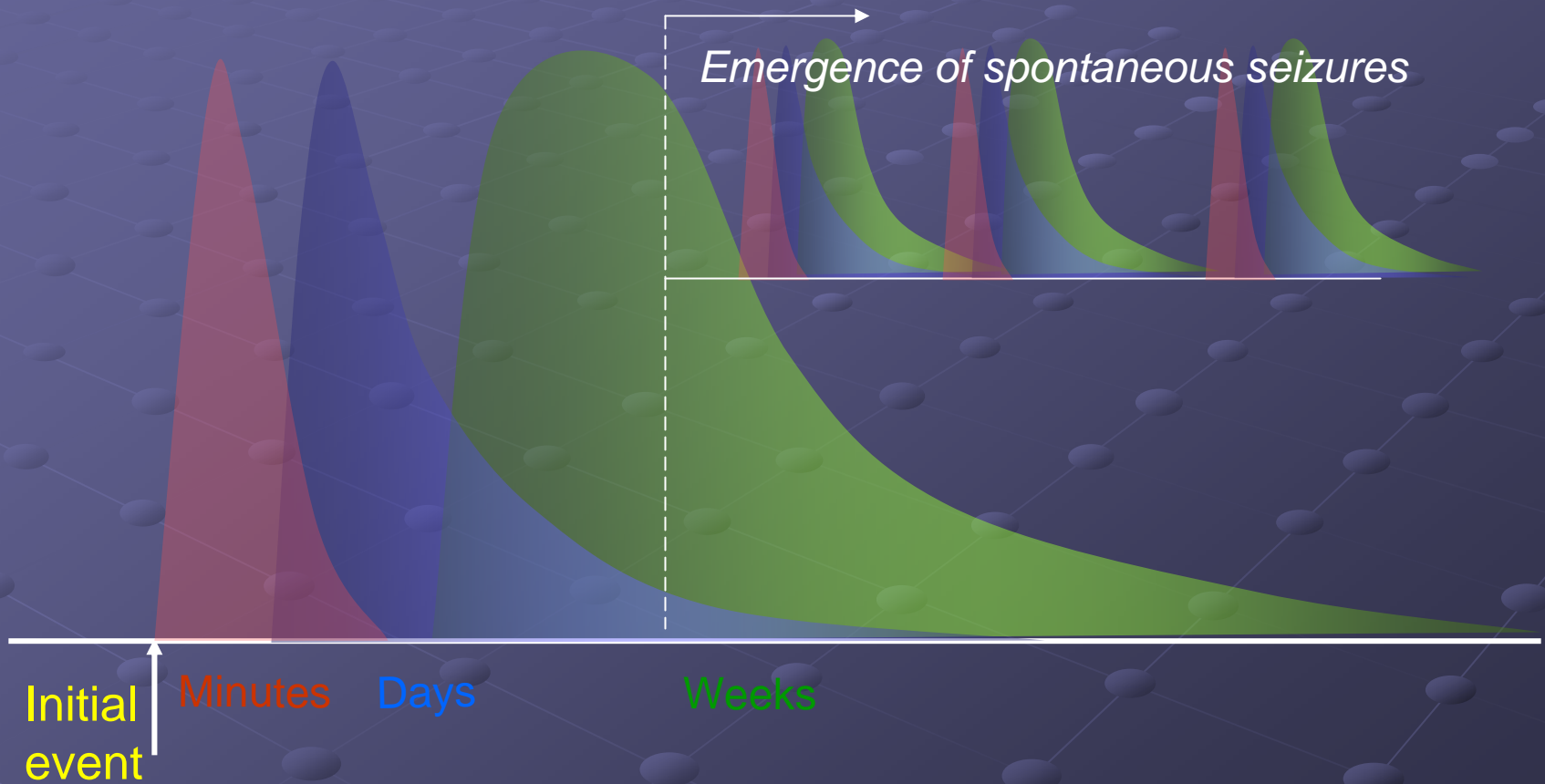
What may represent novel biomarkers for use in clinical diagnosis and treatment?



# Discussants

Where might basic neuroscience research contribute to the development of new diagnostic tools, treatment strategies, and biomarker development?

## CROSS-TALK



# Key Topics

- Detecting epileptogenesis of paramount importance
  - Application of new technologies
- Translating between experimental and human studies
- Multiple targets for therapeutic intervention along timeline
  - Disease modification
  - Antiepileptic versus antiepileptogenic therapy