

Monitoring the developing brain in crisis

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***The developing brain is
expensive and privileged***



***The developing brain
sustains injury
quietly
and on our watch***



***The developing brain is
unforgiving when injured***



Current neuromonitoring is limited

- mechanisms translating insult-to-injury are incompletely understood
- *the optimal target signals remain unclear*



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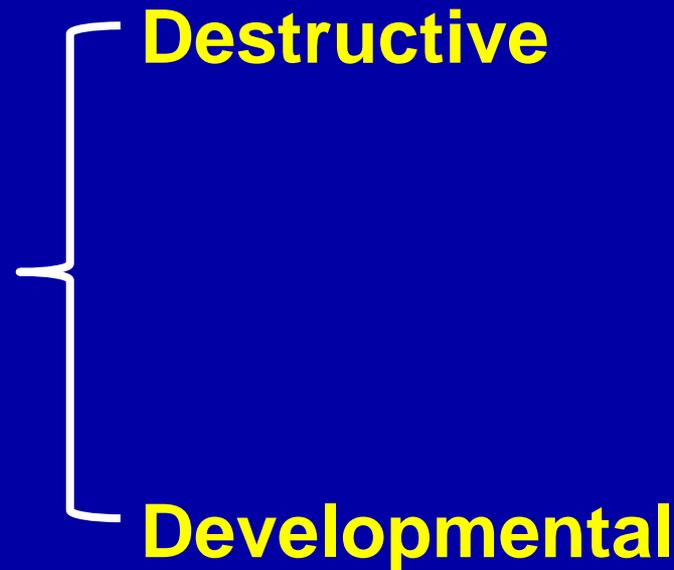
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- techniques have strengths and limitations
- *tools are used without a clear understanding of their limitations*

Pathways from insult to injury in the immature brain

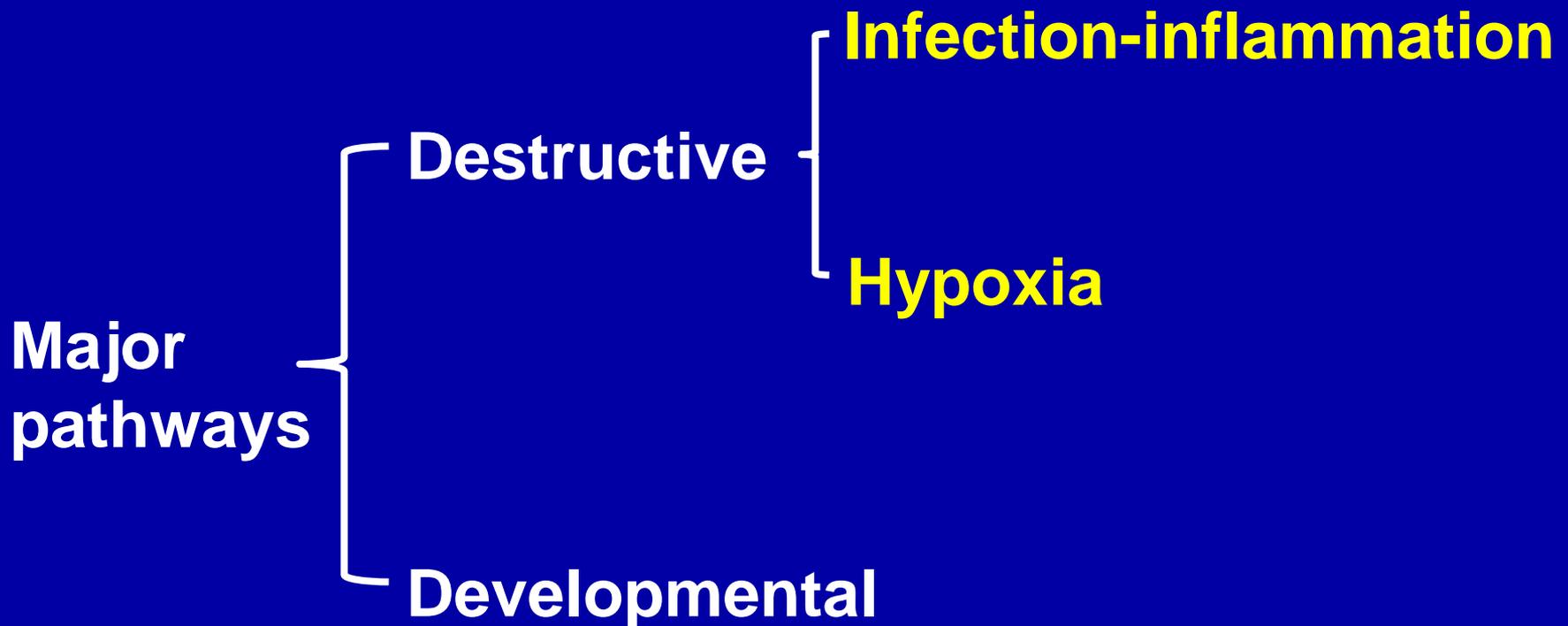


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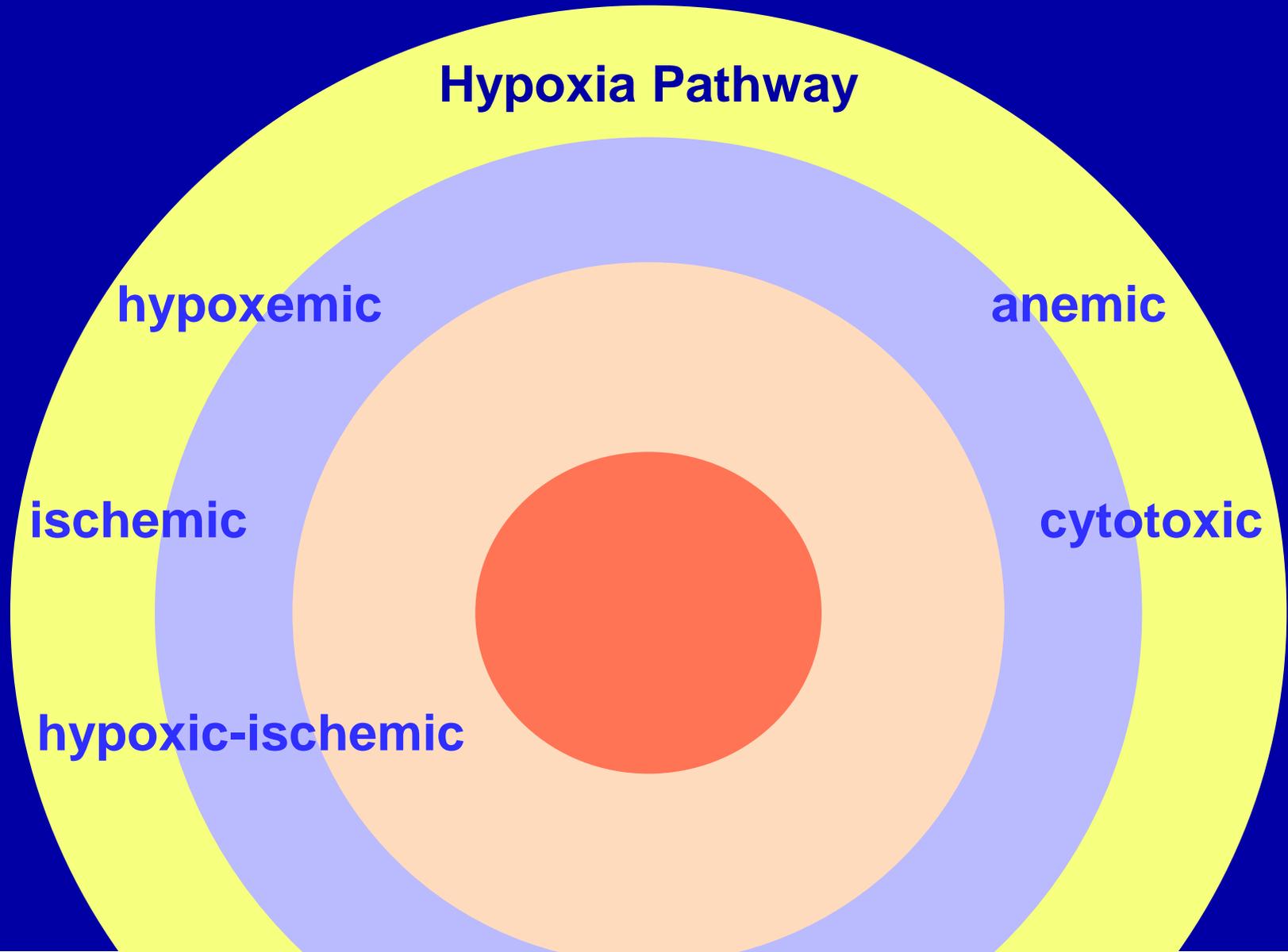
Two major pathways



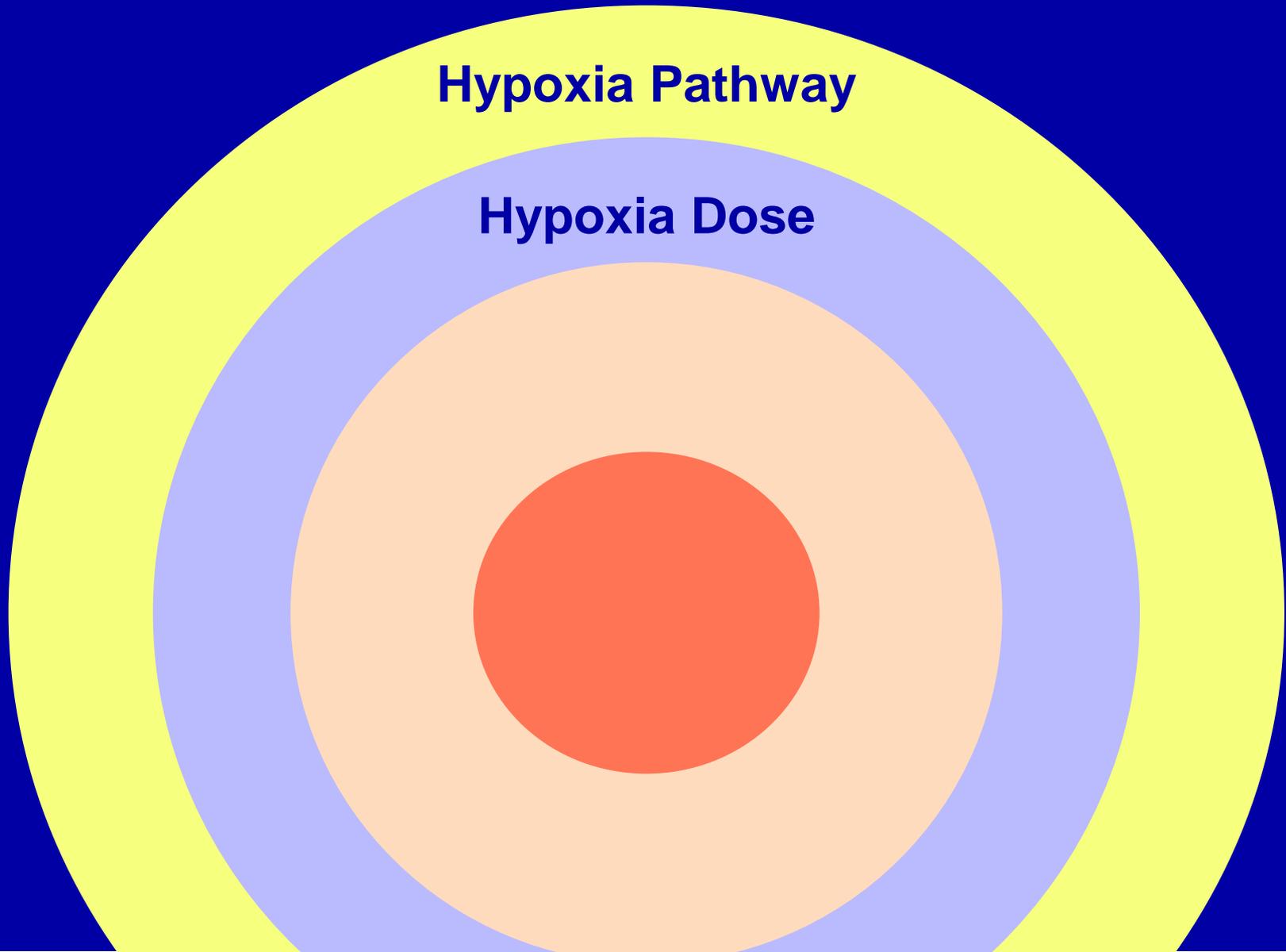
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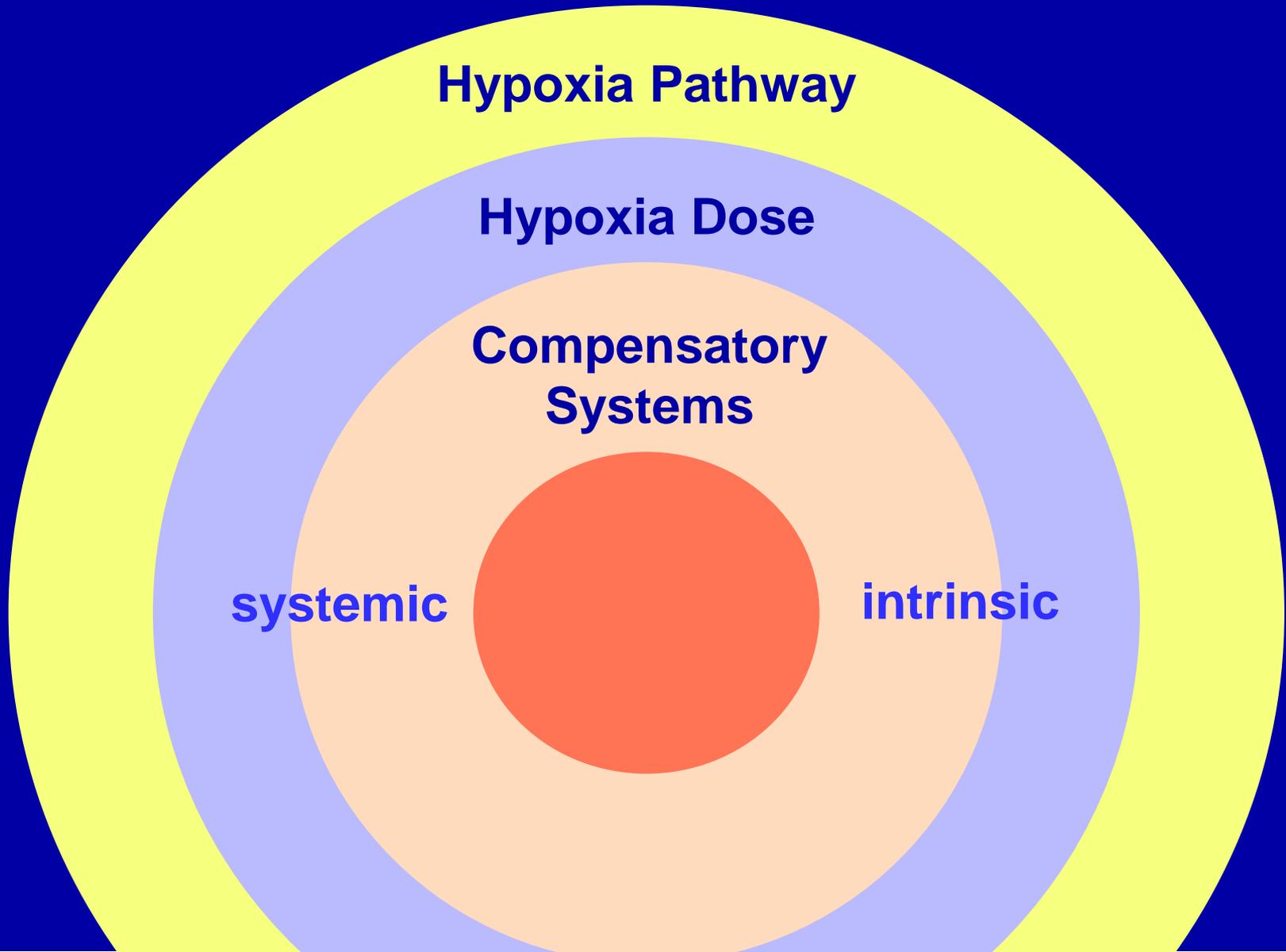
The multiple determinants of hypoxic brain injury



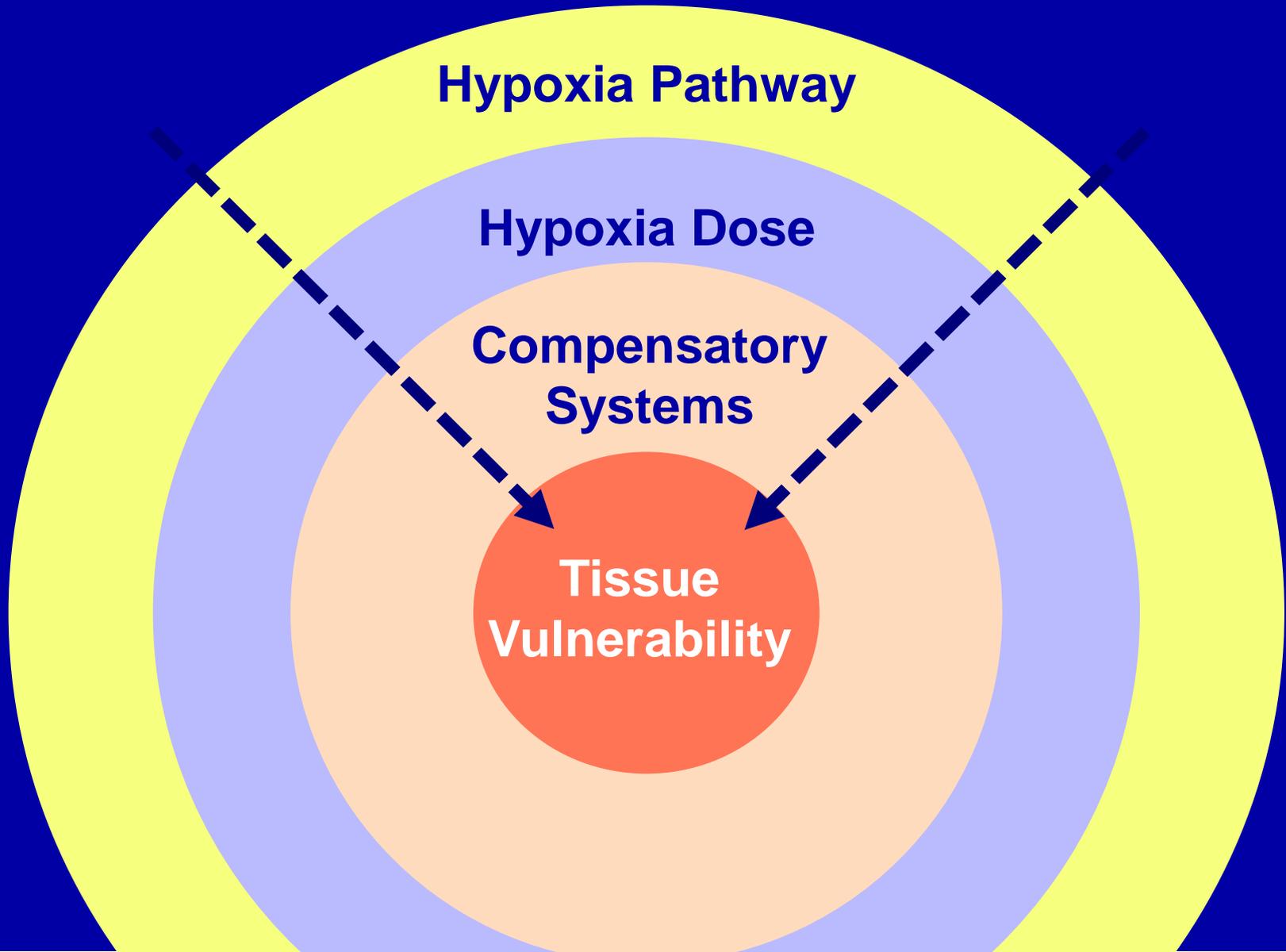
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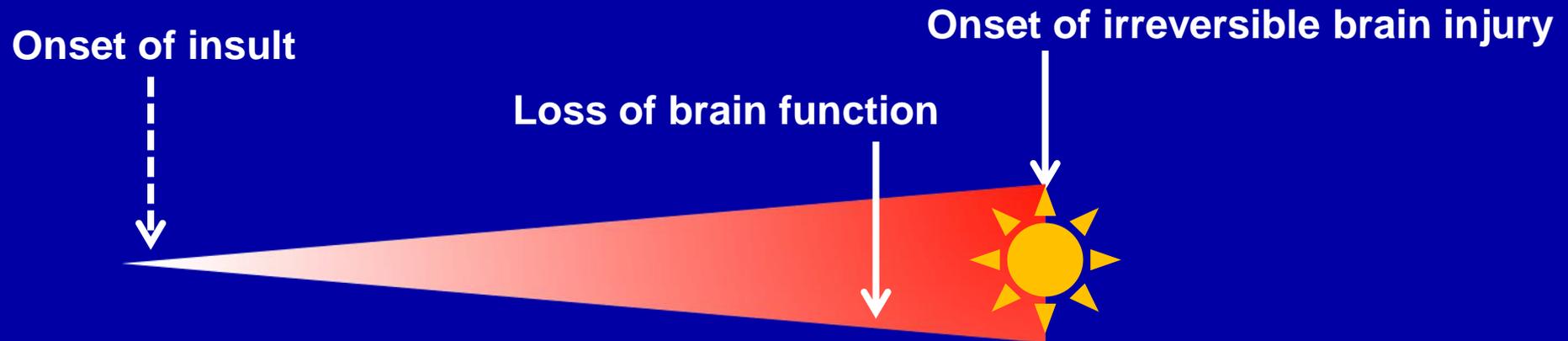
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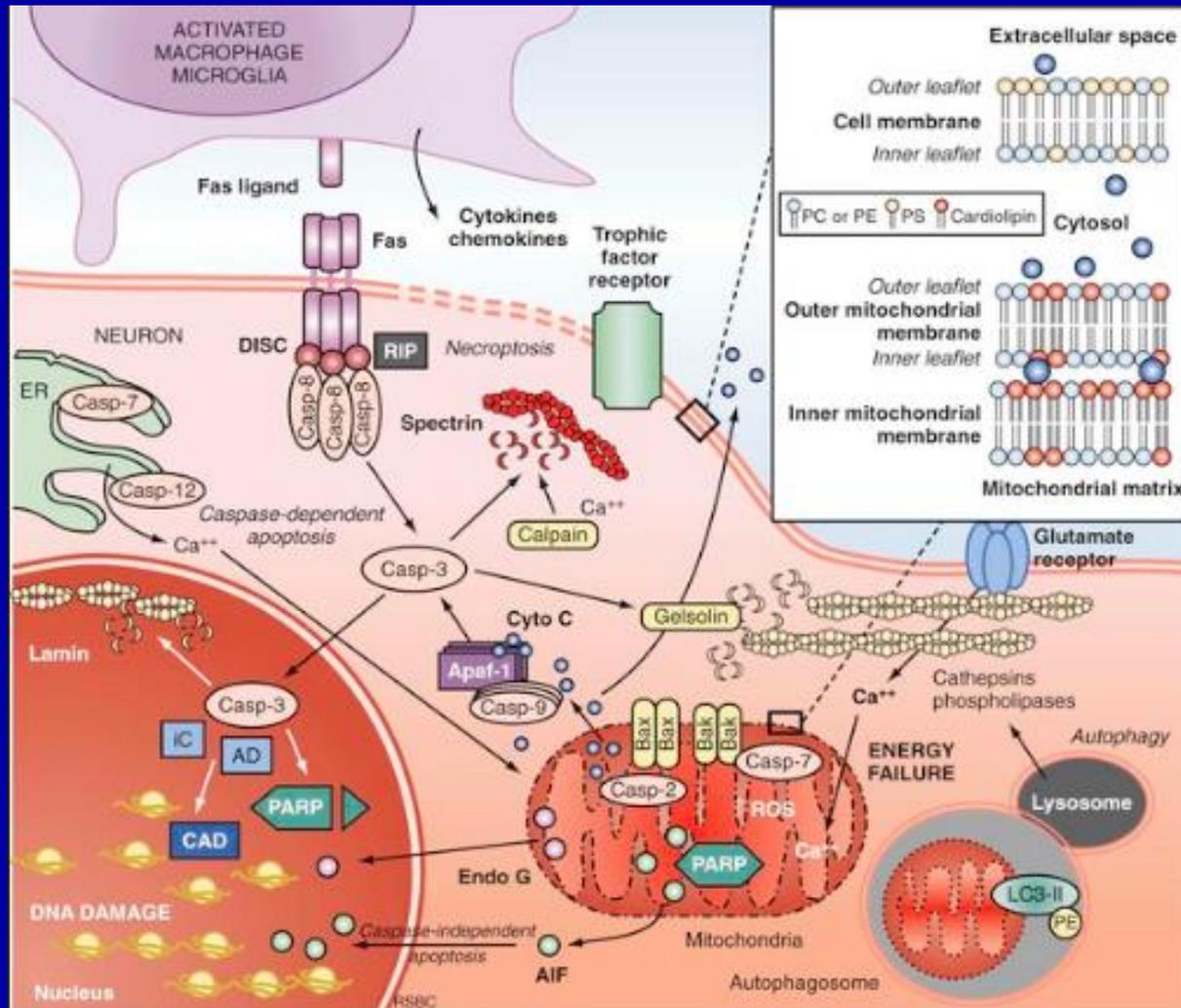


**Critical periods of development,
vulnerability and plasticity**

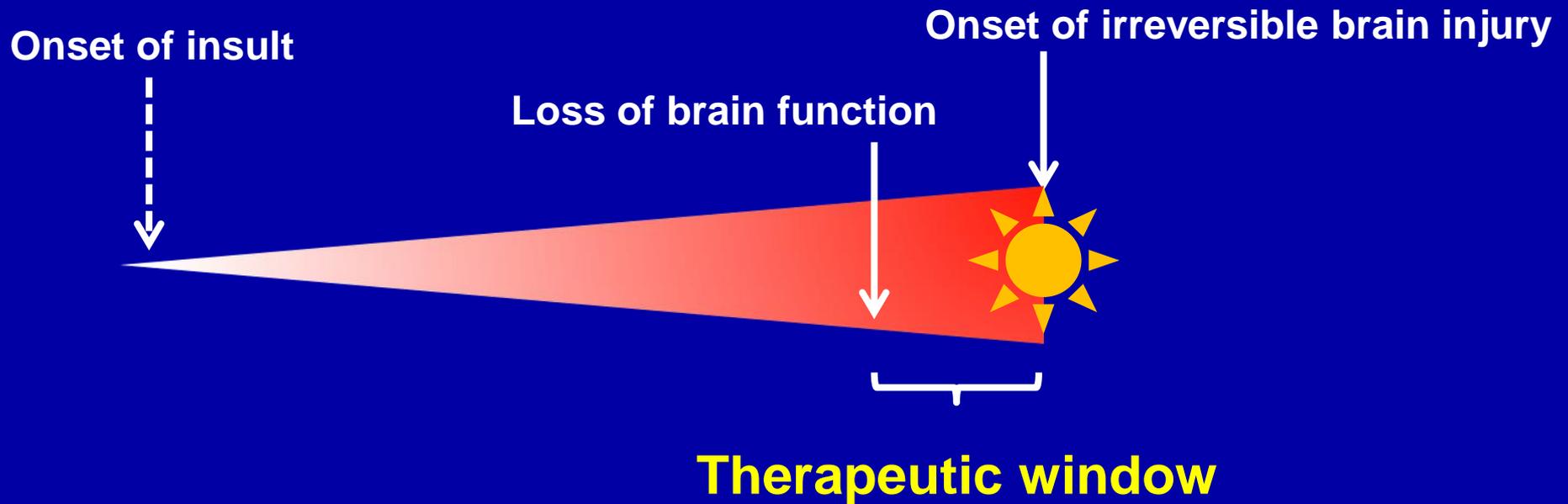
Insults may be well tolerated but once function fails structure soon follows



Post-insult cascades of brain injury

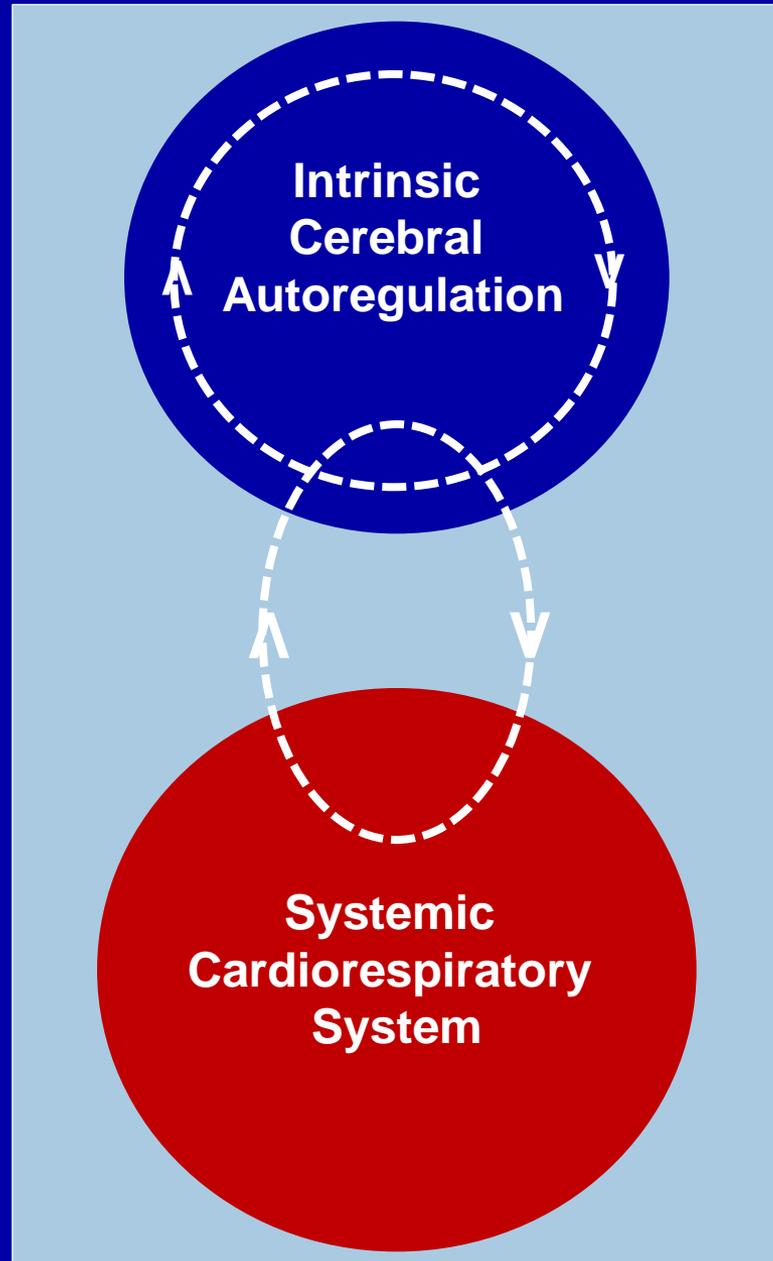


The therapeutic window

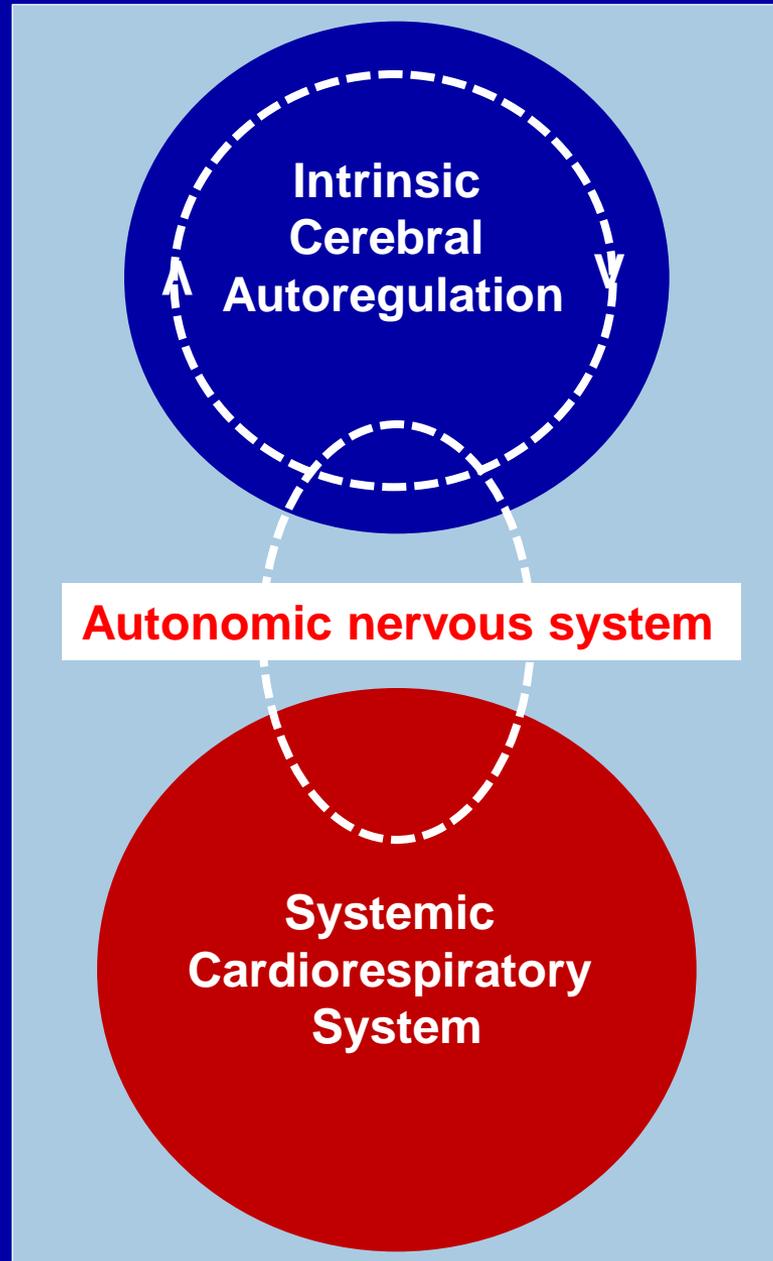


**The fundamental goals for neuromonitoring
are to open the therapeutic window,
to enable preventive neuroprotection, and to
guide brain-oriented neonatal care**

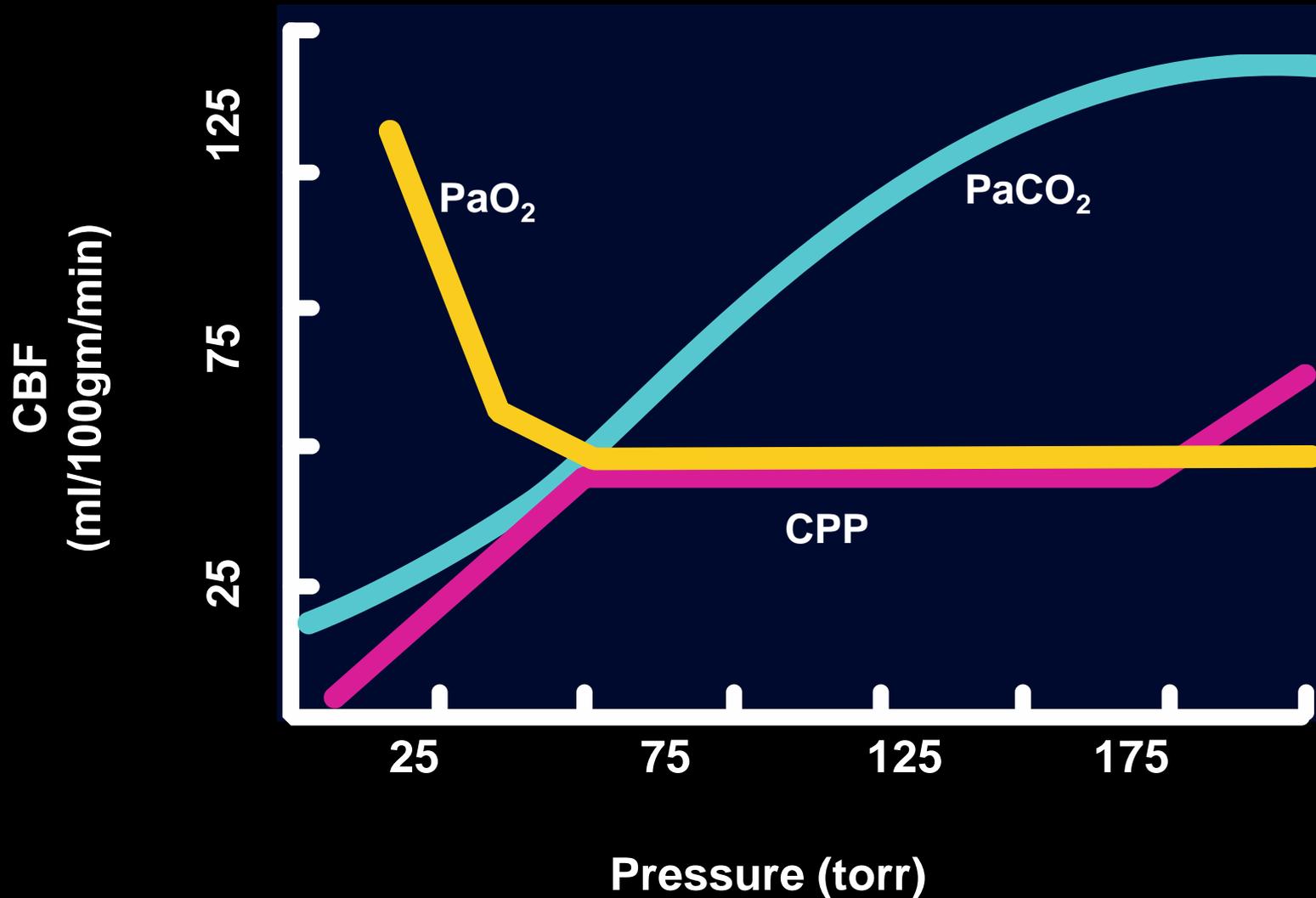
Endogenous neuroprotective systems



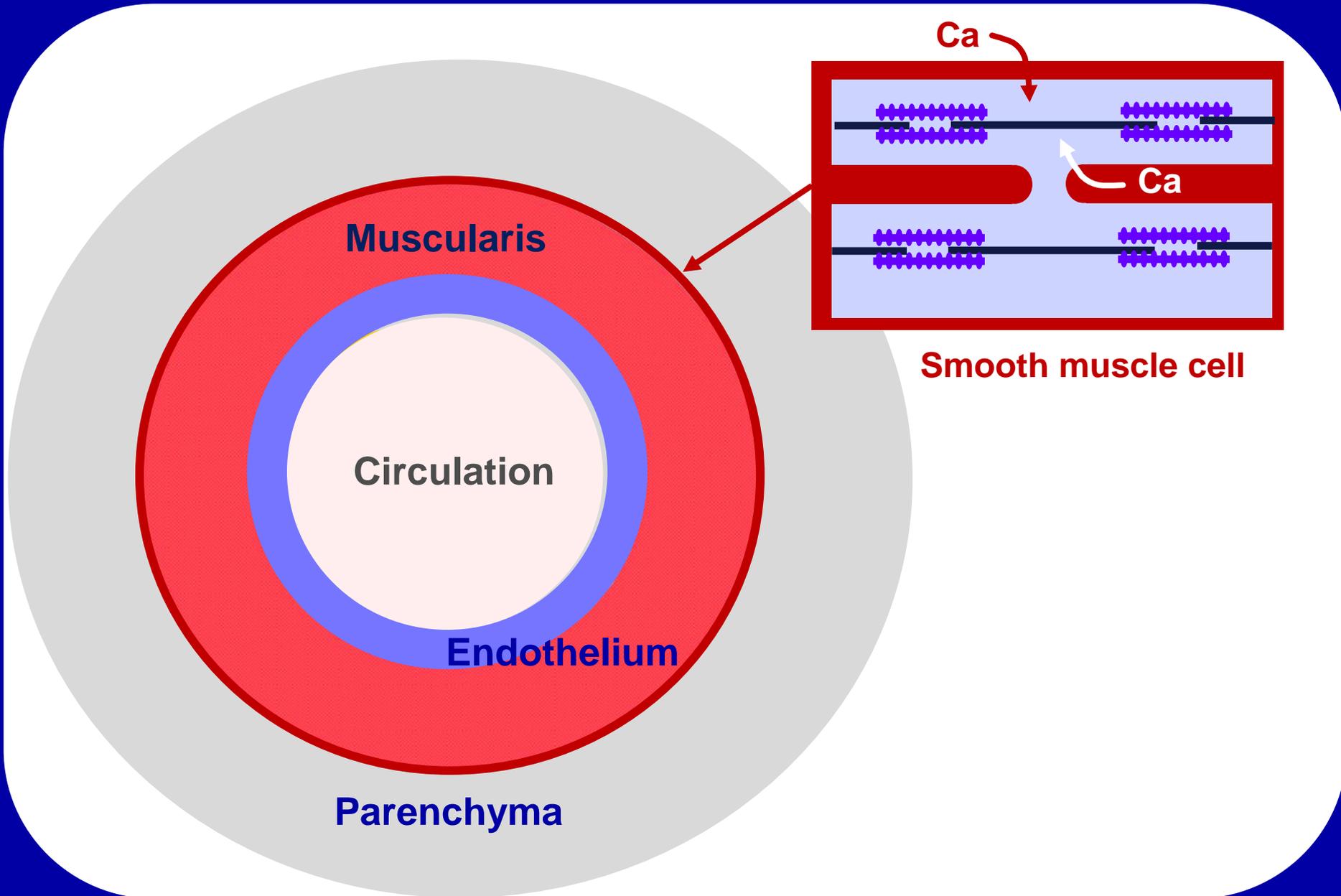
Communication between systems is costly



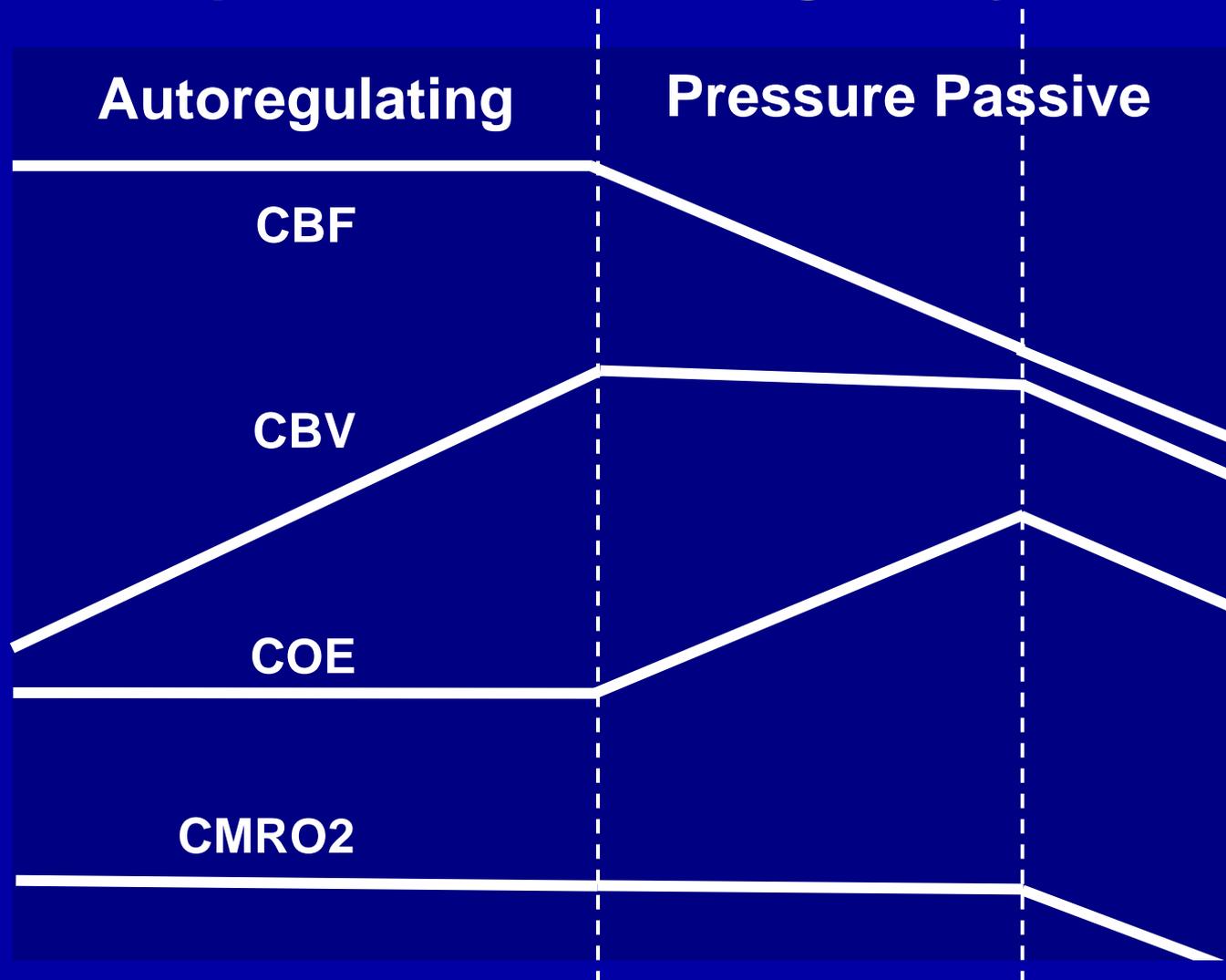
Intrinsic Cerebral Autoregulation



Intrinsic Regulation of Cerebrovascular Tone



Cerebral pressure-flow autoregulatory failure



Falling Blood Pressure

Near Infrared Spectroscopy

Measures absolute *change* in cerebral concentration of

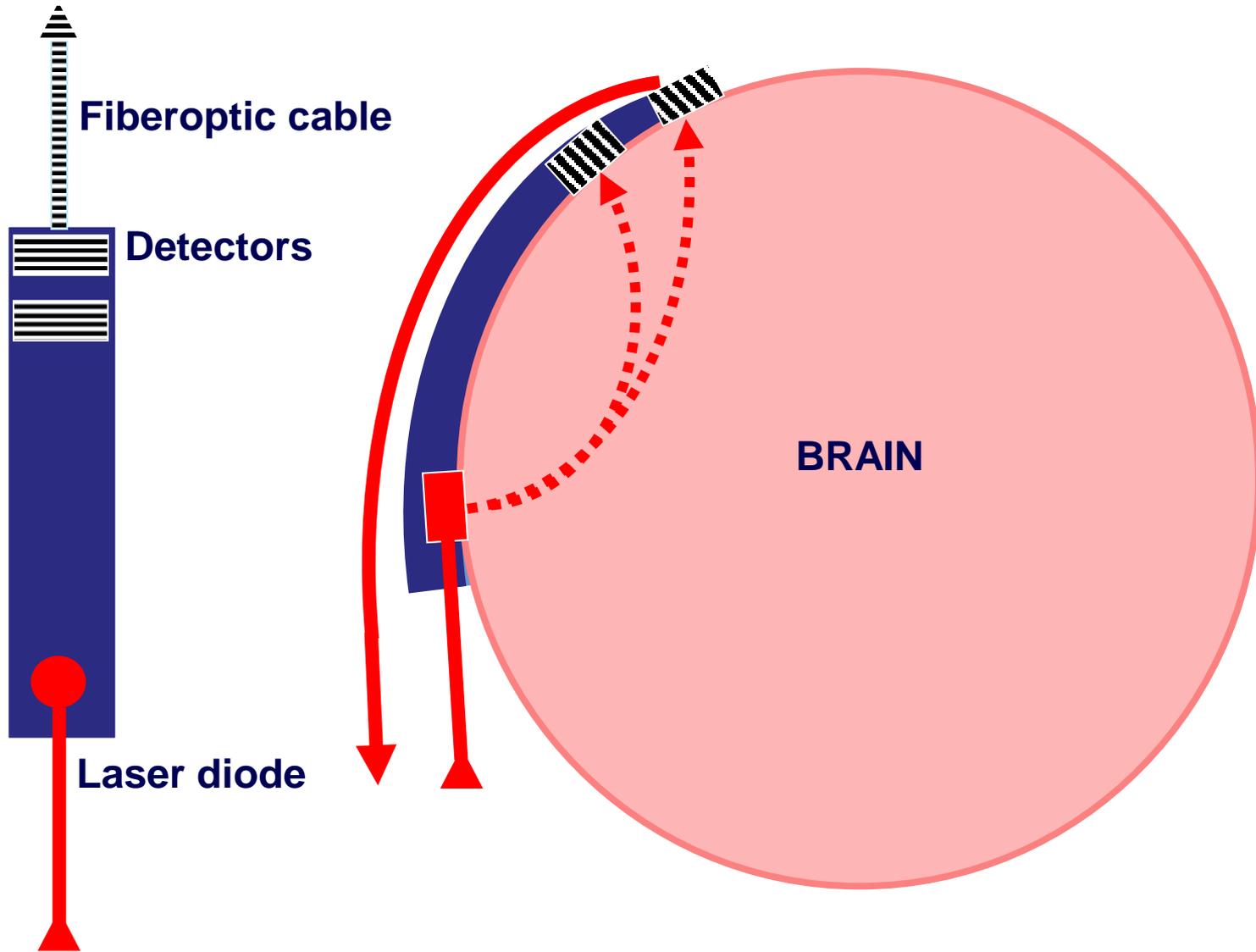
- oxygenated hemoglobin (HbO₂) (900 nm)
- deoxygenated hemoglobin (Hb) (760 nm)

Derived indices of cerebral hemodynamics and oxygenation

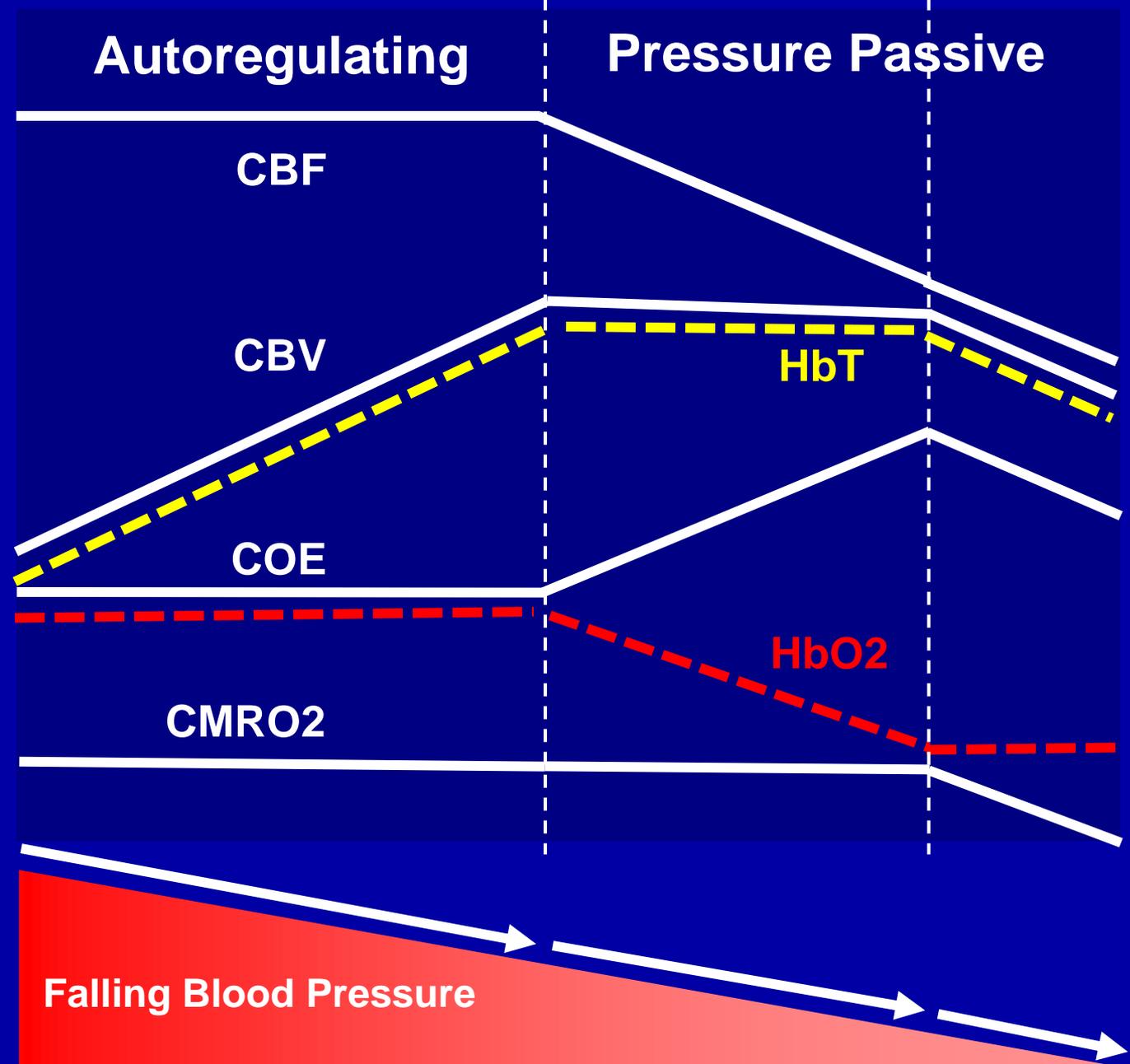
- $\text{HbT} = \text{HbO}_2 + \text{Hb}$ (~ CBV)
- $\text{HbD} = \text{HbO}_2 - \text{Hb}$ (~ CBF)
- HbO_2/HbT ~ cerebral hemoglobin saturation



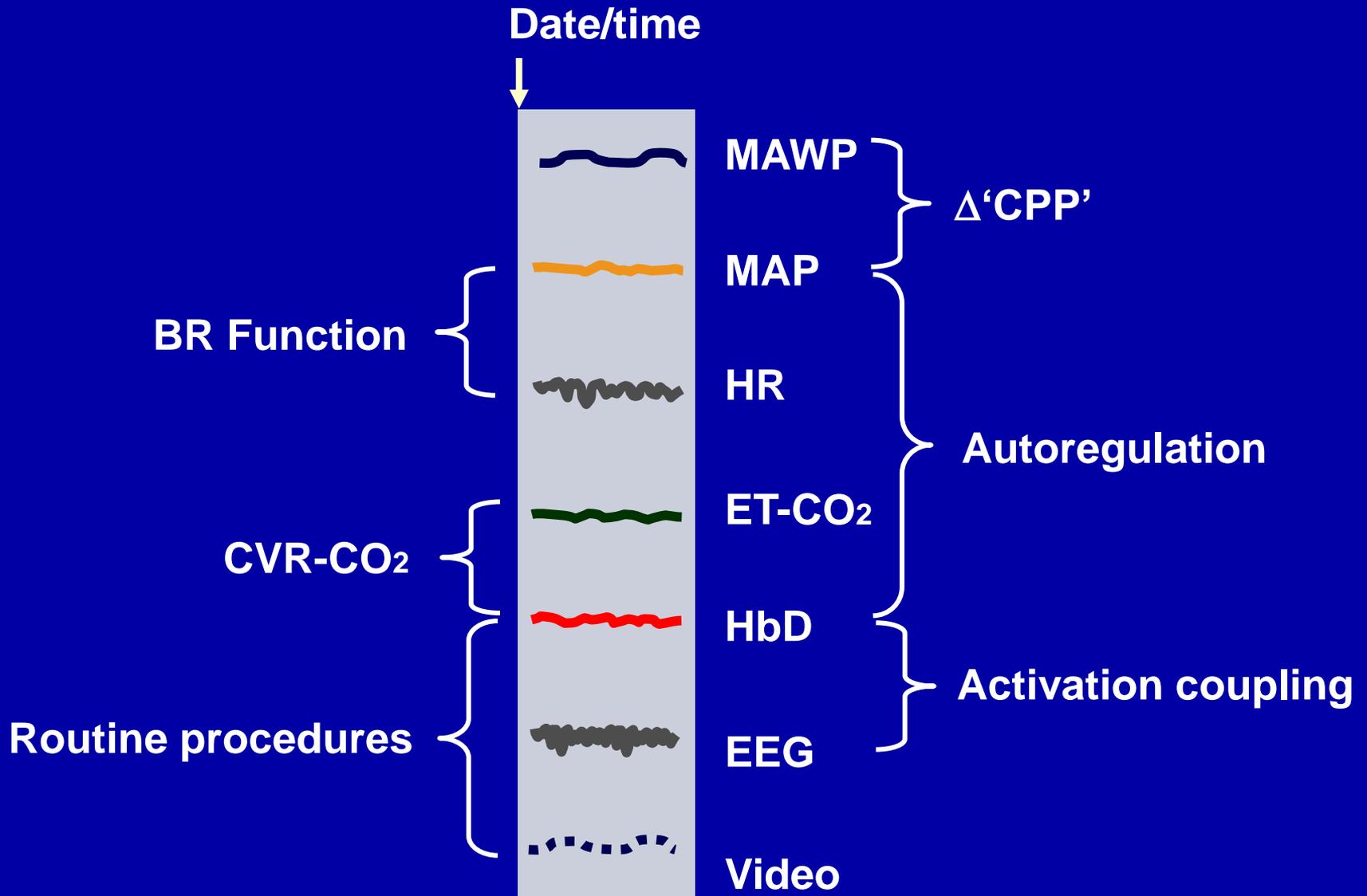
Near-infrared Spectroscopy



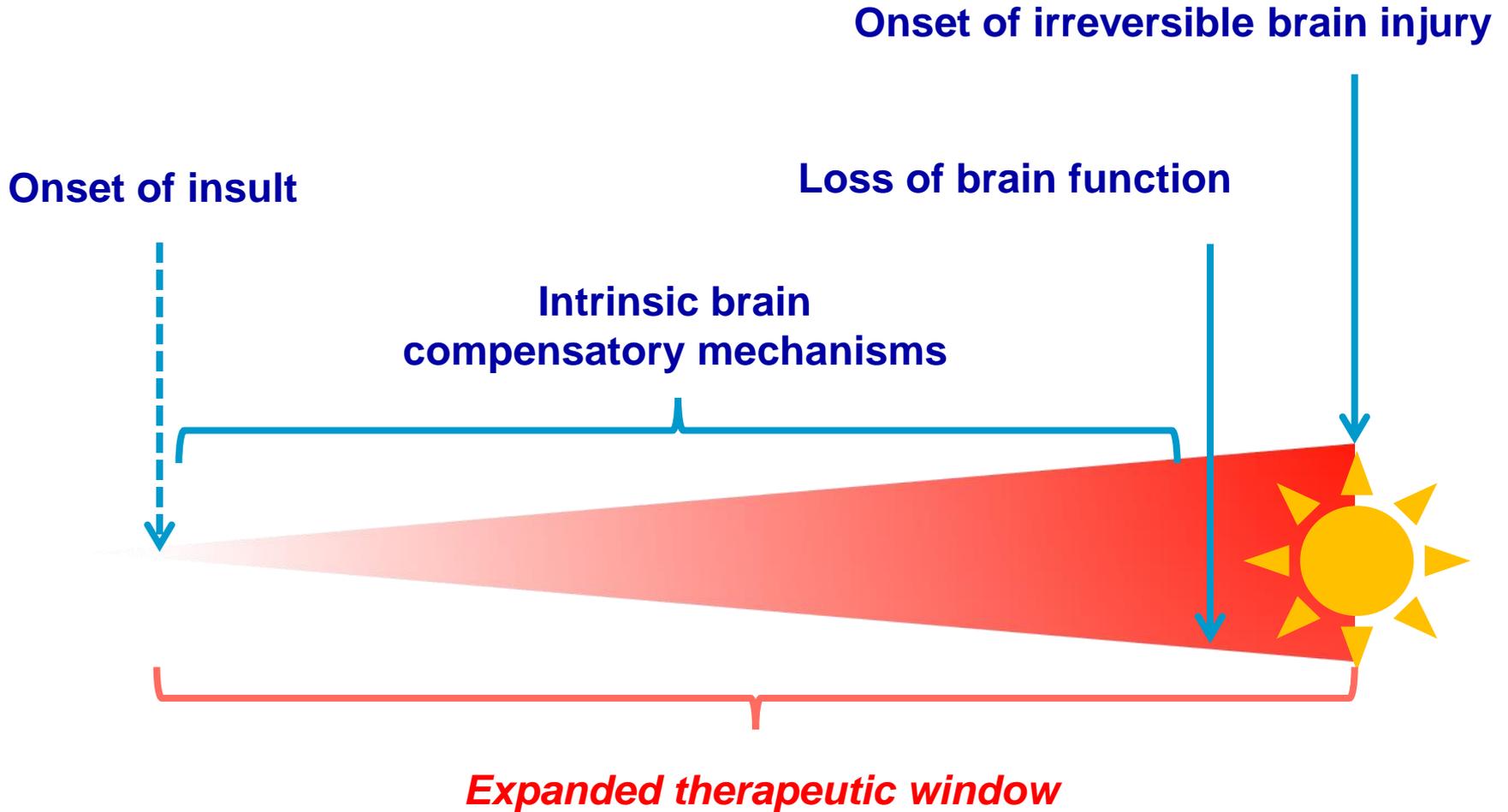
Cerebral pressure-flow autoregulatory failure



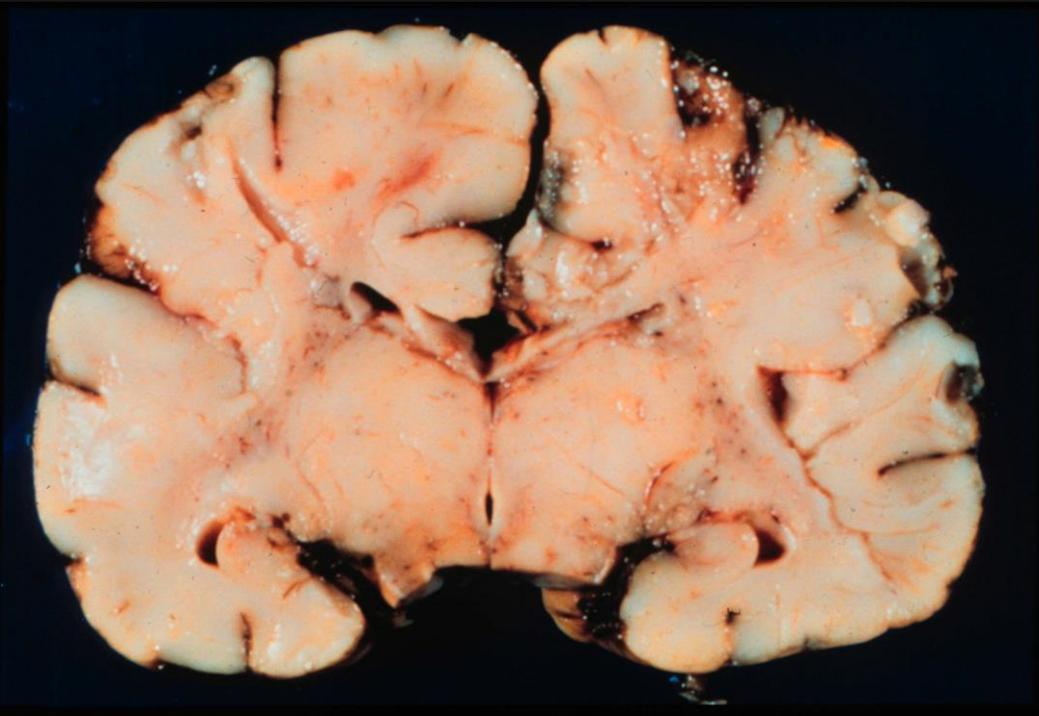
Multimodal Monitoring



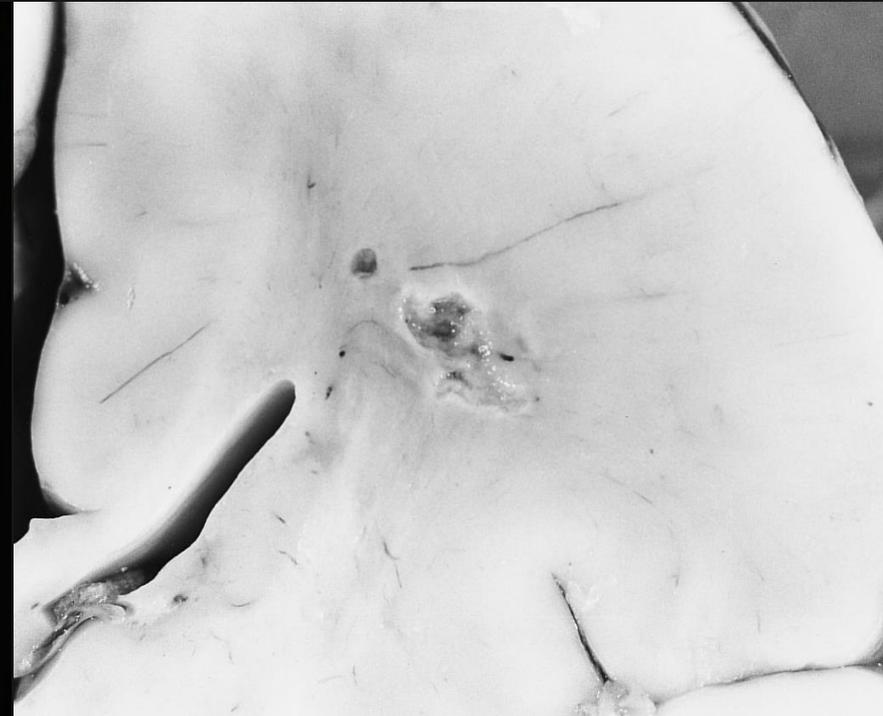
Pathway from insult to injury



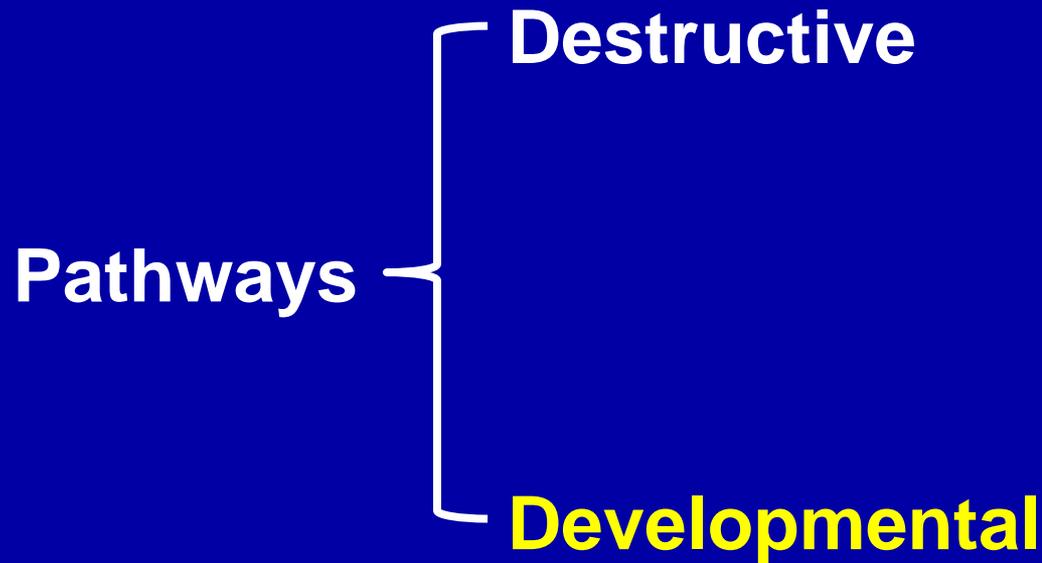
Destructive Lesions of the Immature Brain



Term



Preterm



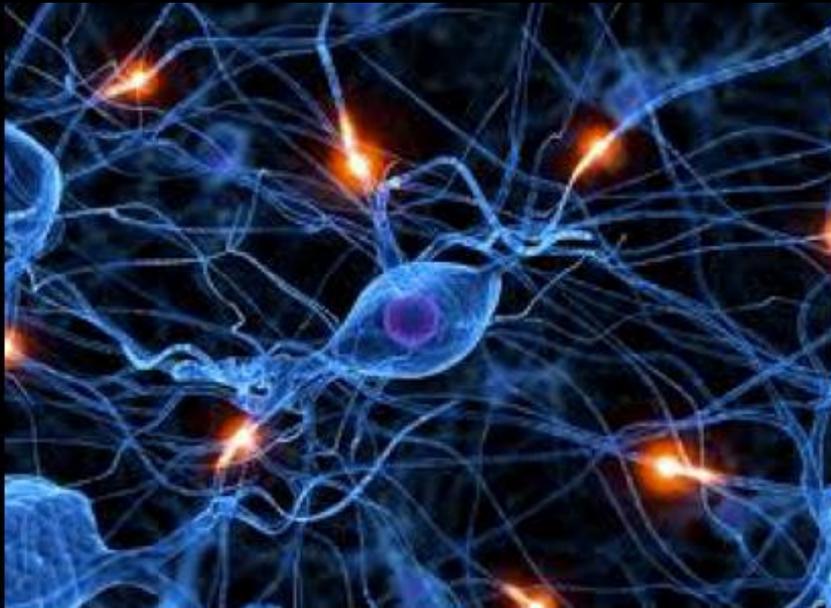
Developmental disruptions are increasingly implicated in neurologic compromise after early-life neurologic insults

**Chronic, recurrent insults
below the level of cellular destruction
may cause
developmental disruption
of the immature brain**

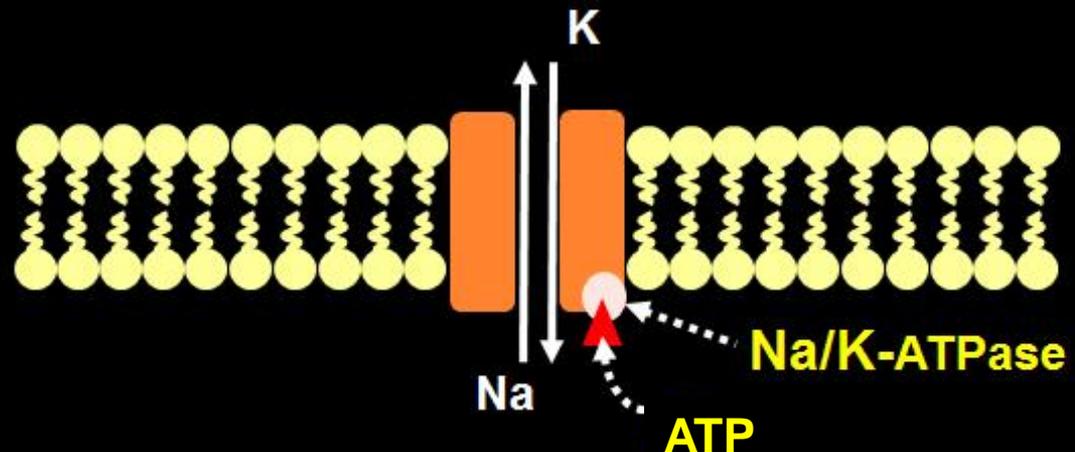
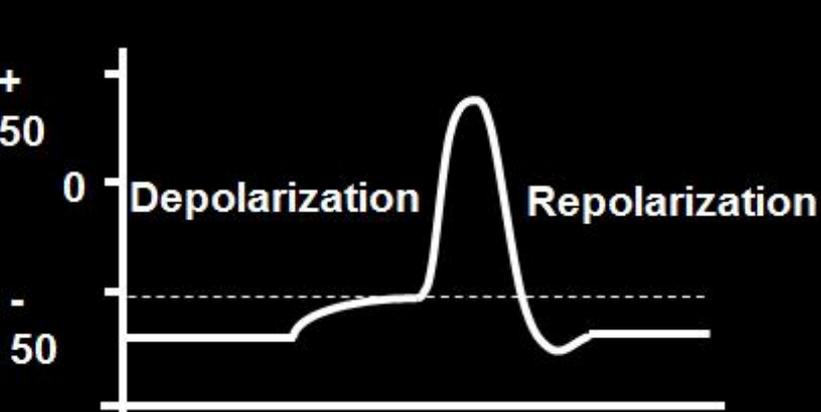
Developmental disruption of the immature brain

- **Chronic low-grade hypoxia**
 - **functional deafferentation, developmental diaschisis**
- **Allostasis (“stability through change”) and allostatic load**
(Sterling and Eyer, 1988; McEwen, NEJM, 1998)
- **Epigenetic mechanisms**
- **Developmental imprinting / programming**

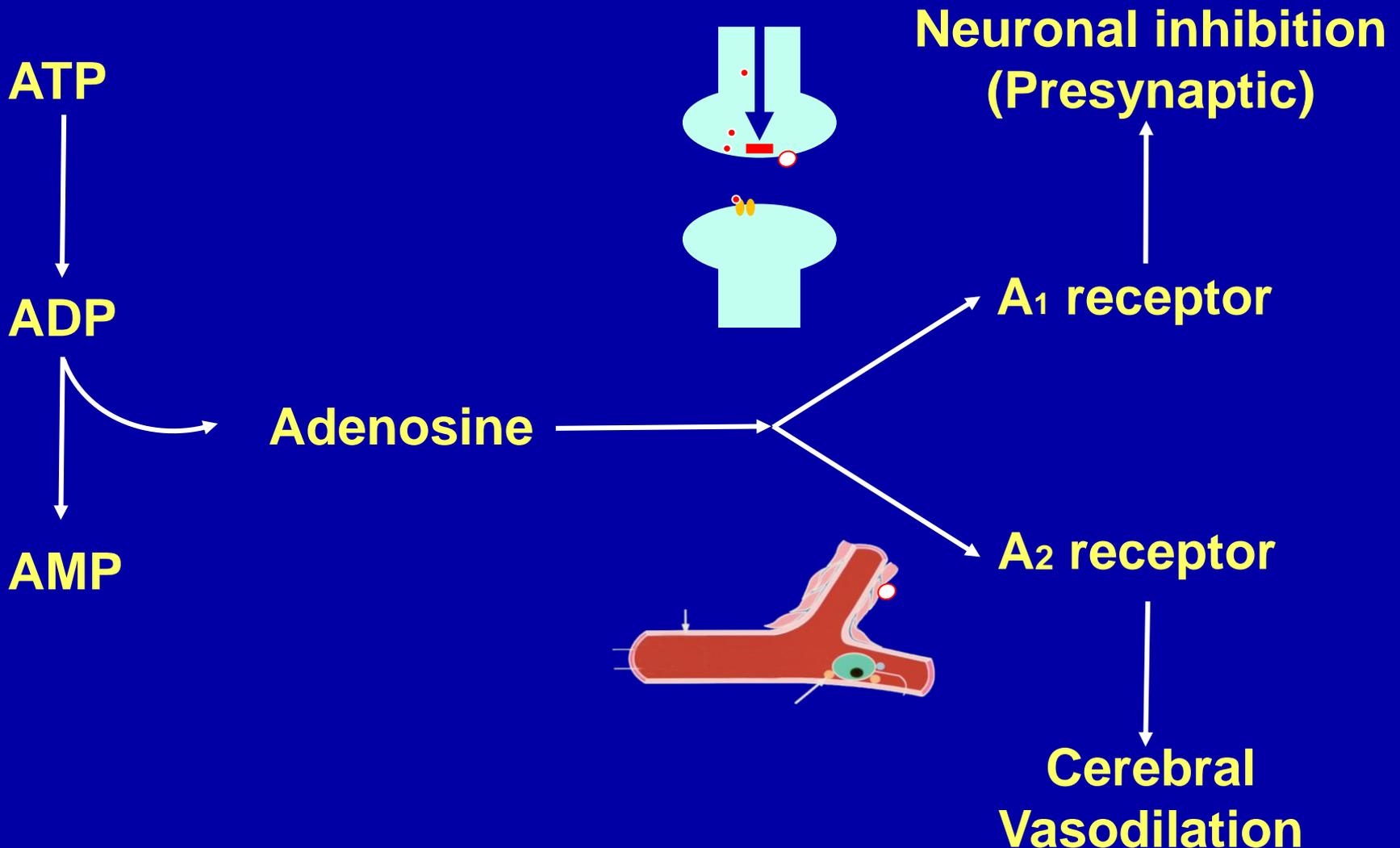
Neuronal activation consumes 60% of cerebral energy supply



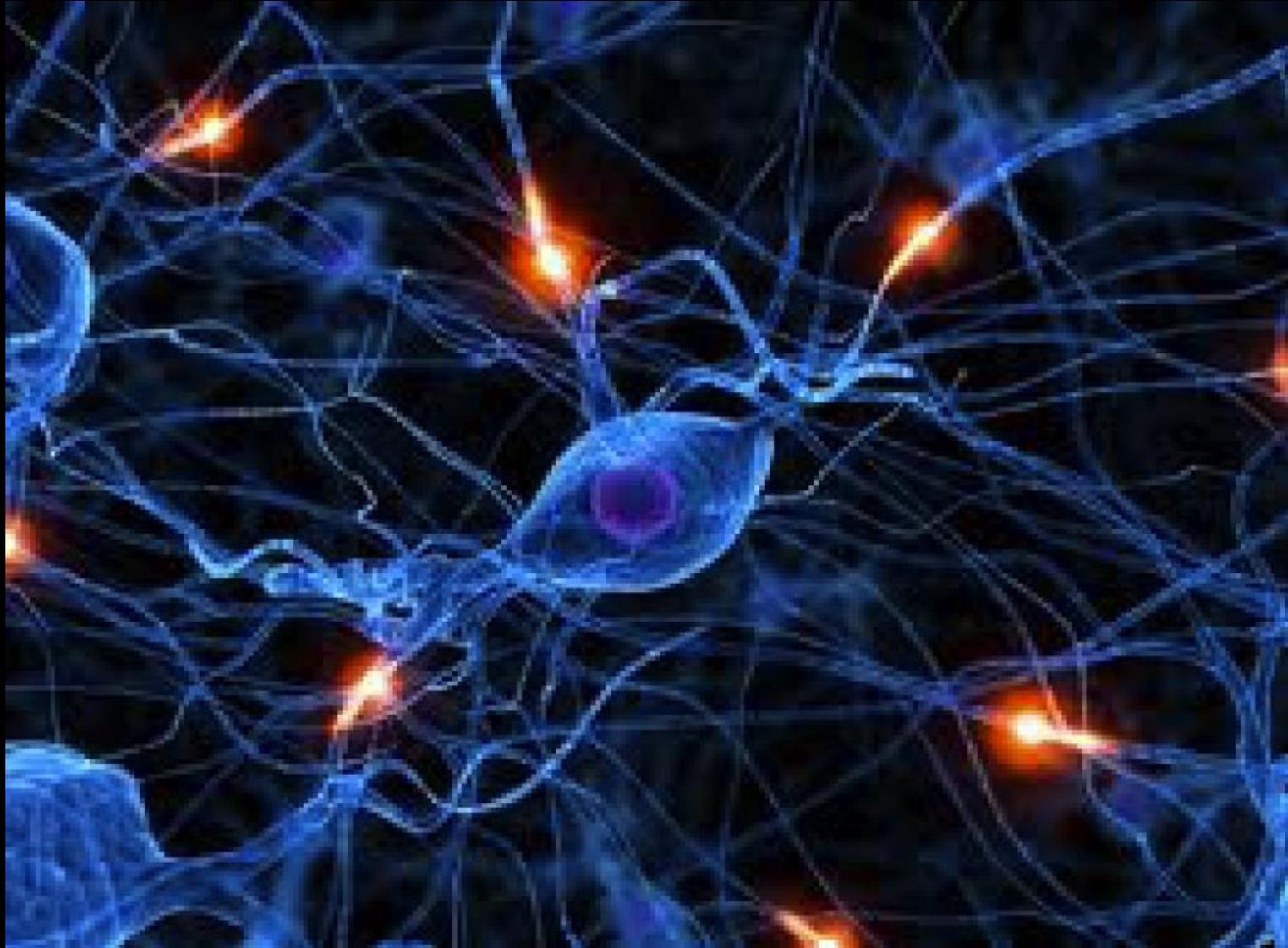
- Nerve action potentials are
- highly energy dependent
 - critical for brain development



Hypoxia, adenosine and neuroprotection



**‘Neurons that fire together wire together,
those that don’t wont’**



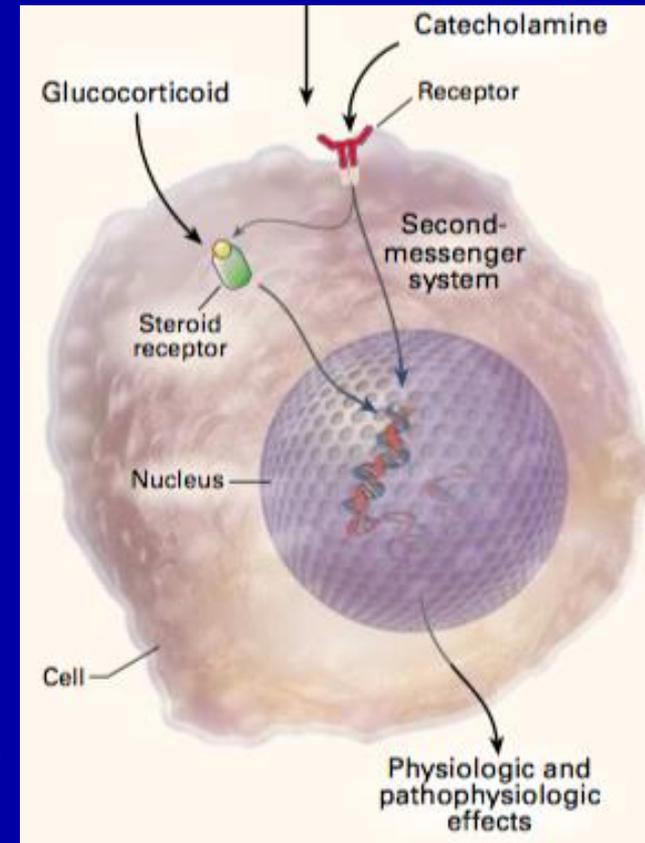
Allostasis and Allostatic Load

Allostasis ('stability through change')

- steady state change keeping regulated variables stable
- compensatory and adaptive
- longterm trade-off (allostatic load) - "wear and tear"

Allostatic responses

- initiated by autonomic and adrenal catecholamines and glucocorticoids
- adaptive processes alter cell function and structure



McEwen, NEJM, 1998

Concluding remarks

- Preventive neuroprotection and brain-oriented care of the human fetus and newborn remains limited by the lack of effective neuromonitoring
- Effective brain monitoring will demand
 - an increased understanding of the pathophysiology
 - more precise targeting of the relevant causal pathways
 - an informed and appropriate response to signals
- Investment in development of effective neuromonitoring and preventive neuroprotection for the fetus and newborn is desperately needed

The fundamental goal for neuromonitoring is to open the window for neuroprotection

