



PROGRAM

MAC 2015

The 9th International Conference
on Mechanisms of Anesthesia

June 17th – 19th
Bonn, Germany

www.mac2015.uni-bonn.de

Gsi
Gustav-Stresemann-
Institut e.V.
Europäische Tagungs-
und Bildungsstätte Bonn



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Tuesday, June 16th

Get-together



Inner court of the Gustav-Stresemann-Institute (GSI)

6:00 pm – open end

“Rheinischer Abend“ (A Rhenish Evening)

(Location at the GSI: Römerkeller)

(foods from the Rhineland and beer from Cologne)

Wednesday, June 17th - Morning Sessions

8:00 am **Welcome**

8:05 am – 10:05 am **Symposium 1**

Identification of anesthetic binding sites and mechanisms on ligand-gated ion channels
(Chairs: Tomoyoshi Seto, Shiga University and Sheldon H. Roth, University of Calgary)

8:05 The sites and allosteric actions of general anesthetics on GABA_ARs (Keith W. Miller, MGH - Harvard Medical School)

8:25 The crystal structure of a human GABA_AR (Radu A. Aricescu, University of Oxford)

8:45 Architecture, gating and modulation of GluCl, an anion-selective Cys-loop receptor (Ryan Hibbs, University of Texas Southwestern)

9:05 The locations and selectivities of general anesthetic binding sites in GABA_ARs and nAChRs (Jonathan Cohen, Harvard Medical School)

9:25 Structure–function mapping of anesthetic allosteric agonist sites in GABA_A receptors (Stuart A. Forman, MGH - Harvard Medical School)

9:45 Sites and actions of general anesthetics: a perspective from cation channels (Pei Tang, University of Pittsburgh)

10:05 am – 10:30 am **Posters, Informal Discussion and Coffee Break**

10:30 am – 12:30 pm **Symposium 2**

Role of GABA_A receptors in anesthetic action (Chairs: Uwe Rudolph, McLean Hospital-Harvard Medical School and Hugh C. Hemmings, Weill Cornell Medical College)

10:30 A structural view on anesthetic binding sites in GABA_A receptor subtypes (Margot Ernst, Medical University of Vienna)

10:50 A mechanism for GABA receptor desensitization (Trevor Smart, University College London)

11:10 GABA_AR phosphorylation and neurosteroid induced hypnosis (Paul A. Davies, Tufts University)

11:30 Bifunctional neurosteroids for photolabeling and "click chemistry"- based enrichment (Douglas F. Covey, Washington University in St. Louis)

11:50 Propofol analogues for photolabeling, imaging and enrichment (Edward H. Smith, Imperial College London)

12:10 Structured Discussion

12:30 pm – 2:00 pm **Posters and Lunch (GSI)**

Wednesday, June 17th - Afternoon Sessions

2:00 pm - 4:00 pm Symposium 3

Anesthetic sites and effects on voltage-gated ion channels (Chairs: [Jeremy Lambert, Dundee University](#) and [Bernd W. Urban, University of Bonn](#))

- 2:00 Are sodium channels important targets for general anesthetics? ([Hugh C. Hemmings, Weill Cornell Medical College](#))
- 2:20 Anesthetic sites on potassium and sodium channels as revealed by photolabeling ([Roderic G. Eckenhoff, University of Pennsylvania](#))
- 2:40 Sites and mechanisms of anesthetic action on voltage-gated potassium and sodium channels ([Manuel Covarrubias, Thomas Jefferson University](#))
- 3:00 Structural dynamics and sites of anesthetic action on sodium channels as revealed by NMR ([Yan Xu, University of Pittsburgh](#))
- 3:20 HCN ion channels ([Peter A. Goldstein, Weill Cornell Medical College](#))
- 3:40 Structured Discussion

4:00 pm – 4:30 pm Posters, Informal Discussion and Coffee Break

4:30 pm – 6:30 pm Symposium 4

Transmitter-gated CNS chloride channels – New targets for emerging drugs combating chronic pain (Chairs: [Martin Leuwer, University of Liverpool](#) and [Pei Tang, University of Pittsburgh](#))

- 4:30 GABA_A receptors as analgesic drug targets ([Hanns Ulrich Zeilhofer, University of Zurich](#))
- 4:45 Glycine-mediated tonic and phasic inhibition in the spinal cord ([Veit-Simon Eckle, University of Tuebingen](#))
- 5:00 Multiple binding sites for propofol and propofol derivatives at strychnine-sensitive glycine receptors (SSGRs) ([Bodo Laube, Technical University of Darmstadt](#))
- 5:15 Medicinal chemistry-based optimization of positive allosteric modulators of strychnine-sensitive glycine receptors (SSGRs) ([Neil Berry, University of Liverpool](#))
- 5:30 Studying neuropathic pain in laboratory animals ([Stephen McMahon, King's College London](#))
- 5:45 Glycine re-uptake inhibitors ([Robert Werdehausen, Heinrich Heine University Duesseldorf](#))
- 6:00 Structured Discussion

6:30 pm – 8:00 pm Posters and Dinner (GSI)

Wednesday, June 17th – Evening Sessions

8:00 pm – 10:00 pm

Workshops 1 – 5

W 1: Neuroprotection by anesthetic inert gas xenon and argon (Chairs: Robert Dickinson, Imperial College London and Mark Coburn, RWTH Aachen)

- Mechanisms of xenon neuroprotection (Robert Dickinson, Imperial College London)
- Xenon neuroprotection in in vivo models of brain injury (Rita de Campos Pires Santos e Sousa, Imperial College London)
- Argon neuroprotection (Mark Coburn, RWTH Aachen)
- Current and future clinical trials with xenon & argon (Rolf Rossaint, RWTH Aachen)

W 2: How do anesthetics interact with the molecular mechanisms of channel gating? (Chairs: Keith W. Miller, MGH - Harvard Medical School and Pei Tang, University of Pittsburgh)

- Structural basis for modulation of gating by general anesthetics (Vincenzo Carnevale, Temple University)
- Paths of channel signaling and routes of anesthetic action, where are we now? (Pei Tang, University of Pittsburgh)
- Mass spectrometric identification of neurosteroid binding sites using photolabeling and click chemistry (Alex Evers, Washington University in St. Louis)
- Conformation changes and anesthetic action in functionally reconstituted GABA_ARs (Keith W. Miller, MGH - Harvard Medical School)
- Open Discussion: What are our best approaches going forward? (Discussants: Radu A. Aricescu, University of Oxford, Ryan Hibbs, University of Texas Southwestern and others)

W 3: Modulation of cortical network dynamics by anesthetics: from synaptic transmission to global networks dynamics (Chairs: Aeyal Raz, University of Wisconsin - Madison and Berthold Drexler, University of Tuebingen)

- Differential effects of anesthetics on synaptic pathways in sensory cortex (Aeyal Raz, University of Wisconsin - Madison)
- Cortical dynamics during anesthetic-induced loss and recovery of consciousness (Yuval Nir, Tel Aviv University)
- The clinical neurophysiology of anesthesia: insights on the pediatric and the elderly brain (Patrick Purdon, MGH - Harvard Medical School)
- Three different anesthetics, similar cortical dynamics (Aryeh H. Taub, Weizmann Institute of Science)
- Excitatory and inhibitory actions of volatile anesthetics (Hailong Dong, Xijing Hospital, Xi'an)

W 4: Extrasynaptic GABA_A receptors and general anesthesia (Chairs: [Stuart A. Forman, MGH - Harvard Medical School](#) and [Paul A. Davies, Tufts University](#))

- Which receptors produce tonic neuronal chloride currents? ([Trevor Smart, University College London](#))
- Extrasynaptic receptors in anesthesia-induced memory loss ([Beverley A. Orser, University of Toronto](#))
- Interfacially selective anesthetics as probes of extrasynaptic GABA_A subunit arrangement ([Stuart A. Forman, MGH - Harvard Medical School](#))
- Modulatory binding sites in extrasynaptic GABA_A receptor subtypes ([Margot Ernst, Medical University Vienna](#))

W 5: Molecular and cellular pathways of anesthetics impact pathophysiology and disease (Chairs: [Gerhard Rammes, Technical University of Munich](#) and [Christopher G. Parsons, Merz, Frankfurt](#))

- Pathomechanisms in Alzheimer's disease - relevance for general anesthesia ([Christopher G. Parsons, Merz, Frankfurt](#))
- Molecular interaction of anesthetics with the pathophysiology of Alzheimer's disease: focus on in vitro studies ([Pravat Kumar Mandal, National Brain Research Centre, India](#))
- Anesthesia, delirium and dementia: is there a relation? ([Bettina Jungwirth, Technical University of Munich](#))
- Modulation of PDZ interactions with ion channels by general anesthetics ([Roger A. Johns, Johns Hopkins University](#))
- A mouse model linking anesthetic sensitivity to mitochondrial function ([Philip Morgan, University of Washington](#))

Thursday, June 18th - Morning Sessions

8:00 am – 10:00 am Symposium 5

Anesthetic mechanisms in memory, consciousness and sleep (Chairs: Bernd Antkowiak, University of Tuebingen and Raz Aeyal, University of Wisconsin - Madison)

- 8:00 Hippocampal subregion-specific functions of alpha5-containing GABA_A receptors in learning and memory (Uwe Rudolph, McLean Hospital - Harvard Medical School)
- 8:20 Electrophysiological signatures of cortical disconnection during anesthetic unconsciousness (Anthony Hudetz, Medical College of Wisconsin)
- 8:40 Anesthetic-induced loss of consciousness and natural sleep - similarities and differences (Nick Franks, Imperial College London)
- 9:00 Sleep and synapses: a two-step hypothesis for general anesthesia (Bruno van Swinderen, The University of Queensland)
- 9:20 Genetic dissection of the hypothalamic circuitry underlying anesthetic-induced loss of consciousness (Bill Wisden, Imperial College London)
- 9:40 Structured Discussion

10:00 am – 10:30 am Posters, Informal Discussion and Coffee Break

10:30 am – 12:30 pm Symposium 6

Zeitgeist and anesthetic research: is the reductionist approach passé? (Chairs: Misha Perouansky, University of Wisconsin - Madison and Christopher D. Richards, University College London)

- 10:30 Investigating the effects of general anesthetics on sleep and circadian rhythms in different phyla to understand the commonalities in mechanisms (Guy Warman, University of Auckland)
- 10:50 Added layers of complexity: inhibitory control of synaptic plasticity (Robert Pearce, University of Wisconsin - Madison)
- 11:10 Emergent properties of complex neural systems: a passing fashion, or the only true explanation of anesthesia? (Jamie W. Sleight, University of Auckland)
- 11:30 Emergent oscillatory brain activity and its perturbation by anesthetic action (David Liley, Swinburne University of Technology, Melbourne)
- 11:50 Molecular and cellular mechanisms underlying anesthesia-induced modulation of neural plasticity (Lazlo Vutskits, University of Geneva)
- 12:10 Structured Discussion

12:30 pm – 2:00 pm Posters and Lunch (GSI)

Thursday, June 18th - Afternoon Sessions

2:00 pm – 4:00 pm Symposium 7

General anesthetic action: generalized suppression or dedicated network? (Chairs: [Beverley Orser, University of Toronto](#) and [Trevor Smart, University College London](#))

- 2:00 Mesopontine node in a network for transitioning between wake and anesthesia ([Marshall Devor, The Hebrew University of Jerusalem](#))
- 2:20 Modulation by general anesthetics of connectivity and stimulus representation in sensory cortex ([Matthew I. Banks, University of Wisconsin - Madison](#))
- 2:40 Functional connectivity and cortical information transfer with sevoflurane: changes during loss of consciousness and "deep" anesthesia (EEG burst suppression) ([Eberhard Kochs, Technical University of Munich](#))
- 3:00 The influence of etomidate on thalamic synaptic and extrasynaptic GABA_A receptors ([Jeremy Lambert, Dundee University](#))
- 3:20 Selective anesthesia neurotoxicity in developing brain - the role of Tau protein phosphorylation ([Zhongcong Xie, MGH - Harvard Medical School](#))
- 3:40 Structured Discussion

4:00 pm – 4:30 pm Posters, Informal Discussion and Coffee Break

4:30pm – 6:30 pm Symposium 8:

Developmental neurotoxicity: mechanisms, phenotype and clinical relevance (Chairs: [Roderic Eckenhoﬀ, University of Pennsylvania Medical Center](#) and [Gerhard Rammes, Technical University of Munich](#))

- 4:30 Morphology, distribution and modulators of anesthetic neurotoxicity in the developing brain ([Andreas Loepke, Cincinnati Children's Hospital Medical Center](#))
- 4:50 Effects of sevoflurane anesthesia on the developing brain: results from the EuroStar consortium ([Niccolo Terrando, Duke University Medical Center](#))
- 5:10 Functional impairments resulting from exposure to anesthetics at young age and potential neuroprotective strategies ([Ansgar Brambrink, Oregon Health & Science University](#))
- 5:30 Is there a human phenotype of anesthetic neurotoxicity and what clinical research is necessary to provide definitive evidence? ([Andrew Davidson, The Royal Children's Hospital Melbourne](#))
- 5:50 Anesthesia-induced developmental neurotoxicity: do we understand the mechanisms ([Vesna Jevtovic-Todorovic, University of Virginia](#))
- 6:10 Structured Discussion

6:30 pm – 8:00 pm Posters and Dinner (GSI)

Thursday, June 18th – Evening Sessions

8:00 pm – 10:00 pm Workshops 6 – 10:

W 6: Modulation of thalamocortical circuits by anesthetics: insights from in vitro studies
(Chairs: Harald Hentschke, University of Tuebingen and Gerhard Rammes, Technical University of Munich)

- Introduction: Role of the thalamus in anesthesia
(Peter A. Goldstein, Weill Cornell Medical College)
- Effects of xenon on thalamocortical circuit function (Gerhard Rammes, Technical University of Munich)
- Modulation of thalamocortical afferent signals by propofol (Stephan Kratzer, Technical University of Munich)
- Modulation of thalamocortical afferent signals by sevoflurane (Matthias Kreuzer, Technical University of Munich)
- Interaction of thalamocortical and cortico-cortical afferents; modulation by isoflurane (Harald Hentschke, University of Tuebingen)

W 7: Same or different: anesthetic neurotoxicity in the developing brain versus the aging brain
(Chairs: Ansgar Brambrink, Oregon Health & Science University and Vesna Jevtovic-Todorovic, University of Virginia)

- Mechanisms of anesthetic neurotoxicity in the developing brain (Vesna Jevtovic-Todorovic, University of Virginia)
- Synaptic dysfunction as the underlying mechanisms of anesthesia neurotoxicity in the developing brain (Zhongcong Xie, MGH - Harvard Medical School)
- Factors that determine acute or delayed vulnerability for anesthetic-induced injury in the developing brain (Laszlo Vutskits, University of Geneva)
- Anesthetic-induced neuromodulation in the developing brain (Barbara Sinner, University Hospital Regensburg)
- Biomarkers (CSF, serum, imaging, clinical, etc.) of anesthetic-induced injury in the developing brain (Ansgar Brambrink, Oregon Health & Science University)

W 8: Waking up to a world of pain: how external stimuli and their perception influence unconsciousness (Chairs: [Paul Garcia, Emory University School of Medicine, Atlanta](#) and [Jamie W. Sleight, University of Auckland](#))

- How deep is deep? The influence of opioids in combination with anesthetic drugs on measures of anesthetic depth ([Gerhard Schneider, University of Witten/Herdecke](#))
- Sensory input vs integration. The different neural circuits involved in response to noxious and non-noxious stimuli in near unconscious states ([Katie Warnaby, University of Oxford](#))
- Unresponsiveness $\neq$ unconsciousness but does consciousness during anesthesia = perception of surgery? ([Rob Sanders, University of Wisconsin - Madison](#))
- The heterogeneity of cortical and subcortical arousal in the presence of external stimuli ([Paul Garcia, Emory University](#))
- EEG hallmarks of analgesia vs anesthesia. Stimulation, spindles, and slow wave saturation ([Jamie W. Sleight, University of Auckland](#))
- Neurotransmission of the basal forebrain and general anesthesia ([Zhi-Li Huang, Fudan University, China](#))

W 9: Side effect targets of general anesthetics (Chairs: [Huafeng Wei, University of Pennsylvania](#) and [Serge C. Thal, Johannes Gutenberg University Mainz](#))

- Anesthetic activation of IP3 receptors; critical outcome switch ([Huafeng Wei, University of Pennsylvania](#))
- A new side effect target of propofol: Sirtuin2 deacetylase (SIRT2) ([Roderic G. Eckenhoff, University of Pennsylvania](#))
- Propofol induces neurotoxicity after brain injury ([Serge C. Thal, Johannes Gutenberg University Mainz](#))
- Leukocyte adhesion and anesthetics ([Koichi Yuki, Boston Children's Hospital](#))
- Myofilament proteins and anesthetics ([Wei Dong Gao, Johns Hopkins University](#))
- 11 β hydroxylase and etomidate ([Douglas E. Raines, MGH - Harvard Medical School](#))

W 10: From bench to bedside: Does it happen? (Chairs: [Bernd Antkowiak, University of Tuebingen](#) and [Andreas Hoeft, University Bonn](#))

Speakers provide a focused 10-minutes-statement, putting emphasize on one of these questions: 1) Anesthesia and perioperative care: almost perfect? 2) New treatments without novel drugs? 3) Benzodiazepines with lesser side effects: is there still hope? 4) Laws, politics and product marketing: what do we need to know? 5) How much does it cost to transform ideas into products? 6) Industry-academia interactions: who wins, who loses and why?

- [Robert Pearce, University of Wisconsin - Madison](#)
- [Christian Grasshoff, University of Tuebingen](#)
- [Uwe Rudolph, McLean Hospital-Harvard Medical School](#)
- [Ute Brauer, B. Braun Melsungen AG](#)
- [Klaus Fink, Merz Pharmaceuticals GmbH, Frankfurt](#)

Friday, June 19th - Morning Sessions

8:00 am – 10:00 am Symposium 9

Neural circuit mechanisms of general anesthesia (A) (Chairs: Hailong Dong, Xijing Hospital, Xi'an and Robert Pearce, University of Wisconsin - Madison)

- 8:00 Alpha-2 adrenergic stimulation of the ventrolateral preoptic nucleus (VLPO) destabilizes the anesthetic state ([Max Kelz, University of Pennsylvania](#))
- 8:20 Dynamics of recovery from general anesthesia ([Alex Proekt, Weill Cornell Medical College](#))
- 8:40 Computational models for anesthesia-induced EEG rhythms ([Patrick Purdon, MGH - Harvard Medical School](#))
- 9:00 Ventral tegmental area (VTA) stimulation induces reanimation and cognitive recovery from general anesthesia ([Ken Solt, MGH - Harvard Medical School](#))
- 9:20 Anesthesia and PET imaging in the study of human consciousness ([Harry Scheinin, University of Turku, Finland](#))
- 9:40 Structured Discussion

10:00 am – 10:30 am Posters, Informal Discussion and Coffee Break

10:30 am – 12:30 pm Symposium 10

Neural circuit mechanisms of general anesthesia (B) (Chairs: Nick Franks, Imperial College London and Jamie W. Sleight, University of Auckland)

- 10:30 Closing the gap between the molecular and systemic actions of anesthetic agents ([Bernd Antkowiak, University of Tuebingen](#))
- 10:50 Neurophysiological and neuroanatomical insights into how anesthetics work ([Emery Brown, MGH - Harvard Medical School](#))
- 11:10 Slow-wave activity saturation and thalamocortical isolation during anesthesia ([Irene Tracey, Oxford University](#))
- 11:30 Awake versus anesthetized: modulation of micro- and mesoscale cortical dynamics and functional connectivity ([Flavio Frohlich, University of North Carolina](#))
- 11:50 Propofol-induced network changes on the systemic level of the brain: loss of functional connectivity and fronto-parietal feedback interaction ([Gerhard Schneider, University of Witten/Herdecke and Denis Jordan, Technical University of Munich](#))
- 12:10 Structured Discussion

12:30 pm – 1:30 pm Posters and Lunch (GSI)

Friday, June 19th - Afternoon Session

1:30 pm – 1:50 pm

- Human stem cells and developmental anesthetic neurotoxicity ([Zeljko Bosnjak, Medical College of Wisconsin](#))

1:50 pm – 3:30 pm

Symposium 11

Memory formation during anesthesia: dark side of the moon (Chairs: [Alex Evers, Washington University in St. Louis](#) and [Emery Brown, MGH - Harvard Medical School](#))

- 1:50 Current concepts of memory – a quick overview ([Robert Veselis, Memorial Sloan Kettering Cancer Center](#))
- 2:10 Anesthetic modification of memory ([Beverley Orser, University of Toronto](#))
- 2:30 Mind the gap: the perennial divide between model, theory and reality ([Misha Perouansky, University of Wisconsin - Madison](#))
- 2:50 The effects of anesthetics on medial temporal lobe memory systems in humans ([Kane Pryor, Weill Cornell Medical College](#))
- 3:10 Structured Discussion

3:30 pm – 3:40 pm

Closing Remarks



Our catamaran boat the "Filia Rheni"

4:15 pm

Departure of buses from the GSI for the Rhine cruise

4:45 pm – approx. 11:30 pm

Rhine Cruise with the "Filia Rheni", including conference dinner and wine tasting on board

The conference will finish off with the conference dinner as part of an extended guided boat tour on the Rhine. Experiencing the beauty of the Rhine valley while sampling its wines and regional dishes should facilitate the transition from serious discussions to relaxed conversations with colleagues and friends, old and new, as the final highlight of an intense conference.

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Ground Floor Gustav-Stresemann-Institute:

