Information on the Activity of the Institute

The Institute mission

Motto: *Cutting-edge science for health*

The **Institute of Physiology (IPHYS)** of the Czech Academy of Sciences (**CAS**) is a leading biomedical research institution in the Czech Republic (https://www.fgu.cas.cz/en/). We carry out basic research in physiology and pathophysiology. We aim to understand the physiological processes in both healthy and diseased human bodies, which is of utmost social importance. **Our results are applied primarily in biomedicine** in the development of new preventive, diagnostic, and curative procedures, but also in the education of both current and future healthcare professionals.

IPHYS continues the legacy of the greatest Czech physiologist, J. E. Purkinje, who said more than 150 years ago that physiology is most indispensable to doctors, but it cannot be effectively beneficial unless it stands on the foundation of general natural science.

Our research focuses on specific areas of the **nervous system, the cardiovascular system** and **metabolism**. Our **scientific laboratories*** study mechanisms that regulate processes in mammals, including humans, at the levels of cells, organs, and systems, including time regulation of these processes. The results of basic research are applied in the understanding of a wide range of diseases, including those that result from unhealthy lifestyles and ageing of the population. These diseases often have multifactorial origins. Therefore, we study them from an interdisciplinary perspective that involves research of complex regulatory physiological mechanisms. We adopt a developmental perspective, which focuses on physiological processes and related diseases during different stages of human life.

We employ the latest methods of molecular and cellular biology, biochemistry, molecular pharmacology using imaging techniques, mathematical analyses, and modelling. Special animal biomodels help us detect genetic determinants of major diseases. Thanks to a relatively broad professional scope that allows comprehensive research of processes, IPHYS has a favourable and privileged position in comparison with other biomedical institutions, both at home and abroad. Fulfilling the scientific vision of IPHYS is possible only thanks to active cooperation with other institutes of the CAS, various research facilities, universities, and clinical biomedical institutions. Employees of IPHYS cooperate with top foreign teams, engaging the Institute in a large international scientific community.

IPHYS informs the general public effectively and by all available means. We strive to popularise the results we have achieved so that the public perceives the Institute as a leading scientific institution with international significance.

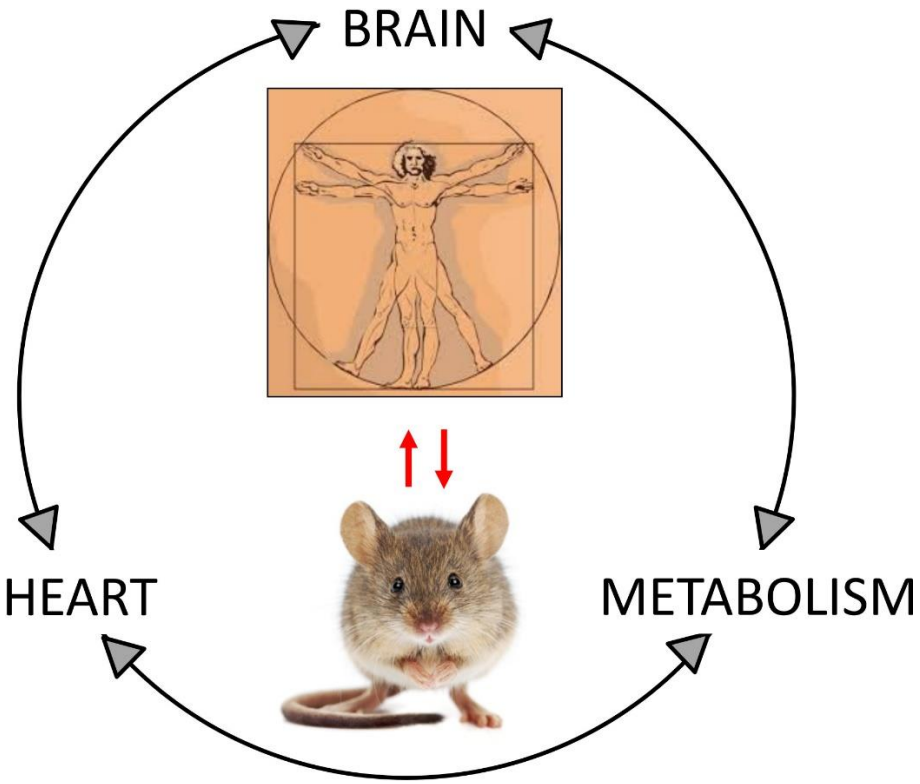
For more information about IPHYS, see the IPHYS brochure (https://www.fgu.cas.cz/upload/files/BRO%C5%BDURA%20FGU%202017small.pdf).

Abbreviations: AD, Alzheimer´s disease; ASD, Autism spectrum disorders; BIOCEV, Biotechnology and Biomedicine Centre; CAS, Czech Academy of Sciences; EpiRec, Epilepsy Research Centre of Prague; FTE, Full Time Equivalent; GLP, Good Laboratory Practise; HR, human resources; IKEM, Institute of Experimental and Clinical Medicine; IOCB, Institute of Organic Chemistry and Biochemistry; IAB, International Advisory Board; IPHYS, Institute of Physiology; MRC, Medical Research Council; OCD, Obsessive-compulsive disorders; OTM-R, Open, transparent and merit-based recruitment; PEN, Project of Excellence in Neuroscience; PerMed, Centre of Personalized Medicine - Diagnostics and Therapy.

*__Note__: IPHYS is organised into scientific units called “laboratories” and service units called “departments”. The previously used term for a scientific unit “department” was changed to “laboratory” in March 2020. The term “laboratory” better reflects the size of units, which is 5 to 19 FTE employees each. Laboratories represent individual “teams” in this evaluation. As of May 2020, IPHYS consists of 22 scientific units.

Description of main research directions investigated by the Institute

The main results published by IPHYS scientists during the evaluated period (2015–2019) in three major fields of research are listed below.



1. Metabolic research

One of the research fields pursued at IPHYS since its early days is metabolism and its regulation. While some research teams concentrate on specific aspects of metabolism, their studies have implications for cardiovascular and neurophysiological research. The IPHYS Laboratories studying metabolism can be clustered into several groups, depending on the level of complexity. Specifically, this includes research into the activity and regulation of **selected protein complexes and transport proteins**, the function of **mitochondria** and the impact of mitochondrial dysfunction on health, the mechanisms underlying **obesity-associated metabolic disorders** (the metabolic syndrome), including their prevention and treatment by nutritional interventions and pathophysiology of the **gastrointestinal tract**.

The array of methods employed in metabolic research ranges from a cell biology level to advanced **whole-body phenotyping** in rodents, including behavioural testing and the use of sophisticated **animal models** of human biology. For all of our studies, animal models represent an essential tool. The Institute has always been recognised for its research on laboratory **rats** (namely the SHR model) and the development of unique recombinant inbred

strains, and congenic, transgenic, and knockout models (gene editing, ZFN and TALEN nucleases, Sleeping Beauty transposon system). Thus within several years, on-demand rat models could be used in mitochondrial (e.g. TMEM70 or DAPIT knockout) and metabolic studies of human genetic diseases and other pathologies. In recent years, increasing use of **mice** and new facilities on Krč campus of biological institutes of the CAS accelerated the development of transgenic murine models (e.g. tissue-specific and conditional knockouts).These models are essential for the elucidation of molecular mechanisms and genetic determinants of both rare and common diseases, such as the metabolic syndrome associated with aberrant lipid and glucose metabolism and hypertension.

Phenotyping “omics” methods are also important for our metabolic research. We have systematically developed **proteomics analysis** and **metabolomics** for targeted and untargeted LC-MS characterisation and quantification of complex lipids including anti-inflammatory and antidiabetic lipokines (Paluchova et al., *Diabetes* **69**: 300, 2020), polar metabolites, and various food components and drugs in diverse sample types.

The characterisation of activity and regulation of selected protein complexes and transport proteins represents the very first step towards understanding molecular aspects of cellular physiology. In research of protein structures, our primary focus lies in studying the regulation of selected signalling proteins whose functions are controlled through protein-protein and phosphorylation-dependent interactions. We elucidated the molecular basis of 14-3-3 protein-dependent activation of yeast neutral trehalase Nth1, in which 14-3-3 activates Nth1 by stabilizing the flexible part of its active site, and we highlighted its ability to function as an allosteric effector (Alblova et al., *Proc Natl Acad Sci U S A* **114**: E9811, 2017). Our structural studies also characterised 14-3-3 regulation of caspase 2 or kinases ASK1 and CaMKK2**.** In the case of the forkhead transcription factor FOXO3 involved in cancer cell regulation, we have identified small molecular compounds (S9 and its oxalate salt) that interact with FOXO3. We showed that they are able to inhibit its activity in cancer cells (Hagenbuchner et al., *Elife* **8**: 2019). The expertise in protein structure analysis is further used in collaboration with other cellular physiology groups.

Membrane transporters represent a broad and diverse group of proteins involved in the transport of solutes across cytoplasmic or organellar membranes. The yeast cell serves as an important experimental model in studies of cell transport systems at the molecular level and the protein level. Our studies on cell cation and pH homeostasis focused on Na^+/H^+ antiporters and described a hydrophobic filter determining cation selectivity and transport activity (Kinclova-Zimmermannova et al., *J Mol Biol* **427**: 1681, 2015) and characterised cargo receptors of the secretory pathway ERV14 (Zimmermannova et al., *Biochim Biophys Acta Mol Cell Res* **1866**: 1376, 2019), in both yeast and plants (Rosas-Santiago et al., *Biochim Biophys Acta Mol Cell Res* **1864**: 1809, 2017). We were first to show that yeast Na^+/H^+ antiporter is negatively regulated via interaction with 14-3-3 proteins (Smidova et al., *Biochim Biophys Acta Mol Cell Res* **1866**: 118534, 2019). The characterszation of antifungal activity of antimicrobial peptides and the role of plasma membrane lipids in multidrug resistance are important outcomes of our transporter studies (in collaboration with IOCB) (Kodedova et al., *Cell Microbiol* **21**: e13093, 2019).

Mitochondria are key players in cellular energy provision and harbour a number of metabolic pathways, therefore mitochondrial (dys)function has impact on health. Our research into the molecular basis of mitochondrial structure, function and biogenesis was based on the development of numerous cellular and animal genetic models, and it covered several specific areas, all with an increasing impact on human diseases:

(i) Inherited disorders of the mitochondrial oxidative phosphorylation system, focused on ATP synthase depletion due to dysfunction of the TMEM70 biogenetic factor and its role in enzyme biogenesis (Vrbacky et al., *Hum Mol Genet* **25**: 4674, 2016; Kovalcikova et al., *FASEB J* **33**: 14103, 2019); Cytochrome *c* oxidase dysfunction due to the SURF1 factor mutation (Kovarova et al., *Biochim Biophys Acta* **1862**: 705, 2016); and complex I deficiencies caused by altered assembly factors (Hartmannova et al., *Hum Mol Genet* **25**: 4062, 2016; Alston et al., *Am J Hum Genet* **103**: 592, 2018)**.**

(ii) Redox signalling, ROS, and uncoupling proteins in mitochondrial physiology, focused on the essential role of mitochondrial phospholipase iPLA2γ in fatty acid stimulated insulin secretion (Jezek et al., *Antioxid Redox Signal* **23**: 958, 2015); targeting of oxidative stress in pancreatic beta cells by mitochondrial antioxidants (Plecita-Hlavata et al., *Oxid Med Cell Longev* **2019**: 1826303, 2019); and pleiotropic effects of biguanides on mitochondrial ROS production (Pecinova et al., *Oxid Med Cell Longev* **2017**: 7038603, 2017).

(iii**)** Mitochondrial metabolism in cancer cells, namely pharmacological inhibition of fatty-acid oxidation synergistically enhancing the effect of L-asparaginase in childhood ALL cells (Hermanova et al., *Leukemia* **30**: 209, 2016)**;** hypoxic widening of mitochondrial cristae in cancer cells (Plecita-Hlavata et al., *FASEB J* **30**: 1941, 2016); and the role of mitochondrial complex II in cell death initiation (Kluckova et al., *Cell Death Dis* **6**: e1749, 2015).

(iv) Mitochondrial functions specifically involved in heart failure (Melenovsky et al., *Eur J Heart Fail* **19**: 522, 2017)**,** angiogenesis (Wang et al., *Nat Commun* **7**: 12061, 2016) or pulmonary hypertension (Zhang et al., *Circulation* **136**: 2468, 2017).

The major focus is on the adipose tissue function and importance of this tissue for whole-body metabolism, obesity and cancer. We apply dietary (omega-3 fatty acids), environmental (cold exposure), and pharmacological (antidiabetic drugs pioglitazone and MSDC-0160) manipulations to induce the *healthy adipocyte* phenotype. Primarily we use a model of diet-induced obesity in mice and various advanced techniques such as hyperinsulinemic-euglycemic clamps, FACS, and metabolipidomics analyses. We found that changes in adipose tissue metabolism (e.g. triacylglycerol/fatty acid cycling, de novo lipogenesis) during cold exposure reflect susceptibility to obesity (Flachs et al., *Int J Obes (Lond)* **41**: 372, 2017). We also demonstrated that omega-3 supplementation induces novel anti-inflammatory lipid mediators from the FAHFA family in adipose tissue of obese mice and diabetic patients (Kuda et al., *Diabetes* **65**: 2580, 2016).Omega-3 supplementation also differentially regulates the levels of endocannabinoids in adipose tissue and circulation in mice and patients (Rossmeisl et al., *Biochim Biophys Acta Mol Cell Biol Lipids* **1863**: 712, 2018). In older sedentary individuals, omega-3 wax esters (Calanus oil) potentiates insulin-sensitizing effects of exercise training, which itself induces anti-inflammatory and insulin-sensitizing PAHSA lipid mediators in adipose tissue and circulation (Brezinova et al., *Biochim Biophys Acta Mol Cell Biol Lipids* **1865**: 158576, 2020). We also demonstrated that Nrf2-mediated antioxidant defence and peroxiredoxin 6 are linked to the biosynthesis of 9-PAHSA regioisomer (Kuda et al., *Diabetes* **67**: 1190, 2018) and that 5-PAHSA is regulated by adipose triglyceride lipase and primes adipocytes for glucose metabolism (Paluchova et al., *Diabetes* **69**: 300, 2020). With regard to cancer cachexia, we showed that it may reflect aberrant metabolism of adipose tissue itself by inhibiting AMPK activity by high levels of CIDEA in adipocytes, leading to increased lipolysis and “burning” of released fatty acids in skeletal muscles and other tissues (Rohm et al., *Nat Med* **22**: 1120, 2016).

Gastrointestinal research was focused on the intestinal transport system, endocrine regulation and intestinal pathologies (colitis, inflammatory bowel disease). Our studies characterised psychophysiological and inflammatory stress-induced modulation of glucocorticoid (the HPA axis) signalling, glucocorticoid metabolism, and cardiovascular response. We elucidated the role of gut microbiota in shaping the chronic response at the periphery of the HPA axis (Vodicka et al., *Brain Behav Immun* **73**: 615, 2018) and in peripheral tissue (Vagnerova et al., *Front Immunol* **10**: 2655, 2019). We also characterised the role of corticosteroid hormones in the regulation of the peripheral circadian clock in the intestine.

2. Neurophysiological research

Neurophysiology research carried out at IPHYS covers a selected spectrum of topics ranging from the molecular mechanisms of actions of transmitters on their receptors and the effects of cellular context on neurotransmission to highly integrative functions of the central nervous system, such as memory and temporal regulation of physiological processes (circadian rhythms). We also studied pathological mechanisms, namely those of neuropathic pain, cerebral ischemia, neurological diseases (such as epilepsy), and psychiatric conditions

(such as Alzheimer's disease (AD), autism spectrum disorder (ASD), obsessive-compulsive disorder (OCD), and schizophrenia). We correlated some experimental approaches from experimental animals with healthy volunteers andcomplement our neurophysiology research with computational methods.

At the molecular level, we investigated mechanisms of operation of fast-acting ion channels (glutamate NMDA receptors, transient receptor potential (TRP) ion channels, purinergic (PTX) channels), and slow-acting metabotropic G-protein coupled receptors (muscarinic acetylcholine receptors) in both peripheral and central nervous systems. In the research of NMDA receptors, we identified residues that are key to extracellular channel gate function (Ladislav et al., *Front Mol Neurosci* **11**: 113, 2018). Further, we found that polymorphism of NMDA receptors of schizophrenia patients and individuals diagnosed with ASD leads to enhanced sensitivity to steroids (Vyklicky et al., *Front Mol Neurosci* **11**: 110, 2018). In the research of TRP channels, we investigated activation of the channel by heat and cold (Sinica et al., *Cells* **9**: 2019; Macikova et al., *Int J Mol Sci* **20**: 2019) and allosteric mechanism of channel gating (Zimova et al., *Sci Signal* **11**: 2018). In the research of P2X channels, we identified transmembrane residues that regulate receptor conductivity and agonist sensitivity (Jindrichova et al., *J Neurochem* **133**: 815, 2015). Further, we identified new allosteric modulators of P2X receptors (Sivcev et al., *J Neurochem* **150**: 28, 2019) and analysed allosteric modulation of P2X receptors (Zemkova et al., *Pflugers Arch* **467**: 713, 2015; Mackay et al., *PLoS Comput Biol* **13**: e1005643, 2017). Concerning muscarinic receptors, we investigated molecular mechanisms of receptor activation and signalling bias (Randakova et al., *Pharmacol Res* **97**: 27, 2015; Randakova et al., *Neuropharmacology* **133**: 129, 2018; Randakova et al., *Br J Pharmacol* 2020). Further, we studied structure-activity relationships underlying the selectivity and long-lasting action of muscarinic antagonists (Jakubik et al., *J Mol Model* **21**: 284, 2015; Boulos et al., *Chem Biol Drug Des* **91**: 93, 2018; Randakova et al., *Br J Pharmacol* **175**: 1731, 2018). We also studied common mechanisms of allosteric modulation of muscarinic receptors (Jakubik et al., *Sci Rep* **7**: 40381, 2017; Jakubik et al., *Sci Rep* **9**: 4637, 2019; Jakubik et al., *PLoS One* **14**: e0214255, 2019).

At the level of the cellular context, we investigated the modulation of neurotransmission by various cellular and membrane components, especially membrane cholesterol and neurosteroids. We also investigated receptor regulation and trafficking at the cellular level. We found that membrane cholesterol and neurosteroids modulate the function of both NMDA receptors (Korinek et al., *J Physiol* **593**: 2279, 2015; Vyklicky et al., *Sci Rep* **5**: 10935, 2015; Vyklicky et al., *J Neurosci* **36**: 2161, 2016) and muscarinic acetylcholine receptors (Randakova et al., *Neuropharmacology* **133**: 129, 2018). We identified several mechanisms of TRP channels regulation including phosphoinositide binding (Macikova et al., *FEBS J* **286**: 3664, 2019), and phosphorylation and N-glycosylation (Hynkova et al., *Sci Rep* **6**: 28700, 2016; Marsakova et al., *Front Mol Neurosci* **10**: 16, 2017). At the cellular level, we investigated expression and trafficking of glutamate receptors (Petrovic et al., *Nat Neurosci* **20**: 529, 2017; Skrenkova et al., *Front Mol Neurosci* **11**: 188, 2018; Skrenkova et al., *Sci Rep* **9**: 12303, 2019), P2X receptors (Ivetic et al., *Front Cell Neurosci* **13**: 284, 2019). and the involvement of these mechanisms in the regulation of neurotransmission.

Within the tissue context, we focused on functional remodelling of neural tissues during development or various physiological and pathological processes. We identified and analysed action of ion channels involved in electrical activity and calcium signalling in pituitary corticotrophs (Zemkova et al., *Endocrinology* **157**: 1576, 2016; Fletcher et al., *J Neurophysiol* **117**: 2298, 2017). We identified cellular mechanisms responsible for the modulation of nociceptive synaptic transmission that involve TRP receptors (Li et al., *J Neurosci* **35**: 13487, 2015). Further, we investigated how various intracellular and extracellular signals mediate mechanical allodynia and enhanced responses to TRPV1 agonist capsaicin (Nerandzic et al., *Br J Pharmacol* **175**: 2322, 2018; Adamek et al., *Neuropharmacology* **146**: 163, 2019). At the tissue/organ level, we studied various aspects of neurodevelopment. Namely, we studied the role of signalling proteins (Sema3F, Pin1, CRMP2) in axon guidance, axon pruning, and dendritic spine remodelling. We demonstrated

that CRMP2 mediates Sema3F-dependent synapse pruning and that its dysfunction shares histological and behavioural features of ASD (Ziak et al., *EMBO Rep* **21**: e48512, 2020).

At the system level, we studied neuroinflammatory changes in the central nervous system, circadian rhythms, epilepsy, and learning, memory, and cognitive functions related to schizophrenia, AD, OCD, and narcolepsy. In the research of ***neuroinflammation***, we found that losartan treatment attenuates the development of neuropathic thermal hyperalgesia (Kalynovska et al., *Life Sci* **220**: 147, 2019) and that the sodium channel blocker protoxin II reduces burn injury-induced spinal nociceptive processing (Torres-Perez et al., *J Mol Med (Berl)* **96**: 75, 2018).

In the research of **circadian rhythms,** we focused on the changes of the circadian clock during the lifespan, the role of hormones and neuromodulators in the circadian regulation, the circadian clock in brain function and memory, and the human circadian system in neuropsychiatric disorders. We found that although the adult master clock in suprachiasmatic nuclei (SCN) is resilient to glucocorticoids, these hormones can entrain the fetal and neonatal master clock in SCN. The clock located in the maternal placenta serves as a glucocorticoid sensitive gatekeeper to control and deliver proper levels of glucocorticoids to the fetal SCN (Cecmanova et al., *J Biol Rhythms* **34**: 307, 2019). Proper maternal care may protect offspring from the development of pathological symptoms even if they are genetically programmed (Olejnikova et al., *Chronobiol Int* **32**: 531, 2015; Olejnikova et al., *J Physiol* **596**: 5757, 2018; Olejnikova et al., *Acta Physiol (Oxf)* **223**: e13020, 2018). Ageing does not impair the ability of the circadian clock in the SCN and the pancreas to generate a rhythmic signal, but it impairs their ability to control output rhythms (Polidarova et al., *Chronobiol Int* **34**: 1, 2017; Novosadová Z. et al., *Sci. Rep.* **8**:11668, 2018). The functional state of the circadian system in patients with bipolar disorder may vary depending on arousal state as accompanied with the episodes of mania and depression (Novakova et al., *Bipolar Disord* **17**: 303, 2015).

In the research of **epilepsy**, we focused on the mechanisms of epileptogenesis, epilepsy-related comorbidities, and the long-term impact of early pharmacological intervention on brain development. We developed new diagnostic techniques for epilepsy, and we searched for new potential anti-seizure drugs. To this end, we found that the activation of endothelin B receptors results in the development of non-ischemia related seizures associated with an inflammatory process (Vondrakova et al., *Exp Neurol* **328**: 113255, 2020). We found that hyperthermia aggravates long-term outcome of status epilepticus (Suchomelova et al., *Neuroscience* **305**: 209, 2015), and we identified the key role of oxidative stress in the pathogenesis of epilepsy (Folbergrova et al., *Front Cell Neurosci* **10**: 136, 2016; Folbergrova et al., *Mol Neurobiol* **55**: 7512, 2018). In the research of the long-term impact of early brain insults on brain development, we found that early exposure to benzodiazepines has long-term impacts (Kubova et al., *Front Mol Neurosci* **11**: 382, 2018) and that long-term neonatal stress affects habituation to the experimental environment and impairs an ability to sustain attention to stimuli in adulthood (Holubova et al., *Behav Processes* **149**: 59, 2018). In our research of epilepsy-related pharmacology, we identified two possible therapeutic targets in early-life seizures, the adenosine A_1 and glutamate NMDA receptors (Fabera et al., *Front Pharmacol* **10**: 656, 2019; Szczurowska et al., *Epilepsy Res* **109**: 106, 2015). Moreover, $GABA_A$ antagonists have anti-convulsive effects at certain stages of brain development (Mares, *Eur J Pharmacol* **818**: 26, 2018). In the development of new antiepileptics, we focused on neurosteroids and NMDA antagonists. In the development of new diagnostic methods, we focused on biomarkers of epileptogenesis, such as the integrity of the blood-brain barrier (Svoboda et al., *Physiol Res* **68**: 37, 2019), and monitoring of brief interictal epileptiform discharges. We found that the transition to seizure is not a sudden phenomenon, but it is instead a slow process characterised by the progressive loss of neuronal network resilience (Chang et al., *Nat Neurosci* **21**: 1742, 2018; Chvojka et al., *Epilepsy Behav* 106591, 2019).

In the research of **learning, memory, and cognitive functions**, we focused on brain areas and neurotransmitter systems (cholinergic, glutamatergic) related to cognitive symptoms in AD and schizophrenia. We showed that specific brain areas, namely the

hippocampus, anterior cingulate and retrosplenial cortices, and neuronal circuits and cell populations, are involved in spatially- and task-oriented behavioural processes (Brozka et al., *Neurobiol Learn Mem* **141**: 93, 2017; Levcik et al., *Neurobiol Learn Mem* **155**: 127, 2018; Svoboda et al., *Front Psychiatry* **8**: 215, 2017). We thoroughly examined multiple biological levels in search of a common neurophysiological mechanism of cognitive symptoms in schizophrenia (Buchtova et al., *Hippocampus* **27**: 134, 2017; Krajcovic et al., *Acta Physiol (Oxf)* **226**: e13282, 2019; Uttl et al., *Front Pharmacol* **9**: 42, 2018; Szczurowska et al., *Prog Neuropsychopharmacol Biol Psychiatry* **81**: 275, 2018) and AD *(Petrasek et al., Front Aging Neurosci **10**: 250, 2018; Petrasek et al., Front Aging Neurosci **8**: 83, 2016; Horak et al., Prog Neuropsychopharmacol Biol Psychiatry **75**: 54, 2017)*. We showed that 7-methoxy derivative of tacrine is the open-channel blocker of the NMDA receptor and has neuroprotective and pro-cognitive effects that may be beneficial in the treatment of AD (Rambousek et al., *Neuropharmacology* **105**: 594, 2016; Kaniakova et al., *Neuropharmacology* **140**: 217, 2018; Wesierska et al., *Neurobiol Learn Mem* **162**: 59, 2019; Laczo et al., *Neurobiol Aging* **51**: 67, 2017). In two mouse models of AD, we have showed that lipid-based diets improve cholinergic neurotransmission in the hippocampus (Janickova et al., *Curr Alzheimer Res* **12**: 923, 2015; Dolejsi et al., *J Neurochem* **136**: 503, 2016). These results demonstrate that lipid-based diets represent a viable complement to the pharmacological treatment of AD.

In healthy volunteers, we focused on the translation of rodent model tasks to humans and basic research into the electrophysiology of human spatial orientation concerning AD and schizophrenia. Our methods testing visual and non-visual spatial navigation exert high discrimination accuracy among AD, mild cognitive impairment, and healthy control groups (Laczo et al., *Neurobiol Aging* **51**: 67, 2017; Mokrisova et al., *Behav Brain Res* **307**: 150, 2016). In the research related to schizophrenia, we focused on visuospatial abilities and how they influence patients' quality of life (Rodriguez et al., *Front Behav Neurosci* **9**: 322, 2015). In our current research, we describe extensive networks of the spatial-scene or object selective brain areas consisting of the occipital place area, the parahippocampal area, and retrosplenial complex and object processing in the lateral occipital complex area.

In the **computational approach**, we employed theoretical methods to describe and understand particular processes in neural systems on the level of single cells or populations. The focus was mainly on the neural coding problem, mathematical models of neuronal activity, and biophysical modelling of axon growth and circuit formation. Namely, we showed how olfactory receptor neurons adjust their encoding to pheromone fluctuations (Levakova et al., *PLoS Comput Biol* **14**: e1006586, 2018). We described mechanisms of axon fasciculation and network formation (Smit et al., *Elife* **6**: 2017), the rate coding capabilities of neurons (Barta et al., PLoS Comput Biol 15: e1007545, 2019) and established a critical size of the neural population for reliable information transmission (Kostal et al., Phys Rev E 100: 050401, 2019). We studied the entropy factor for randomness quantification in neuronal data (Rajdl et al., *Neural Netw* **95**: 57, 2017) andthe instantaneous firing rate of neurons (Kostal et al., *Chaos* **28**: 106305, 2018).

3. Cardiovascular research

The IPHYS research into physiology and pathophysiology of the cardiovascular system may be divided into four main closely related directions: (i) systemic hypertension, ii) myocardial ischemia and heart failure, (iii) cardiac development, and (iv) vascular replacement.

In the research of **systemic hypertension**, we mainly studied the role of principal vasoactive systems in the mechanisms of blood pressure regulation in various hypertensive rat models. We showed that augmented sympathetic vasoconstriction plays a major role in the development and maintenance of hypertension in spontaneously hypertensive rats (SHR) (Behuliak et al., *Hypertension* **72**: 676, 2018), Ren-2 transgenic rats (TGR) with angiotensin II-dependent hypertension (Vaneckova et al., *J Hypertens* **33**: 161, 2015), and Dahl rats with salt hypertension (Zicha et al., *Physiol Res* **68**: 873, 2019). We also demonstrated (i) different changes of the sympathetic nervous system in prehypertensive SHR and in SHR with established hypertension (Vavrinova et al., *Hypertens Res* **42**: 949, 2019; Vavrinova et

al., *Hypertens Res* **42**: 1872, 2019), (ii) the hypotensive effect of gabapentin mediated by voltage-dependent calcium channels (Behuliak et al., *Hypertension* **72**: 676, 2018), and (iii) the diverse contribution of calcium influx and calcium sensitization to blood pressure regulation in various forms of hypertension (Behuliak et al., *Biomed Res Int* **2017**: 8029728, 2017). In hypertensive TGR, the enhanced blood pressure reduction induced by either the calcium channel blocker nifedipine or the Rho-kinase inhibitor fasudil is related to impaired baroreflex efficiency (Vaneckova et al., *Hypertens Res* **42**: 145, 2019). Regarding the involvement of the endothelin vasoconstrictor system, we showed that the reduced calcium influx is responsible for the antihypertensive action of a selective ETA receptor blocker in TGR (Vaneckova et al., *J Hypertens* **33**: 161, 2015). Importantly, a substantial reduction of blood pressure was achieved by sodium nitrate or beetroot supplementation in salt-sensitive hypertensive Dahl rats (Morris et al., *Hypertension* **73**: 1042, 2019). Our results also provide evidence for a new role of Plzf (promyelocytic leukaemia zinc finger) in the regulation of blood pressure, cardiac hypertrophy, and fibrosis (Liska et al., *Hypertension* **69**: 1084, 2017).

Regarding **myocardial ischemia and heart failure**, we focused on beneficial effects of a therapy based on synthetic analogues of epoxyeicosatrienoic acids (EETs) and inhibitors of soluble epoxide hydrolase, an enzyme responsible for conversion of EETs to inactive metabolites. We showed that cardioprotection induced by EETs analogue is mediated by stabilisation of hypoxia-inducible factor-1α (Hif-1α) due to downregulation of its degrading enzyme prolyl hydroxylase-3 at reperfusion (Neckar et al., *Am J Physiol Heart Circ Physiol* **315**: H1148, 2018). We also demonstrated that EETs analogue attenuates post-infarction heart failure progression in normotensive rats (Hrdlicka et al., *Front Pharmacol* **10**: 159, 2019) and in SHR without affecting blood pressure (Neckar et al., *Clin Sci (Lond)* **133**: 939, 2019). EET-based therapy in the setting of myocardial infarction was ineffective in hypertensive Ren-2 transgenic rats, except for reducing blood pressure and life-threatening ventricular arrhythmias (Cervenka et al., *J Hypertens* **36**: 1326, 2018). In rats with chronic heart failure induced by volume overload, we showed that severity of morphological phenotype (hypertrophy) correlated with a drop of connexin 43 phosphorylation and electrophysiological changes related to arrhythmogenesis (Sedmera et al., *Front Physiol* **7**: 367, 2016).

Research into the molecular mechanism of **myocardial protection** induced by chronic hypoxia revealed a crucial role of antioxidant defence activated by tumour necrosis factor-α via its type-2 receptor signalling (Chytilova et al., *Acta Physiol (Oxf)* **214**: 97, 2015). Using the conplastic SHR strain harbouring mitochondrial genome of normotensive rats, we showed that mitochondrial DNA modulates the cardioprotective effects of chronic hypoxia (Neckar et al., *Clin Sci (Lond)* **131**: 865, 2017). Regular exercise during hypoxia does not further augment the improved ischemic tolerance, suggesting a common protective mechanism dependent on persisting antioxidant response (Alanova et al., *J Appl Physiol (1995)* **122**: 1452, 2017).

In the research of **cardiac development**, we participated in a study which showed that conditional deletion of Hif-1α suppresses the embryonic development of cardiac sympathetic innervation and results in coronary artery anomalies and decreased cardiac contractility (Bohuslavova et al., *Proc Natl Acad Sci U S A* **116**: 13414, 2019). Global reduction of Hif-1α gene dosage increases the predisposition of mouse offspring exposed to maternal diabetes to cardiac dysfunction (Cerychova et al., *Cardiovasc Diabetol* **17**: 68, 2018). These results underscore Hif-1α as a critical transcription factor in the fetal programming of adult cardiovascular disease. We also revealed the novel role of mitochondrial tryptophanyl-tRNA synthetase WARS2 as a determinant of angiogenesis in the heart and other tissue (Wang et al., *Nat Commun* **7**: 12061, 2016). In studies on developing hearts, we showed that the presence of a specialised conduction system in the vertebrate ventricle is linked to the ventricular septum rather than to homeothermy, as was believed previously (Hanemaaijer et al., *Development* **146**: 2019).

Regarding **vascular replacement**, we succeeded in reconstructing a continuous endothelial cell layer on the inner surface of synthetic polymeric vascular prostheses used in current clinical practice, i.e. prostheses made of expanded polytetrafluoroethylene or

polyethylene terephthalate. Their inner surface is coated with fibrin layers of nanofibrous morphology, which allowes for the development of a confluent, mature endothelial cell layer. These vascular prostheses are not suitable for reconstruction of tunica media containing vascular smooth muscle cells (VSMC). Therefore, we used decellularized porcine matrices, which maintain a similar structure and composition as the original tissue *in vivo*. For recellularisation of decellularised blood vessels or pericardium, we used human adipose tissue-derived stem cells obtained by liposuction and expanded *in vitro* in our dynamic bioreactors for planar and tubular tissue (Musilkova et al., *Biomed Mater* **15**: 015008, 2019). These cells can easily differentiate towards VSMC as demonstrated in our laboratory. Three main factors for the differentiation were used: (i) scaffolds with appropriate mechanical properties for soft tissue engineering, i.e. decellularised matrices or fibrin gel, (ii) appropriate composition of the cell culture media containing transforming growth factor-β and bone morphogenetic protein-4, and (iii) appropriate mechanical stress generated in the bioreactor. Under these conditions, the ASCs synthesise alpha-actin, an early marker of VSMC differentiation, and calponin, an intermediate marker of VSMC differentiation (Bacakova et al., *Muscle Cell and Tissue: Current Status of Research Field*, **book chapter**, 2018). We also used porcine ASCs for recellularisation of porcine blood vessels and started implantations of these constructs into pigs in collaboration with the Institute for Clinical and Experimental Medicine (**IKEM**).

Cooperation within the international research area

To classify international cooperation activities, we designated three main types of cooperation.

1. Formalised cooperation

During the evaluation period, IPHYS was a recipient of a number of bilateral and multilateral *international grants* from the following providers:

Provider	**No. of projects**
The Czech Science Foundation (GAČR)	2
Ministry of Education, Youth and Sports (MŠMT)	14
The Czech Academy of Sciences (CAS)	4

This next list includes both general cooperation, based on broader *Memoranda* or *Letters of Cooperation,* and specific cooperation described in *Project Agreement* or similar documents.

Nencki Institute of Experimental Biology (Poland)
Document: Memorandum of Understanding
Concluded: 23/10/2017
Objectives: General collaboration
Outputs: Conference on Bioenergetics, IPHYS 2017

Centre of Experimental Medicine, Slovak Academy of Sciences
Document: Memorandum of Understanding
Concluded: 10/4/2019
Objectives: General collaboration in the field of neurosciences
Outputs: PhD student exchange, publication in preparation

University of Central Lancashire of Preston (United Kingdom)
Document: Memorandum of Understanding
Concluded: 22/6/2017
Objectives: Research, funding and commercialisation in the field of electrophysiological imaging, behavioural and molecular biology methods

National Institute of Informatics, NII (Japan)
Document: Memorandum of Understanding
Concluded: 7/11/2016
Objectives: Research collaboration in the field of artificial intelligence and computational neuroscience, staff exchange
Outputs: 2 publications, annual mutual visits, 2 internships at NII

EPTRI Consortium
Document: Consortium Agreement
Concluded: 12/1/2018
Objectives: Implementation of the ID-EPTRI project under H2020
Outputs: Successful implementation of the project

University of California (USA)
Document: 3 Memoranda of Cooperation
Concluded: 11/12/2017, 26/2/2018, 14/3/2018
Objectives: Internships for postdoctoral researchers
Outputs: 3 six-month internships at UC

University of Arizona (USA)
Document: 1 Memorandum of Cooperation
Concluded: 27/3/2018
Objectives: Internship for postdoctoral researchers
Outputs: 1 six-month internship at UA

University of Padova (Italy)
Document: 2 Memoranda of Cooperation
Concluded: 28/11/2017, 18/12/2017
Objectives: Internships for postdoctoral researchers
Outputs: 2 six-month internships at UP

University of Padova (Italy)
Document: 2 Agreements on Scientific Cooperation
Concluded: 17/5/2018, 20/6/2018
Objectives: Partnership in a mobility project
Outputs: 2 two-year mobilities at UP

Medical Research Council (UK)
Document: Agreement on Scientific Cooperation
Concluded: 28/7/2018
Objectives: Partnership in a mobility project
Outputs: Two-year mobility at MRC

2. Natural cooperation

Most of the collaboration activities of IPHYS come through without a formal document. Such collaboration consists of cooperation on specific research projects, preparation of publications, and other outputs. These activities are summarised in the following **publication statistics.**

Institutes/organisations with the most collaborative publications

Institute/organisation	**Country**	**No. of Publications**
Slovak Academy of Sciences	Slovakia	25
University of Minnesota	USA	13
University of California San Francisco	USA	13
Polish Academy of Sciences	Poland	12
University of Colorado	USA	10
Medical College of Wisconsin	USA	10
University of Ghent	Belgium	8
Imperial College London	UK	8
Max Delbrück Centre for Molecular Medicine in the Helmholtz Association	Germany	8
Comenius University	Slovakia	8

Most frequent countries in publications with international co-authorship

Country	**No. of Publications**
USA	184
Germany	82
England	81
France	66
Spain	51
Slovakia	41
Poland	31
Japan	28
Italy	27
Australia	21

Furthermore, the number of researchers from foreign countries employed by IPHYS has been growing since 2015:

Year	2015	2016	2017	2018	2019
Researchers	26	35	48	49	59

3. Internship programmes

We consider internship programmes as a special category of cooperation, as it is not usually predated by specific collaboration or output, but it provides the base for further collaboration and training for our researchers.

Since 2018, IPHYS started offering funding for short (1-2 months) internships to young researchers. In 2018, 2 internships at foreign institutes received funding; in 2019, 5 internships were funded. These internships are gaining increased popularity among young researchers, and the Institute plans to increase the number of internship in the coming years.

HR policy of the Institute

1. The recruitment process at IPHYS contains:

- Identifying the jobs vacancy;
- Analysing the job requirements;
- Advertising the position;
- Reviewing applications;
- Shortlisting;
- Conducting interviews;
- Selecting the suitable candidate.

First, the Laboratory Head contacts the Human Resources (**HR**) Department to announce they have a job opening. Together they analyse the position and its requirements. Afterwards, the HR Specialist and the Laboratory Head decide which advertising websites and newspapers will be used. The position is advertised for at least 30 days.

When the position is advertised, the HR Specialist collects applications and contacts the applicants about the selection process. Then the candidates are filtered for the further selection process. In this process, the resumes of the candidates are reviewed and checked for the candidates' education, work experience, and overall background matching the requirement of the job. After that, the HR Specialist sends a rejection e-mail to candidates who did not meet the requirements.

The top candidates are invited to an interview by telephone, video call, or face to face. Interviews are held before a committee that evaluates the candidate's abilities. The committee is composed of both men and women (scientists and people from HR) to ensure transparency of the selection process. After the interviews, the committee chooses the suitable candidate and writes a selection process report.

IPHYS has substantially changed its recruiting process so that it could meet the HR Award standards. Thanks to this, the recruiting process has become more transparent, and it has enhanced cooperation among scientists and employees from the HR Department. The Institute also started to cooperate with *Euraxess*, which provides great support in this area. As a result, the Institute is now able to provide better help for foreign applicants with their visa process.

In the coming years, the Institute will endeavour to achieve further modernisation in the recruiting process. It will be necessary to continue monitoring new trends in the field of HR, recruiting, and HR marketing so that the Institute is perceived as an attractive employer for scientists from the entire world.

2. HR Award

IPHYS received the HR Award (guaranteed by *Euraxess*, financially supported by *Operational Programme Research, Development and Education*) in March 2019 with commendation and is currently in the middle of the implementation phase. The GAP analysis needed for receiving the HR Award has not shown any major shortcomings in the HR practice of the Institute

The Action Plan, published on the IPHYS webpage (https://www.fgu.cas.cz/en/articles/836-hr-excellence-in-research-award)), sets two primary goals: to implement an OTM-R compliant recruitment process, which mainly consists of better documentation of current practice, and to improve career development options of researchers, especially in the postdoctoral phase. In order to do that, the Institute will support, both financially and otherwise, its researchers in gaining their abroad research experience and also provide them with options to gain more independence in their research activities, including the possibility of establishing their own laboratory. Enacting measures to support work-life balance can also be considered a part of this objective.

3. Work-life balance

IPHYS understands the importance of equal opportunities, gender equality, and healthy work-life balance and its advantages for both the Institute and its employees. That is why the Institute tries to create the best working environment and work culture. The work-life balance policy is divided into three parts:

- Flexible working practices
- Attractive working environment
- Family/ Employee benefits

Flexible working practices help the employees combine their work with their personal life. The Institute commonly offers part-time contracts along with flexible working hours, which helps especially parents with smallchildren.

Attractive working environment is one of the most important points for the employees to like going to work, and the Institute always tries to enhance it. At present, the Institute provides many benefits: there are subsidised lunches in the canteen, a buffet, and food/drink machines. Moreover, there are several sports activities available within the Krč campus, such as squash, volleyball, dancing, and yoga lessons.

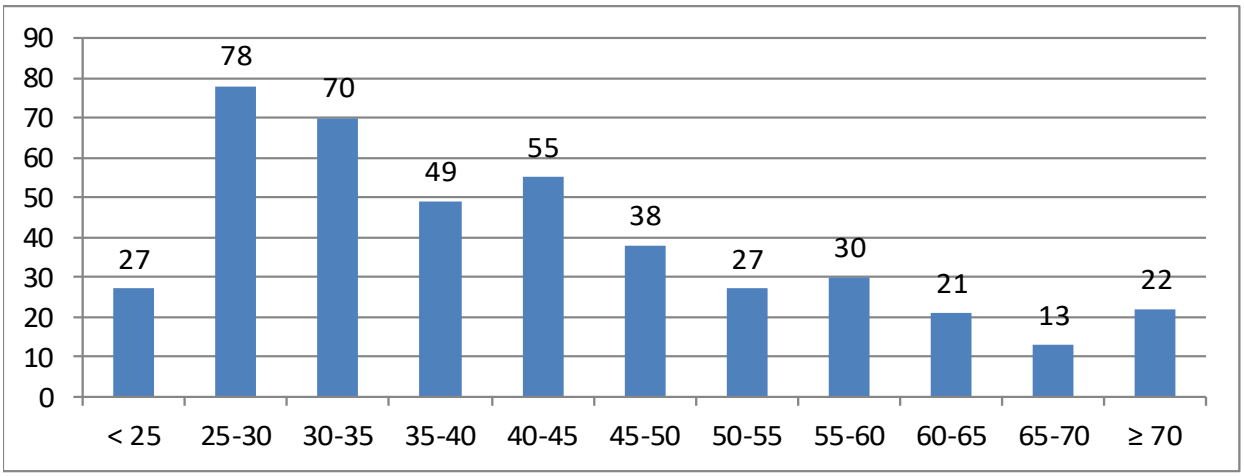
Finally, the Institute offers family/employee benefits. The Institute offers one week of additional holidays for employees working in a standard environment, two weeks for employees working in a high-risk environment, and three sick days for everyone. Moreover, there is a kindergarten and a children's group for parents with young children. The Institute also offers foreign language courses at a reduced price, lunch vouchers, and pension insurance for those working at IPHYS for more than three years.

Work-life balance policy is an important part of the IPHYS culture. There are several high-level benefits which are regularly used by our employees. IPHYS plans to improve this area constantly. The HR Department is currently negotiating with the Institute management about implementing work from home into the benefits system.

The age structure of the Institute

As of 31 December 2019

Age category	**< 25**	**25-30**	**30-35**	**35-40**	**40-45**	**45-50**	**50-55**	**55-60**	**60-65**	**65-70**	**≥ 70**
Number of members	27	78	70	49	55	38	27	30	21	13	22



Age category > 65 includes 10 emeritus scientists

Strengths and weaknesses of the Institute

For complementary information, see also the section below: *Implementation of recommendations from past evaluation*.

1. Strengths

A clear focus on important scientific topics, building on a decades-long tradition of excellence, while being open to novel approaches

(i) IPHYS's scientific research is focused on studies of physiological and pathophysiological processes at the molecular, cellular, organ, and whole-body levels, with the aim to understand the fundamental principles of human diseases. It has **a high socio-economic impact**, as it leads to more reliable prevention, diagnostics, and therapy of major human diseases and disorders.

(ii) IPHYS has a decades-long **tradition of excellence** in the above fields of research.

(iii) We are proud of the tradition of excellence; at the same time, we are **open to new topics and novel approaches**, as relevant to the IPHYS's research focus. Since 2014, two Junior groups have been established thanks to the *IPHYS StartUp Research Programme.*

(iv) Research in the above areas, as performed at IPHYS, gave rise to a high and stable scientific performance, as documented by a robust publication record and a number of important results outreaching to applied research. In fact, both the Impact factor (IF) and the Article Influence Score (AIS) per publication, and the percentage of first-quartile outputs (AIS) have been increasing steadily since 2014.

(v) The high quality of the teams and their research projects is reflected by above-the-mean success in the competition for the domestic grant resources.

Highly-qualified, multidisciplinary scientific staff trained in modern methods and technologies, with a balanced scientific level, i.e. strong human potential

(i) The staff of IPHYS is **highly qualified**, possessing a broad range of knowledge and research skills required to employ **a broad spectrum of methodological strategies**, ranging from molecular and cellular techniques to systemic (whole animal) approaches.

(ii) This means that the staff is truly **multidisciplinary**, comprising specialists not only in physiology but also in biochemistry, molecular biology, genetics, biophysics, bioinformatics, biomathematics, and biomedical engineering. Novel methodological approaches are introduced, especially metabolomics and proteomics, to support the infrastructure.

(iii) IPHYS is a **top biomedical research institution in the country**. All teams are internationally well-recognized, and some of them highly competitive world-wide.

A wealth of collaborative projects within the Institute, as well as at national and international levels

(iv) A wealth of **internal collaboration** among the Institute's teams has been established, as well as collaboration **with other Czech institutions**. It should be emphasized that the critical "know-how" often comes from within IPHYS itself in such collaborative pursuits.

(v) Six teams participate in the **Biotechnology and Biomedicine Centre (BIOCEV)** funded by the EU structural funds and have opportunities to exploit the offered cutting-edge core facilities.

(vi) We are deeply involved in the **Strategy AV21** (see also the specific section below) initiated by the CAS. We coordinate two of its programmes: **the QUALITAS Programme** with the main goal to develop more effective strategies to prevent and

treat lifestyle-choice related diseases; and the **Preclinical Testing of Potential Pharmaceuticals Programme**, which is focused on the integrated use of facilities at several CAS institutes in the translational biomedical research.

(vii) Active **international collaboration** is documented in team reports, see also the Cooperation within the international research area section.

Teaching activities and training of young researchers

(i) IPHYS is involved in extensive teaching activities at many faculties of several universities.

(ii) Top-quality young researchers are trained at the Institute; many Institute's alumni have joined prestigious laboratories abroad or run their own laboratories at universities or clinics.

Improved research infrastructure.

New essential equipment was acquired in 2015-2019, resulting in a broader range of available techniques. Sharing of equipment among the laboratories within the Institute guarantees high utilisation and cost-efficiency. In 2020, an extensive reconstruction of the main animal facility of IPHYS was initiated (in collaboration with the Institute of Microbiology, CAS), which is scheduled for 3 years. Projected cost is 193 mil CZK (ca. 6.9 mil EUR, funded by the CAS). The *newly reconstructed animal facility* will provide an optimal environment for studies on laboratory rodents – the key element of research conducted at IPHYS. The *Service Laboratory of Metabolomics* was established at IPHYS in 2019, and the *Joint Laboratory of Proteomics of IPHYS and the Institute of Molecular Genetics* was founded in 2020 (see below, the *Administration of research infrastructure*).

Transfer of knowledge from basic to applied research - see the *Research for practice* section below.

Improved dissemination of our results and achievements to the general public

In past years, we have strengthened our public relations activities, which we find important for convincing the general public and politicians about the importance of our research to society as a whole.

2. Weaknesses

Problems with attracting highly motivated and talented young researchers

The multidisciplinary focus of IPHYS and a broad range of state-of-the-art methods employed translate to an ever-increasing **demand on the new prospective colleagues,** as they have to broaden their expertise gained during their university studies in relatively narrow disciplines by acquiring a vast range of new knowledge and skills. This requires hard work and much effort, but not everybody is capable and willing of acquiring additional skills. Although more young and talented researchers are still needed, **important progress in this respect has been made**, see the section below *Implementation of recommendations from past evaluation.*

Relatively low recognition of the CAS academic performance by the government and relatively low funding of science in the Czech Republic in general

A rather fuzzy system of basic research funding represents a major risk for the Institute's future. The financial insecurity results in deepening the core weaknesses and in missing opportunities. Unfavourable financial situation has adverse effects on human resources. The unclear situation concerning the support for basic research discourages especially young people from pursuing a scientific career. Inadequately trained researchers, inability to recruit new ones, and the difficulty to retain necessary expertise are all serious, long-term

challenges. Limited budgets of the Czech grant-giving agencies are connected with the necessity to limit the grant support duration to 3 years and to reduce budgets of individual grants (in average less than 60 thousand EUR per grant per year). This results in fragmentation of research topics, short-term goals, and a necessity for each team to apply for grant support frequently, which increases the administrative burden for researchers.

Exaggerated bureaucratic burden regarding this document
In our opinion, the structure of this document should be simplified for the sake of better efficiency of the next evaluation. Thedocuments from *Phase I* of the evaluation and the on-site visits by the commissions are more important for understanding the overall environment, quality, potential, impact, and possible problems of the performance of the whole Institute as well as its individual scientific teams.

The threat of the budget cuts due to the global economic downturn resulting from the coronavirus pandemic – see the ***Contingency plan*** in the section below*: Strategy plan of the institute as a whole for the period of 2020–2024*

Assessment of the strategic plan of the Institute for the period of 2015-2019

Since the strategic plan of IPHYS for the 2015 – 2019 period might not be available for the reviewers, **the main specific highlights** of this plan are listed below:

- Use of novel transgenic models developed by the newly introduced, high-efficiency technique of germline transgenesis, as well as all other unique biomodels, to characterise basic physiology and genetic mechanisms of the studied diseases
- To initiate collaborative efforts among several teams to uncover basic mechanisms of functioning of the signalling and transport proteins, while applying state-of-the-art structural biology, morphology, and membrane biophysical approaches
- To further uncover the role of mitochondria in the development of severe diseases, including “classical” mitochondrial diseases, as well as obesity-associated diseases including cancer, and to use this knowledge for diagnosis and treatment
- To further characterise the mechanisms behind beneficial effects of omega-3 fatty acids on health and test the potential of these lipids in the treatment of obesity-associated diseases
- To elucidate possible mechanisms through which particular humoral systems, such as endothelin or angiotensin II, contribute to hypertensive end-organ damage in the kidney or the heart
- To delineate endogenous adaptive mechanisms of sustainable cardiac protection against acute ischaemia/reperfusion injury with respect to developmental aspects and lifestyle-related risk factors
- To develop new materials /approaches for biocompatible replacement of blood vessels
- To advance the understanding of molecular and cellular mechanisms underlying the activation, allosteric regulation and post-translational modification of ion channels and receptors involved in nerve excitation and synaptic transmission (NMDA, AMPA, P2X, TRP, mAChR) and to explore highly integrative functions of the central nervous system, such as memory and temporal regulation of physiological processes
- To elucidate mechanisms of temporal regulation of physiological processes on a daily basis and the role of their alignment with environmental cues for our health
- At the molecular, cellular, functional, and cognitive levels, to further uncover pathophysiological mechanisms of neurological, neuropsychiatric, and

neurodevelopmental disorders, including cerebral ischemia, epilepsy, neuropathic pain, Alzheimer's disease, schizophrenia, depression, and others

As apparent from the reports of the individual teams, these specific aims have been mostly accomplished. **Thus, the overall IPHYS strategy of biomedical research, which is based on *The institute mission* (see the first section of this report) has been successfully followed.**

Implementation of recommendations from past evaluation

The evaluation of 23 research teams of IPHYS was performed by 5 different commissions:

- Commission No. 2: *Computer and information sciences*
  One team: Computational Neuroscience
- Commission No. 4: *Chemical sciences*
  One team: Analysis of Biologically Important Compounds
- Commission No. 6*: Biochemistry and molecular cell biology, biophysics, virology*
  Five teams: Bioenergetics, Membrane Transport Biophysics, Genetics of Model Diseases, Membrane Transport, Protein Structures
- Commission No. 8*: Engineering and technology*
  One team: Biomathematics
- Commission No. 9: *Medical and health sciences*
  Fourteen teams: Experimental Hypertension, Adipose Tissue Biology, Biomaterials and Tissue Engineering, Cellular and Molecular Neuroendocrinology, Cellular Neurophysiology, Epithelial Physiology, Functional Morphology (new name: Pain Research), Cardiovascular Morphogenesis, Neurochemistry, Neurophysiology of Memory, Neurohumoral Regulations (new name: Biological Rhythms), Developmental Epileptology, Developmental Cardiology, Biochemistry of Membrane Receptors

The Commissions were impressed by the generally high quality of biomedical research in IPHYS. However, due to their large number, and uneven numbers of teams evaluated by different Commissions, the evaluation of IPHYS as a whole was difficult to accomplish. The most valuable conclusions were the conclusions of Commission No. 9: *Medical and health sciences* that evaluated 14 teams, and Commission No. 6*: Biochemistry and molecular cell biology, biophysics, virology* that evaluated 5 teams (see above). Collectively, these Commissions stressed that:

- the main research topics represent a clear strength for IPHYS, which addresses highly relevant issues for healthcare;
- the synergistic, multidisciplinary approach incorporates both *in vitro* and *in vivo* research;
- the track record of the Institute is strong in national and international collaboration with other academic and medical research centres;
- IPHYS has many highly experienced PI's with strong international visibility;
- participation of PhD students in the research programs of the Institute is very good; and
- the Institute has a very good publication record.

Both commissions identified several weaknesses and gave several recommendations, as listed below (*in italics*). Our action in response during the 2016-2019 period is also specified.

- .. *several of the smaller "Departments" (or more appropriately, groups) lack critical mass and so represent weak points for achieving the global strategy and vision of the Institute. This tendency to "fragment" research efforts is in part exacerbated by the domestic funding landscape*…In response to this criticism:

(i) four individual smaller "Departments" were merged to form two larger "Departments" (Pain Research and Developmental Cardiology, now called Laboratories);
(ii) in 2020, all scientific teams at IPHYS, formerly called "Departments", were renamed to "Laboratories" in order to make the nomenclature compatible with other scientific institutes internationally,;
(iii) based on the call by the Ministry of Education of the Czech Republic in 2019, IPHYS participated in two major "Strategic projects" with most of its Laboratories involved (i.e. the projects "Obesity and Diabetes-Related Cardiovascular Disease: An Integrated Prevention and Treatment Research Programme", and "Progress Brain – National Centre of Applied Neurosciences"). The projects were rated highly (the 4th and the 14th place/48 projects in total) in the first step of the evaluation. However, due to the ongoing economic crisis, the fate of these projects is not clear at present. If funded, they will bring the required support for long-term conceptual research in IPHYS Laboratories.

- *…. there is room for improvement in the arenas of translational activities and intellectual property rights……..*

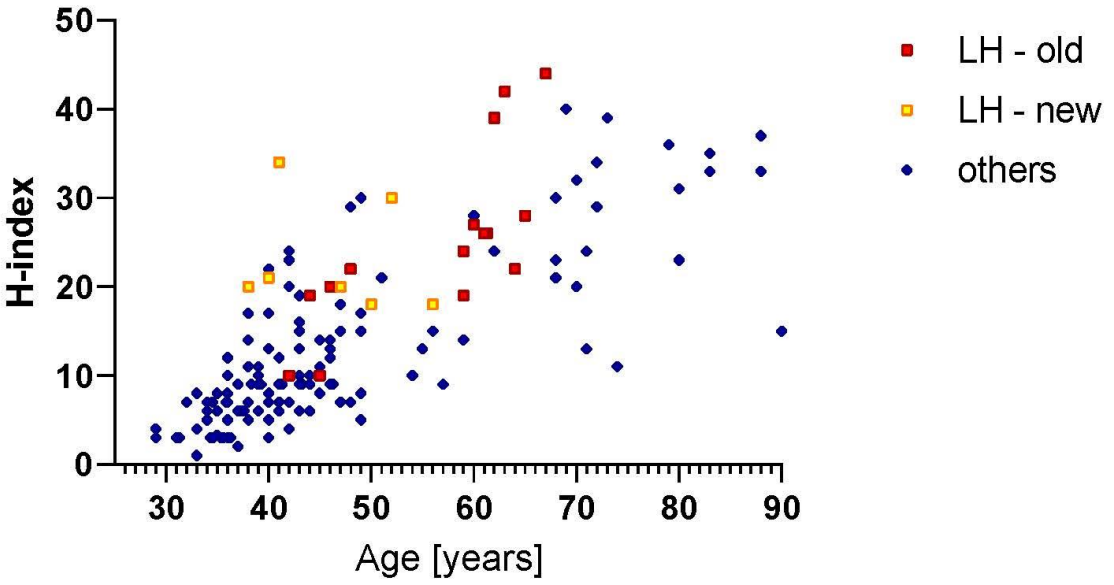
  This problem was fixed completely (see the "Research for practice" below).

- *weakness in the age structure….. problems to attract and maintain middle career scientists, in large part due to internationally non-competitive salaries and so there is an inevitable "brain drain" effect. These problems are compounded by funding constraints which for example retard investment in new infrastructure that would be needed to competitively recruit new senior scientists….*

  This important recommendation was enforced in several aspects:

(i) based on the *internal Start-Up Research Programme*, a new scientist with several-year-experience in the USA, Dr. M. Tencerova, was selected to head the new *Laboratory of Physiology of Bone* in 2019;
(ii) the new *Laboratory of Metabolism of Bioactive Lipids* headed by Dr. O. Kuda was established in 2019, based on the prestigious *award Lumina quaeruntur* by the CAS;
(iii) the *Junior group* of Dr. M. Balastik, was transformed into a standard *Laboratory of Molecular Neurobiology;*
(iv) five senior scientists who served as heads of various Laboratories were replaced by younger and capable scientists, based on open competitions;
(v) based on the internal IPHYS competition to provide 3-year-support for postdocs with long-term experience outside the Czech Republic, in total 7 such individuals were selected to join various IPHYS Laboratories.

As a results of all these changes, 10 out of 22 heads of IPHYS Laboratories are 50 years old or younger in 2020, as compared with 5 such scientist under 50 years of age serving as heads in 2015. The research performance of all Institute's scientists (including postdocs, but not PhD students) expressed by the Hirsch index as a function of age is shown below. The laboratory heads are also indicated, including the specification of the time of their appointment.



Performance (Hirsch index) versus age of Institute's researchers (in May 2020)
(LH - old, Laboratory Head appointed before December 2015; LH – new, Laboratory Head appointed after December 2015).

Moreover, in order to improve IPHYS infrastructure, a new *Service Laboratory of Metabolomics* was founded in 2018, headed by Dr. T. Čajka. Most importantly, to improve the conditions for performing animal experiments, a large-scale reconstruction of the IPHYS animal facility started in 2020, which is scheduled for 3 years. This is the most significant reconstruction at IPHYS to date; it is funded by the CAS.

- …… *recommendation to strengthening the links with clinical partners*……This recommendation was followed by:
  - (i) the engagement of IPHYS in the applications for the clinically oriented "*Strategic projects*" (see above);
  - (ii) involvement in a newly founded consortium of several partners, EPIREC (http://epirec.cz/), which is focused on innovative epilepsy treatment;
  - (iii) organisation of two bilateral meetings of IPHYS and the Institute of Experimental and Clinical Medicine – **IKEM** (2015, 2019);
  - (iv) involvement in many projects in collaboration with domestic clinical partners that have been funded by domestic grant agencies, namely the Czech Science Foundation, the Czech Health Research Council (AZV), and the Technology Agency of the Czech Republic (TACR);
  - (v) involvement in international research consortia/projects with a focus on translational biomedical and clinical research, namely EPTRI (https://www.cvbf.net/eptri/); see also the above section "*Cooperation within international research area*".

- …… *recommendation to establish an external advisory board of the Institute….*
The International Advisory Board of IPHYS (**IAB-IPHYS**) was established in 2019, having 5 scientists from Germany (2), Sweden (2) and Poland (1) as the members (https://www.fgu.cas.cz/en/about/61-institute-management)

Several specific comments regarding individual teams were raised by different commissions. The most serious of those concerned two teams:

- The Department of Analysis of Biologically Important Compounds
  ……*There is not any unifying strategy in the different aspects of the research performed by this team…….. the plans for future research are incompletely developed* ….The head of this Department has resigned. Based on an open competition, a new head was selected, Dr. T. Čajka, an excellent scientist (41 years, H index = 31), after his return to the Czech Republic following a 5-year-stay in the USA. The Department was renamed to the Laboratory of Translational Metabolism, with a focus on collaboration of IPHYS scientists with clinicians using advanced analytical approaches. He is also the head of a new Service Department of Metabolomics (see above).

- The Department of Biomaterials and Tissue Engineering
  …… *no clear vision for an independent research roadmap for the future*……
  We do not agree with this criticism. This team is one of the groups with the most advanced translational research profile at IPHYS, with a clear focus on the improvement of currently-used synthetic tissue replacements by introducing cell and other biological components. See also publications of this team.

Strategy plan of the Institute for the period of 2020–2024

We aim to further strengthen basic **physiological research at the genetic, molecular, cellular, organ,** and **system levels**. We will elucidate pathophysiological mechanisms underlying the development of diseases, namely those associated with selected disorders of metabolism and the cardiovascular and nervous system. These are usually multifactorial and often represent consequences of overeating and a sedentary lifestyle. Diagnosis, prevention, and treatment of these diseases largely depend on a proper understanding of the underlying mechanisms. The ultimate aim of our research programme is **to understand those fundamental processes and to translate the acquired knowledge into innovative and effective diagnoses and treatments.** Even subtle improvements in prevention and treatment strategies may have a high socio-economic impact. For such research to be successful, **an inter-disciplinary approac**h is essential. We are confident that we will achieve it through intense collaboration among our teams and beyond. To achieve our goals, we must combine the efforts in several fields highlighted below.

- The Institute's management, namely its Council and Director, will be responsible for the quality of research and its compliance with the overall Institute's strategy. A newly established (2019) *International Advisory Board of IPHYS* (**IAB-PHYS**) will be involved in various strategic decisions.

- The IPHYS system of the 5-year-evaluation period of its scientists will be improved, with a focus on postdoctoral fellows and team leaders (i.e. the heads of laboratories). We will optimize the evaluation in collaboration with the IAB-IPHYS. Among other requirements, it will be essential that the postdoctoral fellows coming to IPHYS will gain experience from a long-term stay (at least 6 months) in a laboratory abroad, either before they come to IPHYS, or during their 5-year postdoctoral stay at IPHYS.

- We will continue to promote intramural seminars and conferences. Apart from a direct scientific benefit, those activities will improve the training of our PhD students and increase the visibility of the Institute.

- Allocation of a part of the institutional budget to individual scientific Laboratories will reflect the potential and quality of the teams and their research projects. This **internal IPHYS Economy System** will further promote the autonomy and responsibility of the team leaders.

- A part of the institutional budget will be allocated for:
  (i) Recruiting new postdoctoral fellows, based on the scientific merit of projects submitted by individual teams and the experience of the candidates from their long-term stays in laboratories abroad;
  (ii) ***Start-up Research Programme*** for junior scientists (junior group leaders); at least two such positions will be offered during 2021-2022;
  (iii) Financial rewards for excellent publications and also support for publications in high-quality journals, especially those offering the open-access only option.

- Ratification of national and international, ongoing and prospective collaboration with universities and clinical research centers. Importantly, in 2020, the ***MediAim consortium*** (http://www.mediaim.cz/en) was established. It comprises three distinguished Prague-based research institutes specialising in preclinical and clinical research: the Institute for Clinical and Experimental Medicine (**IKEM**), the Institute of Organic Chemistry and Biochemistry (**IOCB**), and **IPHYS**. The project is dedicated to the development of new therapeutic agents and strategies to fight certain serious noncommunicable diseases and selected viral diseases. The collaboration focuses on experimental, preclinical, translational, and clinical research of the nervous and cardiovascular systems with selected aspects of metabolic research. The primary objectives are (i) the characterisation of common mechanisms of pathogenesis associated with the occurrence of selected noncommunicable diseases, (ii) the improvement of strategies to prevent, diagnose, and treat these diseases, and (iii) the treatment of selected viral diseases. The MediAim project responds to the need for a stronger link between experimental and clinical research in the Czech Republic. It undertakes to bridge the gap between basic and translational medical research by facilitating and bolstering unique multidisciplinary collaboration. The project's special added value lies in its embrace of full drug development, from initial synthesis to patented drug candidates. The involvement of IPHYS in the MediAim consortium represents a major opportunity for the future.

Contingency plan

We expect that due to the present coronavirus pandemic the support of science will decrease at both national and international level; see also the section: *Strengths and weaknesses of the Institute.* If this happens, the overall budget of IPHYS could be seriously affected. In order to cope with such a situation, and to preserve the IPHYS performance in the future, the following measures will be needed:

- To maintain sufficient institutional support for services that are essential for IPHYS "*basa*l" performance (i.e. the HR and IT Departments, and the Animal facility), while other services will be supported less – depending mainly on the fees paid by the customers.

- Regarding the scientific Laboratories, some of them might be closed or re-organised, reflecting the *ad hoc* evaluation performed in collaboration among the director, Council of IPHYS, and IAB-IPHYS.

- It may be necessary to merge some of the "smaller" scientific Laboratories to secure their efficient performance, while the "larger" Laboratories may continue with a reduced number of employees. In such a situation, the internal IPHYS Economy System will serve as the lead.

The above measures reflect in part the vision of Dr. J. Kopecky, who was re-appointed as the IPHYS Director for the second 5-year period (with the effect from 1st July 2020).

Research for practice

Identification of research results with application potential

In order to protect intellectual property, IPHYS has an internal directive called "*The Internal Directive regulating the rules for handling the results of research and development and the method of their registration and protection*". (SME FGU 2018/001 effective from March 1, 2018). This Internal Directive regulates legal relations concerning the records and protection of objects protected under the Czech Copyright Act, the Patent Act, and the Act on Utility Models.

The Specialist in Intellectual Property under the Director's Office coordinates protection and records of objects of industrial rights. This position (FTE 1.0) was created on January 1, 2018, and is funded by the HR Award project supported by the Czech Ministry of Education, Youth and Sport. Since January 1, 2020, activities related to the administration of industrial rights have been supported by the Technology Scout (FTE 0.2) funded by the HR Award II project. The Institute's Library maintains administration of employees' scientific publications, which are registered in a database called RIV. This database also includes data concerning granted patents and registered utility models. Responsible IPHYS employees regularly follow updates on the protection of intellectual property and attend training courses, e.g. courses organised by the CAS (CeTTAV), ASTP Proton, and the Industrial Property Office. The Director's Order effective from 1st February 2019 sets the rules on the remuneration of inventors (employee invention 10,000 CZK). The subsequent remuneration is calculated according to the formula included in the Internal Directive.

Table of valid patents/patent portfolios/patent applications, valid utility models, signed licenses, and license fees

patents/patent portfolios/patent applications	14
Utility models	4
Signed licenses	1
License fees received	377,968 CZK

List of patent applications, valid patents/patent portfolios:

- Dental adapter to fibre spectrometer probe (CZ305825, filing year 2009)
- Process for preparing controlled layers of fibrin on solid surfaces (CZ299687, filing year 2006)
- Joint implant and the process for producing thereof (CZ304445, filing year 2012)
- Liposomal, gel-like phthalocyanine composition for photodynamic therapy of tumour diseases and the process for preparing thereof (CZ298978, NO20091595, CA2665762, EP2101732, filing year 2006)

- A liposomal dosage form with light-converting nanoparticles, its preparation and use (CZ307580, PCT/IB2018/057981, filing year 2017)
- Long-acting stable peptide analogues of ghrelin for the treatment of cachexia (PV 2014-429, filing year 2014)
- Amphiphilic compounds with neuroprotective properties (CZ305733, JP6437636, EP3260462, EP3260462, filing year 2014)
- Antimicrobial peptides and their use in the treatment of topical infections (CZ307755, US10160785, EP3280722, filing year 2015)
- Pregnanolone derivatives substituted in position 3 alpha, the process for their preparation and use (CZ 303037, EP2435963, US8575376, filing year 2009)
- Pregnanolone derivatives substituted in position 3alpha with the cationic group, the process of their preparation, their use and composition containing them (CZ 303443, EP2675821, filing year 2011)
- Lipidated peptides lowering the blood glucose level (EP3094643, AU2015207776, CA2935036, JP6342016, US10350271, filing year 2015)
- Targeted influence of the consequence of N-methyl-D-aspartate receptor mutation (PV 2017-757, filing year 2017)
- Neuroactive steroids for the treatment of epilepsy and seizure disorders(PV 2019-216, filing year 2019)
- N-(furan-2-ylmethyl)-7H-purin-6-amin for circadian rhythms modulation, increasing sleep quality, and increasing efficacy and safety of therapy (PV 2019-757, filing year 2019)

Signed license agreements
One license agreement relating to the patent portfolio “Lipidated peptides lowering blood glucose” was signed in 2017 with the company Novo-Nordisk. IPHYS has received license fees of 377,968 CZK so far.

Strategy AV21

IPHYS actively participates in Strategy AV21 (http://www.avcr.cz/en/strategy/research-programmes/programmes-of-strategy-av21/index.html) of the CAS since its formation in 2013/14. IPHYS administers two programmes of Strategy AV21 covering the large field of biomedicine. Our vision is to improve the quality of life by direct scientific discoveries, connecting scientific teams to form aim-oriented multidisciplinary consortia, and direct interaction of scientists with clinical doctors and their patients. We aim to explore current public health needs and find opportunities for new treatments and strategies in improving the quality of life. We have also funded an important facility for preclinical testing of biomolecules possessing the pharmacological potential to facilitate the transfer of important discoveries into the pharma market and thus close to sufferers.

The programme “**QUALITAS - Wellbeing in Health and Disease”** (https://www.fgu.cas.cz/en/research/416-centres-of-excellence-strategy-av-21) was formulated as one of the first research programmes during the formation of Strategy AV21 in 2013/14 and started in 2014. Dr. J. Otáhal, a coordinator of the programme, currently manages thirteen multidisciplinary research teams connecting eight institutes of the CAS with universities and hospitals to cover a broad spectrum of biomedical research topics. The activities of QUALITAS are rather diverse and extend from public awareness and education to high-impact basic research. Prof. P. Jiruska and Dr. Otáhal, IPHYS representatives in the QUALITAS neuroscience branch, participate in Continuing Medical Education of clinical doctors, namely neurologists specialised in epileptology and clinical neurophysiology. They also raise public awareness by giving lectures on epilepsy and neuroscience to the lay public at scientific festivals, the Brain Awareness Week, science cafés, charities, broadcasts and on

television. QUALITAS initiated active collaboration with Czech Teaching Hospitals and health care institutes, which can be documented by signed agreements between the CAS and the Teaching Hospital Kralovske Vinohrady and the Homolka Hospital.

One of the most important activities was the funding of the **Epilepsy** Research Centre of Prague (EpiReC), which connects experts from IPHYS, Charles University, Czech Technical University, and the Teaching Hospital Motol. EpiReC represents a unique platform in the Czech Republic that specialises in epilepsy and combines research with clinical practice, has a strong internationally recognized research team, identifies new global directions in the research and treatment of epilepsy, and uses its outputs in the clinical care of patients with epilepsy, which improve the care but also makes it more efficient. Besides epilepsy, an IPHYS member of QUALITAS, Dr.Balaštík, initiated a fruitful collaboration with paediatric psychiatrists (University Hospital Motol) on **Autism** related research, studying the role of maternal antibodies.

Another activity of QUALITAS is an intensive collaboration with the Institute of Sociology, CAS (Dr. Hamplová), with the aim to perform a **large sociological and health screening of the Czech population**. During the last 5 years, a large important sample of the population was tested, and biological material (blood) was obtained, analysed, and stored. The findings on mitochondrial haplotypes and the omega index (Dr. Mráček) represent a unique dataset on the Czech population and its development after 1989. This unique dataset is now being used as the control sample in the population screening during the **COVID-19** pandemic. In a close cooperation with this project, Dr. Sládek (IPHYS) conducts a large study on **sleep behaviour** and circadian rhythms in the population and their health consequences.

The programme **Preclinical Testing of Potential Pharmaceuticals** (https://www.fgu.cas.cz/en/research/416-centres-of-excellence-strategy-av-21) coordinated by Dr. Kopecký (IPHYS) brings into the scientific community a highly requested facility for effective and comprehensive testing of new promising pharmaceuticals. The preclinical testing of potential pharmaceuticals on animals under OECD GLP conditions (GLP-**Good Laboratory Practice**) is a key element of new pharmaceutical development. The successful completion of preclinical studies is an essential prerequisite for starting clinical trials on humans. The programme integrates excellent research teams from 4 institutes of the CAS. Important and successful preclinical tests have been performed on molecules developed by collaborators from the CAS. This increased their chance to become attractive molecules for further application and transition into clinical trials, which might lead to more effective commercialisation (MitoTax, MitoTam, MitoSen, and MitoDFO).

Cooperation with regions of the Czech Republic

IPHYS collaborates with a variety of public institutions and commercial subjects within regions of the Czech Republic. Besides the important role of our employees in review processes of scientific projects (Czech Science Foundation, Czech Health Research Council, Technology Agency, and the Ministry of Youth, Education and Sports), we intensively collaborate and participate within tertiary education. IPHYS provides experts for evaluation of accreditations of university degree programmes and for the teaching of both graduate and postgraduate students. IPHYS participates in Continuing Medical Education of clinical doctors, especially in the field of neurology, pediatric neurology, and cardiology. In addition to previously mentioned fields, it is worth mentioning an activity of our experts in scientific boards of many scientific institutes and universities/faculties in the region. Finally, we provide support to the government and its authorities. Within the last 5 years, our experts were members of several advisory boards in the field of life sciences, biotechnology, bioengineering, pharmacology, and medicine. We also substantially contribute to raising public awareness by giving lectures on several biomedicine topics to the lay public at

scientific festivals, the Brain Awareness Week, science cafés, charities, broadcasts, and on television.

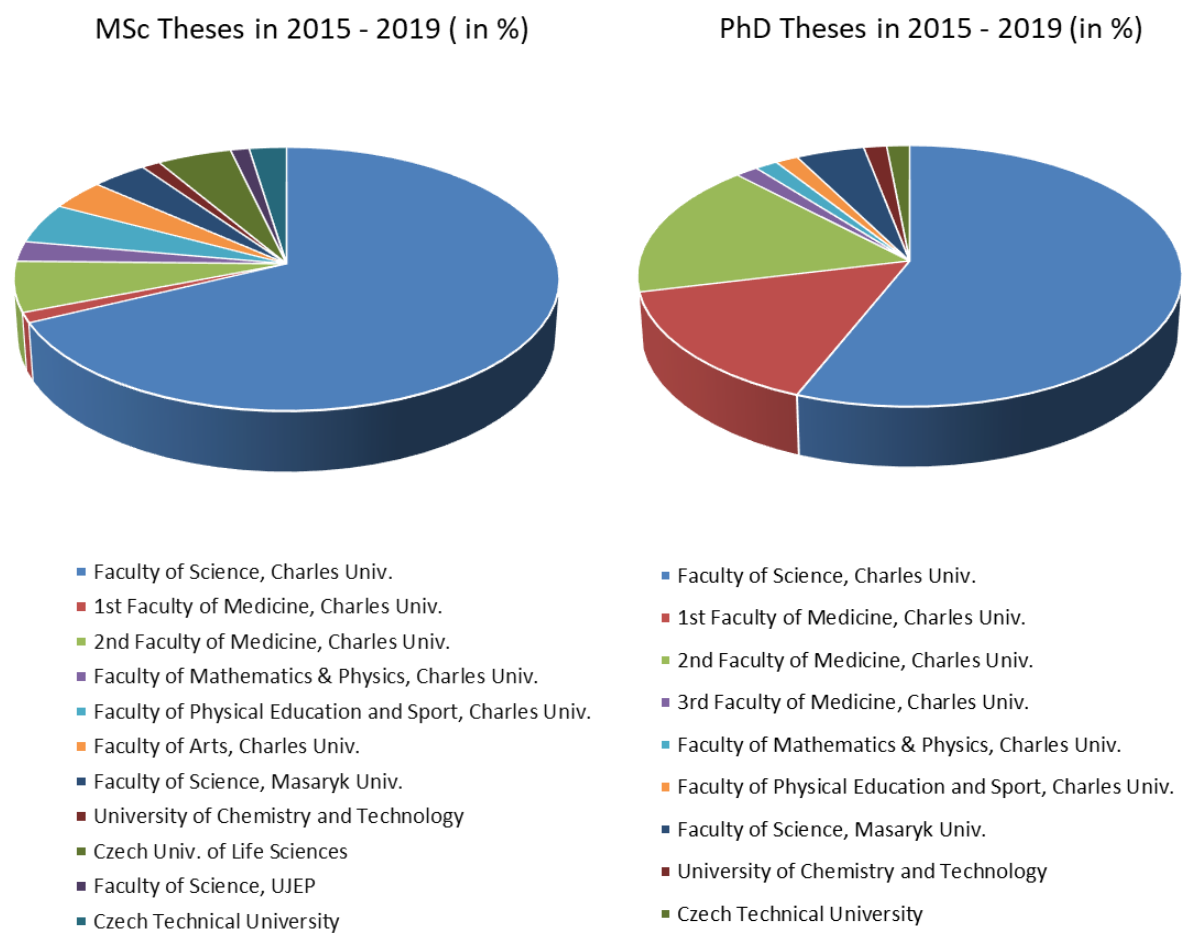
Cooperation with universities

Overview of semester lectures, seminars, and courses

Name of the university	Number of semester lectures, seminars, and courses 2015-2019		
	Bachelor	Master	Doctoral
Charles University in Prague	59	136	25
Czech Technical University in Prague	0	10	0
University of Chemistry and Technology in Prague	4	5	0
J.E. Purkinje University in Ústí nad Labem	19	6	0
University of Pardubice	0	5	5
Masaryk University in Brno	0	10	0
South Bohemian University in České Budějovice	0	5	0
Palestra in Prague	6	0	0

Supervision of students

Type of study	No. of supervisors	No. of consultants	Theses defended 2015-2019
Bachelor	44	11	76
Master	56	16	89
Doctoral	51	18	65



Joint research centres with universities

Although IPHYS is a non-university research institute, it is involved not only in extensive teaching activities but also in research cooperation with numerous universities. To promote cooperation between the CAS and universities, IPHYS participates in 6 research centres, which brought together not only strategic partners but also strengthened research training for students, as they had research supervision from experienced tutors from both institutions. These centres facilitated the establishment of excellent infrastructure and collaboration among the intra- and extra-institutional teams and strengthened research impact and visibility of IPHYS.

- **Centre of Excellence in Biomedicine and Biotechnology (BIOCEV)** is a joint project of six institutes of the CAS including **IPHYS** and **Charles University,** Prague, which started its scientific activities in 2015. IPHYS participates in three research projects, namely *Cellular biology*, *Structural biology and protein engineering,* and *Biomaterials and tissue engineering.*
- **Centre of Mitochondrial Biology and Pathology (MITOCENTRE)**, 2014-2018, a research centre of excellence and a joint project of **IPHYS**, Teaching Hospital in Prague, and **Charles University,** Prague. Funding provider: Czech Science Foundation. The scientific programme of the Centre was to identify and characterise new components and mechanism of mammalian mitochondria with respect to their biological role and possible causal involvement in human diseases.
- **Research Centre "Project of Excellence in Neuroscience" (PEN)**, 2012-2018, a research centre of excellence and a joint project of **IPHYS**; the Institute of Experimental

Medicine, CAS; **Charles University,** Prague; and Teaching Hospital in Prague. Funding provider: Czech Science Foundation. The scientific programme of the Centre was focused on pathophysiological mechanisms underlying the development of neurodegenerative disorders, which are common not only in the ageing population, but also in young adults, and represent a serious socio-economic problem.

- **Centre for Development of Original Drugs**, 2012-2019, a centre of competence and a joint project of the Institute of Organic Chemistry and Biochemistry, CAS; **IPHYS**; the Institute of Experimental Medicine, CAS; **Palacky University,** Olomouc; **University of Chemistry and Technology,** Prague; and several affiliated companies. Funding provider: the Technology Agency of the Czech Republic. The goal of the Centre was to develop new potential drug candidates and enable their transfer into commercial practice.
- **Research Centre "Preparation, Modification and Characterisation of Materials by Radiation",** 2012-2019, a research centre of excellence and a joint project of the Institute of Physics, CAS; **IPHYS;** the Institute of Nuclear Physics, CAS; and the **University of Chemistry and Technology, Prague.** Funding provider: Czech Science Foundation. The programme of the Centre covered preparation of novel micro- and nano-structured materials and systems, their modification by radiation and other techniques, and the study of their chemical, physico-chemical and bio-properties.
- **Centre of Personalized Medicine – Diagnostics and Therapy (PerMedT)**, since 2019, a centre of competence and a joint project of the Institute of Organic Chemistry and Biochemistry, CAS; **IPHYS**; Teaching hospitals in Prague and Brno; **Masaryk Univer**sity, Brno; **Charles University,** Prague; **Palacky University,** Olomouc; **Technical University,** Ostrava; and **University of Chemistry and Technology, Prague;** and affiliated companies**.** Funding provider: the Technology Agency of the Czech Republic. The Centre is focused on applied research in diagnostics and therapy of rare and genetically determined diseases with the aim to develop personalised diagnostic methods and drug candidates/drugs, which would help specific groups of patients.

Research services

1. Research services: library, databases, collections, and others

Library - Centre of Scientific Information

The Centre of Scientific Information of the Institute of Physiology (hereinafter referred to as "the Library") is the **information base** not only of the Institute of Physiology but also of other CAS institutes located on Krč campus: the Institute of Microbiology, the Institute of Molecular Genetics, and the Institute of Experimental Medicine. At the same time, the Library is a **public library** registered in the Register of Public Libraries (under the reg. no.: 3117/2002) and provides specialised services to external users from the general public.

The library collection, systematically built up for almost 50 years, consists of about **80,000 specialised monographs and bound volumes of journals** mostly from the area of biomedicine and related branches. Through its collections, the Library belongs among the largest libraries of the CAS. During the last 15 years, the Library has fully refocused on services using **modern information technologies;** it continues to belong, in terms of its services and offer of information sources, among leading libraries of the CAS, and it is appreciated very positively among other Czech libraries of a similar branch focus.

The Library is divided into its **public** and **non-public** parts. Library visitors can use **a reading room with a reference library,** and a **computer reading room** with necessary technical equipment (printers and copiers). The non-public part includes offices and storage areas. Personal communication with visitors occurs in the area of the information and lending counter. The Library is stabilised in terms of its personnel, and the level of experience and knowledge of all the five staff members is high. The **area of services** of the

Library is relatively wide: in addition to library-information services and administration of catalogues of printed and electronic sources, the Library also processes publishing activities of IPHYS employees and creates outputs from these data for assessment of scientific work and for other purposes. Recently, the Library has actively contributed to the **CAS repository of publications**.

The Library operates its own **web site,** which serves as an intermediary for access to e-sources (http://www.biomed.cas.cz/fgu/knihovna/svi_fgu_eng.html) and includes extensive information associated with e-sources, assessment of science, and necessary instructions. The number of the web site visitors is large (approx. 50,000 visits per year); the Library is used not only by scientific experts and students from the Krč campus institutes but also by the general and professional public.

Within the framework of the Czech Republic, the Library actively participates in the creation of comprehensive **catalogues and portals**. It ensures an extensive **inter-library service** and cooperates with libraries with a similar focus, e.g. in the field of acquisitions.

Since 2000, the Library has been a participant in consortia aimed at purchase of important and financially demanding electronic sources. In 2017, support for the financing of selected electronic information sources changed in the Czech Republic. CzechELib – the National Centre for Electronic Information Resources - was established. The Library is a member of this centre, which allows to draw up to 50% of subsidy for selected resources.

The financial subsidies obtained have helped to create and stabilise an extensive **offer of e-sources, which are available to all employees** of the institutes situated within the **Krč campus**, both in their workplace and remotely. Those interested from other institutions can obtain information from the sources (e.g. articles) through inter-library services, or they are external users of the Library. The use of paid sources is at a high level – e.g. the **number of downloaded articles** oscillates around **170,000 per year**. The detailed monitoring of usage is an important background for effective purchases of e-sources.

Overview of available e-sources:

- Bibliography, citation and combined databases – Web of Science, Scopus, EBSCO, Proquest
- Collection of full-text journals - Elsevier, Springer, Wiley, Nature Publishing Group, Cell Press, American Association for Cancer Research, American Physiological Society, American Society for Microbiology
- Individual full-text journals of various publishers

The Library will endeavour to **further improve** its services. It will be necessary to continue in ongoing monitoring of new trends in the field of **information and information technologies** so that the Library can provide its users with new information in a timely and comprehensive manner. The Library staff will continue to provide important **assistance services,** e.g. during the search and acquisition of information, in citation issues, and other areas of information support of scientific work. The aim is to save the time of scientists for their scientific work and to help create good conditions for high-quality research. In the academic library environment, it is very important to ensure not only **electronic ("virtual") communication**, but also **personal consultations** with individual scientists and students. This requires at least basic knowledge of their work and topics studied, and the knowledge of their information needs. The Library will continue to build relationships with its users and develop the knowledge of its staff.

2. IT Department

The IT Department of IPHYS serves to the whole Krč campus and provides the following technical support:

- Administration of the network (LAN) (domain: biomed.cas.cz) with approx. 1,250 workstations (PC), mailboxes, and system users with group-based security access;
- Administration of servers providing basic infrastructure services (DNS, DHCP, mail, web, mail-antispam and mail-antivirus, campus firewall, and proxy server providing centralized access);
- Administration of network active units (switches, routers) and their renewal process; Planning infrastructure changes, backup ISP connectivity, and new buildings connections;
- Cooperation with local IT departments related to wide-local area network usage.
- Evaluation of the LAN performance and planning further development, taking into account the ever-increasing demands on the LAN performance.
- In cooperation with CESNET active searching for vulnerabilities and botnet.

The following technical support is provided selectively to **IPHYS**:

- Administration and maintenance of the local area network including maintenance and administration of infrastructure services (administration of switches, servers - DNS, DHCP, active directory domain, Exchange mail, web, Intranet, databases, remote access, and VPN)
- User helpdesk and service desk, analysis of users' needs, maintenance of workstations (about 600 PCs) including OS reinstallations, HW upgrades, SW installations and configurations, maintenance of printers, scanners, multifunction and additional devices, data backups, Wi-Fi AP installations, computer renewal process, reservation system, centralized data storage, laboratory network attached storages, workstations and advanced network equipment monitoring.

The IT department is a member of Mentat.

Administration of research infrastructures

Administration of research infrastructures

In the context of investment made with the financial support from the CAS, the Ministry of Education, Youth and Sport, and other national and international funding resources, IPHYS has managed to build high-quality research infrastructures, which are developed further to increase their availability and usability. The present wide range of research infrastructures, including both core facilities and equipment available at the individual laboratories, reflects long-term systematic efforts to build a complex, **cutting-edge research platform for phenotyping** of laboratory rodents **from the cell organelle level to the whole-body level**. Regarding its complexity and the focus on *in vivo* phenotyping of physiological features, the platform is unique and not available in any other biomedical institute in the country. The services of research infrastructures operated by IPHYS are offered to both internal and external users and subjected to a fee. Internal users (from within IPHYS), and to some extent also those affiliated with other CAS institutes enjoy preferential (competitive) rates. Depending on the infrastructure unit, users come mainly from the Institute itself; other users come from other institutes of the CAS, universities, and research institutes of the Ministry of Health. Some infrastructure units (*Animal Husbandry*, *Biological Controls*) have also

attracted private-sector users, while the *Radiometry* unit covers the entire Krč campus, as the sole facility of its kind.

The most important multi-user facilities are listed below:

1. Animal Facility

The Facility is located on the campus of biomedical institutes of the CAS in Krč and produces **outbred laboratory rats** (Wistar, Lewis; approx. 6,500 rats/year), **inbred laboratory rats** (SHR, WKY, and Dahl strains; approx. 400 rats/year), and **inbred mice strains** (Balb/c, C57BL/6; approx. 5,000 mice/year). The Facility also guarantees breeding and housing of **recombinant inbred and transgenic strains of rats and mice**. The Animal Facility serves as a primary quarter for laboratory rodents, which are supplied to internal (90 %) and external users (IKEM, Charles University). The users housing animals in the IPHYS Animal Facility are charged animal care fees based on a per diem rate that includes the cost of labour, food, bedding, and supplies. The Facility has an approved accreditation for the usage of laboratory animals and is **registered as a laboratory animal breeding and supplying facility** with the Central Commission for Protection of Animals of the Ministry of Agriculture. Animal husbandry and care are overseen by the *Institutional Animal Facility Board* and research utilizing vertebrate animals by the *Institutional Animal Care and Use Committee*.

The central building of the Animal Facility is now under an extensive reconstruction to meet the highest international standards of animal care and welfare. The reconstruction includes the renewal of technological equipment, which will improve the care of laboratory animals and animal health conditions. After the reconstruction, the Facility will offer a large number of new possibilities of phenotyping and animal housing in long-term experiments for all scientific laboratories of our Institute. Due to the planned reconstruction of the Animal Facility, the production of rats was decreased in 2019, the mouse breeding facility was closed at the end of 2018, and the mouse breeding colony was transferred to the Institute of Microbiology, CAS.

2. Biological Controls Unit

The Biological Controls Unit is a facility that provides **comprehensive pharmaceutical services** for academic and non-academic entities in the field of toxicological and pharmacokinetic studies based on laboratory animals (rat, mouse, rabbit). The unit is also engaged in quality control of manufacturing operations of medicinal products for human use, pharmacopoeial tests, testing of vaccines and allergens, and testing of substances that have successfully passed through basic research. The unit is a certified GLP laboratory holding the **Certificate of Good Laboratory Practice** issued by the State Institute for Drug Control and the **Authorization for Work with Animals** issued by the Central Commission for Animal Protection of the Ministry of Agriculture. The unit is situated in a newly-constructed building on Krč campus.

3. Service Laboratory of Metabolomics

The laboratory provides fee-based services for liquid chromatography–mass spectrometry-based (LC–MS) metabolomic and lipidomic analysis of biological materials such as plasma/serum, tissues (e.g. liver, heart, lungs, muscle, and adipose tissue), and cells. Specifically, complex analytical workflows are available for (i) combined **untargeted and targeted analysis of complex lipids**, polar metabolites, and exposome compounds; (ii)

targeted analysis of specific low-abundant lipid mediators (eicosanoids, endocannabinoids, fatty acid esters of hydroxy fatty acids), and steroids; (iii) **targeted analysis of metabolites labelled with stable isotopes (fluxomics)**, and (iv) targeted **analysis of pharmaceutical compounds** for ADME studies. The capacity of the laboratory is 4,000 samples per year. Overall, 75% of samples are submitted from different laboratories of IPHYS. Around 10% of samples are analysed for other CAS institutes (Institute of Biotechnology, Institute of Molecular Genetics), and the remaining 15% samples for other clients (Institute of Clinical and Experimental Medicine, Prague; Teaching Hospital, Prague; Charles University, Prague).
The available equipment:

- A high-resolution mass spectrometer (Thermo Q Exactive Plus) coupled with a liquid chromatograph (Thermo Vanquish)
- A quadrupole/linear ion trap mass spectrometer (SCIEX QTRAP 5500) coupled with a liquid chromatograph (Dionex/Thermo Ultimate 3000 RSLC)

Both, the *Biological Control Unit* and the *Service Laboratory of Metabolomics* are engaged in the **Centre for Preclinical Testing**, **CPT** (http://www.prekliniky.cz/en/). The primary mission of the CPT at IPHYS is to perform preclinical testing of substances that have successfully passed through basic research and to contribute towards the development of new pharmaceuticals to combat life-threatening diseases, including those currently difficult to cure. The CPT serves as a tool for the implementation of research programme *Preclinical Testing of Potential Pharmaceuticals*, which is an important part of Strategy CAS 21.

4. BioImaging Facility

The Czech-BioImaging is a national research infrastructure for biological and medical imaging that enables open access to cutting-edge imaging technologies and expertise in imaging to scientists. The IPHYS BioImaging Facility provides fee-based access to numerous types of **confocal microscopes**, with special emphasis on multiphoton microscopic techniques. Further, **optical projection tomography scanners** and a **µCT/PET scanner** enabling imaging of a whole mice and rat (run by the Radiometry Unit) are available. The Facility covers expertise in image acquisition and in image analysis, including the development of new methods and SW modules (in ImageJ, Amira, and Ellipse SW environment) in the field of image processing and analysis, stereology, and spatial statistics.

The available technologies are:

- Laser Scanning Confocal Microscopy (LSM / CLSM)
- Spinning Disc Confocal Microscopy (SDCM)
- Multiphoton Microscopy Systems
- Fluorescence-Lifetime Imaging Microscopy (FLIM)
- Fluorescence Resonance Energy Transfer (FRET)
- Fluorescence Recovery After Photobleaching (FRAP)
- Non-Linear Microscopy Techniques (e.g. CARS, SHG, THG, SRS)
- Optic-fiber Confocal Fluorescence Microscopy
- Optical Projection Tomography (OPT)
- µPET / CT

During the last 5 years, the Facility was exploited by users from IPHYS (83%), other Czech institutions (15%), and institutions from abroad (2%). The facility serves users from the institutes of the CAS (e.g. Institute of Organic Chemistry and Biochemistry, Institute of Microbiology, Institute for Experimental Medicine, Institute of Experimental Botany, and Institute of Molecular Genetics), universities (Charles University, Masaryk University in Brno), and from other institutions (e.g. Institute of Clinical and Experimental Medicine). The facility also participates in **EuroBioImaging ERIC (European Research Infrastructure Consortium)**. In 2016, the facility was involved in COST Action NEUBIAS, focused on building a network of specialists for image analysis of biological objects in Europe and other parts of the world.

5. Radiometry Unit

The unit provides radiometric measurements, orders radioactive substances, conducts dosimetry and radioactive waste management, and supervises radiation safety rules within IPHYS. The unit manages a special animal facility for laboratory animals treated with radionuclides and a radioisotopic laboratory (of grade II) certified for safe handling of unsealed sources of ionizing radiation in higher activities. The unit also runs μCT/PET setup for computerised tomography (CT) and positron emission tomography (PET), which provides imaging of a whole mice and rat with a high resolution. In addition, the unit provides radioactivity measurements and consultations about safe radioactive handling in compliance with the Czech Atomic Law and other legal regulations for other Institutes of the CAS on campus. Radioactivity measurement, storage, and disposal of radioactive waste, handling of animals treated with radionuclides, and the usage of the radioisotopic laboratory are paid services.

6. Proteomic Facility

The Proteomic Core Facility of IPHYS, originally run by the *Department of Analysis of Biologically Important Compounds* (now the *Laboratory of Translational Metabolism*), offered 2D IEF/PAGE electrophoresis and proteome analysis and quantification using a Q-TOF type tandem mass spectrometer MaXis (acquired in 2009) for all laboratories of IPHYS. However, in the last few years, the capacity of the facility and the standard of analysis was not sufficient for the increasing demand for proteomic analyses. Therefore, a new **Joint Laboratory of Proteomics of IPHYS and IMG (Institute of Molecular Genetics, CAS)** was established in 2019 to meet the demands for detailed, untargeted and targeted identification and quantification of proteins in biological samples, identification of protein post-translational modifications, and immunoaffinity experiments. The Laboratory is equipped with necessary instrumentation, above all with the **state-of-the-art HRAM (high resolution, accurate mass) mass spectrometer** coupled with a liquid chromatograph. The project of the Joint Laboratory was supported by the CAS, and the MC/LC setup is to be delivered after a public tender in 2020. Service laboratory personnel, including an LC-MS operator and the operational costs, will be covered by both institutes.

7. Molecular Biology Facility

The Molecular Biology Facility of IPHYS is opened to all users of the Institute free of charge for all apparatuses and other equipment. The facility is based on a **self-service operation of all instruments** after initial training of users by the supervisor. The Facility is equipped with instruments for assessment of quality and quantity of samples, quantitative RT-PCR, and imaging and analysing of the gels:

- Precellys homogeniser with Cryolys cooling system Bertin
- Capillary electrophoresis RNA Agilent Bioanalyser
- Nanodrop spectrophotometer
- Real-time PCR cycler LC480
- Real-time PCR cycler LC96
- Gradient PCR cyclers Eppendorf
- Real-time PCR cycler ViiA 7
- Laser capture microdissection system Leica for isolation of specific single cells or small areas of tissue
- Western blot and gel imaging system Bio-Rad ChemiDoc
- Plate Readers

Outreach activities

1. Research popularisation

During the evaluation period, we stepped up our efforts to increase the awareness of the endeavours of IPHYS not only among the research community but also among the general public. To improve general recognition of IPHYS and all the activities, a **new responsive design of the IPHYS public web page** was created and implemented in 2019 (c.f. http://www.fgu.cas.cz/), where all activities of IPHYS, seminars, and general information are clearly presented. Regularly, newly achieved results are announced via press releases, via interviews with journalists in broadcast media (**Table 1**), and via social media

Table 1. Media coverage of IPHYS in 2015-2019

Type of release	2015	2016	2017	2018	2019	Total
TV and radio	24	20	17	56	30	**147**
Press	38	26	38	53	60	**215**
Internet	26	8	9	108	134	**285**
Total	**88**	**54**	**64**	**217**	**224**	**647**

(https://www.facebook.com/FyziologickyUstavAVCR). **The total number of media coverage increased to 647 releases** in comparison with the last evaluation period (257 activities).

Every year, IPHYS organises a number of regular and irregular events for both the professional public and the general public. Altogether, more than **160 IPHYS employees took part in popular science activities every year**. Outstanding popularisation activities of **three IPHYS scientists received awards of** the President of the CAS (The Award of the President of the CAS for promotion or popularisation of research, experimental development, and innovation: 2015 – Prof. H. Illnerová, 2018 – Prof. F. Vyskočil; The The Vojtěch Náprstek Honorary Medal for Merit in Science Popularisation: 2019 – Assoc. Prof.. A. Sumová).

Table 2 Lectures for professional public in 2015-2019

Type (speakers)	No.
Bureš's	8
International	28
National external	45
IPHYS	67
Methodological	8
Others	5
Total	**161**

2. Activities for the professional public

In 2015, the regular Monday's seminars were initiated at IPHYS. These **publicly accessible lectures** are given by either scientists from IPHYS or by invited scientists from

fields related to IPHYS's scope of research. Invited speakers come from other national research institutions or universities or from abroad. Table 2 shows the number of lectures in the evaluated period.

In 2018, we implemented a new series of **Methodological seminars** for all scientists and students within the Krč campus and the BIOCEV with the aim to share knowledge and methods used in individual institutions and to initiate more collaborative environment.

We also continued in **Bureš's lectures** (the series of lectures initiated in 2013 in honour of Dr. Jan Bureš (1926-2012), an outstanding IPHYS neuroscientist). The lectures are delivered by first-class invited scientists (http://www.fgu.cas.cz/en/about/433-bures-lecture-series).

3. Regular activities for the general public

IPHYS research results were regularly presented at various science festivals organised by the CAS every year. In addition, the physiology of the human body and IPHYS research topics were presented within several successful popular-science interactive programmes:

- During **the Brain Awareness Week** – a unique cycle of lectures on the newest discoveries and trends in brain research and neuroscience, which is a part of the worldwide Brain Awareness Week. In total, ten lectures of IPHYS neuroscientists were provided. Also, an interactive whole-day workshop **Memory Park** with eleven unique physiological tests of memory and orientation skills, some of them developed at IPHYS (Laboratory of Neurophysiology of Memory), were realized every year.
- Since 2015, we have presented our results at the annual **Science Expo**, a large festival of the whole CAS (30,000 of visitors in 2019). The new exhibition of IPHYS entitled **"Research of diseases from a molecule to the whole body"** covering most of the IPHYS's research was created in 2018.
- **The Open House Day** – the laboratories of IPHYS are open to the public during **the Week of Science and Technology** of the CAS (each November). Two half-day series of excursions targeted mainly at high-school students usually comprise of at least **16 presentations of individual IPHYS's Laboratories** and **two interactive exhibitions: Memory Park** and **Purkinje Chamber of Physiology** (interactive activities showing different physiological tests). Each year around 200 attendees visit IPHYS (full capacity).
- Since 2015, we have implemented regular joint presentations (twice a year) of IPHYS's researchers and clinicians called **The Human Body in Health and Disease** with the aim to present the collaboration among experts from basic research and from clinics for the development of novel diagnostic and therapeutical procedures to the general public (10 seminars were organized, each was dedicated to a particular disease studied at IPHYS, more at https://www.fgu.cas.cz/en/about/571-lidske-telo-ve-zdravi-i-nemoci).
- Each year, IPHYS researchers participate in the CAS activity **Open Science** as supervisors in research projects for high-school students (12 projects, 12 supervisors within 2017-2019). In 2019, two students from IPHYS achieved 1st and 3rd place awards at the final Conference of Open-Science Students (supervisors Dr. O. Zimmermannová and Dr. J. Musílková).
- Since 2016, **Epi(c)Run** – we annually participate in the organisation of a charitable run to support people suffering from epilepsy (ca. 400 participants).
- Since 2019, **Mitochondrial Diseases Awareness Week** – a new interactive workshop has been implemented with the aim to spread knowledge about mitochondrial diseases (Laboratory of Bioenergetics, 2019; 30 participants).

4. Irregular activities for the general public

- 2015 – a one-month exhibition of IPHYS research in the "Academia" book store of the CAS.

- 2015 – a press conference dedicated to the **1st International Day of Epilepsy** (Assoc. Prof. J. Otáhal, Prof. P. Jiruška; in collaboration with the organisation Epistop and the Czech League against Epilepsy; 47 releases in media); 2016 – **AFO Olomouc** – a film festival, a special **section dedicated to epilepsy** was realised (Prof. P. Jiruška, Assoc. Prof. J. Otáhal, Assoc. Prof. H. Kubová).
- In 2017, a half-day **educational excursion** of a class of 10-year old pupils from the neighbouring school was organised (Laboratory of Membrane Transport, 30 participants) and a **Discussion Evening about Epilepsy** (Prof. P. Jiruška, Assoc. Prof. J. Otáhal, 150 participants).
- A seminar for the general public **"Autism: a current view of causation and therapy"** (Dr. M. Balaštík, 80 participants).
- Three **panel discussions/workshops** dedicated to human health and diseases were organised with experts from IPHYS: 2017 – *Obesity and related diseases* (Dr. J. Kopecký, Prof. H. Illnerová, Dr. J. Kuneš); 2018 - *Therapy in 21st century* (Assoc. Prof. J. Otáhal, Dr. T. Mráček, Dr. J. Prchal; 2019 – *Scrapping of Daylight Saving Ti*me (Assoc. Prof. A. Sumová, Prof. H. Illnerová).
- During the evaluation period, scientists of IPHYS participated in a high number of Czech **TV and radio broadcasts,** and numerous **articles were published in popular-science magazines** (see Table 1).
- In addition to lectures shown in Table 2, **sixty-eight lectures about IPHYS research for the general public** were realised within 2015-2019.
- **Ten press releases** informing (in Czech) about Institute's achievements were released during the evaluation period (c.f. http://www.fgu.cas.cz/news/pro-media).
- IPHYS continues to support the **"SOČ" project for talented high school students** (11 students 2015-2019; prizes awarded in the Medicine category are under the auspices of IPHYS); 2015 – participants of the final national conference visited IPHYS for a half-day excursion; 2018 and 2019 – students with projects from IPHYS achieved medal places in the project competition at regional and national levels.

Publishing activity concerning scientific books and periodicals

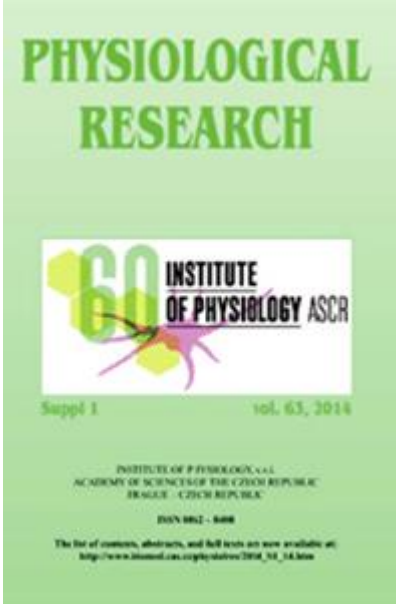
Physiological Research: the Institute's academic forum
http://www.biomed.cas.cz/physiolres/, indexed in Medline and Web of Science.

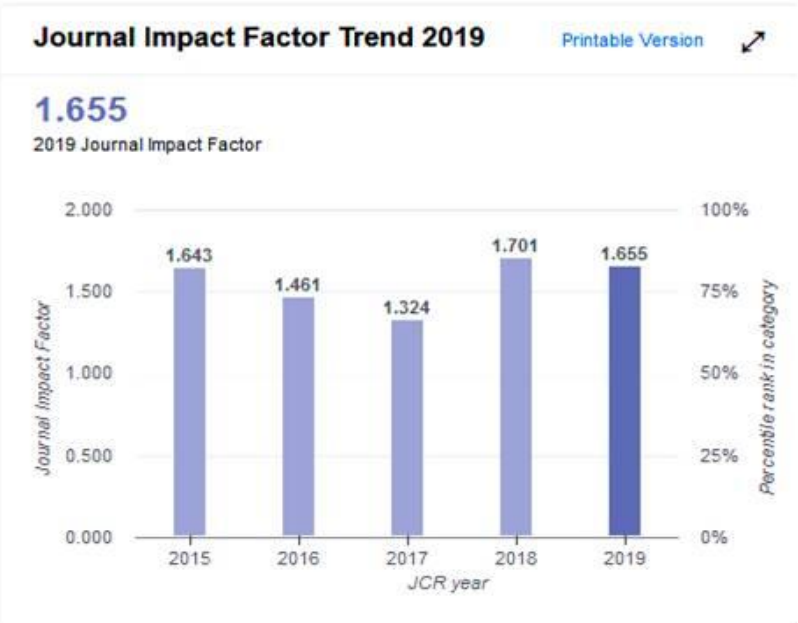
The IPHYS has been publishing its international scientific journal ***Physiologia bohemoslovaca*** since 1952. In 1991, it was transformed into ***Physiological Research*** with Dr. J. Kuneš as the Editor-in-Chief and Dr. J. Zicha as the Managing Scientific Editor; both of them are actively engaged in cardiovascular research.

This journal covers **normal and pathological physiology, biochemistry, biophysics and pharmacology**. Both original papers and reviews are accepted. Typically, 160 to 180 articles are published every year, and 50% of them are contributed by foreign authors from all continents. Its **Impact Factor** (IF) has maintained a stable value of about 1.50 in the last five years (ISI Web of Knowledge database). In 2019, we expect 1.7 for 2-year IF and 1.9 for 5-year IF (based upon citations from WOS Web Core). Currently, *Physiological Research* is an **open-access journal** with a reasonable page charge attractive even for junior authors.

Besides **six regular issues**, several **supplements** (4-5 special issues), devoted to particular topics, prominent scientists, scientific conferences, and foreign scientific institutions are published every year. Some of the supplements surveyed the achievements of the Institute of Physiology (2004 and 2014) and the outcome of major programmes in which the Institute had participated (Neuroscience Centre 2008, Centre for Cardiovascular Research

2009 and 2012). In this context, the journal represents a regional forum that is nevertheless well established in the international scientific community.





Physiological Research Journal published by the Institute of Physiology

Organised conferences and workshops

As an academic institution, IPHYS facilitates the exchange of scientific information by organising major domestic and international workshops, meetings, and conferences or by co-organising these with other institutions. During the evaluated five-year period, more than 20 events were organised and hosted by IPHYS or IPHYS researchers participated in the organisation committees of other events. Among the international events, we can mention:

- 11th Conference on Mitochondrial Physiology, Pec pod Sněžkou 7-11/9/2015, Czech Republic; organised by the MiP Society, co-organised by IPHYS; 71 participants, 80 % from abroad
- DIABAT 4th Annual Meeting, Prague 27-29/9/2015, organised by IPHYS; 82 participants, 82 % from abroad
- Computional Neurosciences 2015, Prague 18—23/7/2015, organised by the Organisation for Computational Neurosciences, co-organised by IPHYS; 530 participants, 96 % from abroad
- ISBI – Special Session 3D Analysis and Stereology in Fluorescence Microscopy, Prague 15/4/2016, organised by IPHYS; 50 participants, 96 % from abroad
- 12th European Congress on Epilepsy, Prague 11-15/6/2016, organised by the International League against Epilepsy, co-organised by IPHYS; 2,850 participants, 96 % from abroad
- The 15th International Conference on Endothelin, Prague 4-7/10/2017, organised by the International Conference of Endothelin, co-organised by IPHYS; 105 participants, 92 % from abroad
- The bilateral seminar of the Nencki Institute of the Polish Academy of Sciences and the Institute of Physiology of the CAS, Prague 25/10/2017, organised by IPHYS; 30 participants, 33 % from abroad

- 28th Conference on Yeast Genetics and Molecular Biology, Prague 27/8-1/9/2017, organised by the Institute of Microbiology of the CAS, co-organised by IPHYS; 550 participants, 82 % from abroad
- 13th Meeting of the New Frontiers in Basic Cardiovascular Research, Prague 11-14/11/2018, organised by IPHYS; 91 participants, 47 % from abroad
- Optical Projection Tomography of Peripheral Nerves, Prague 13/4/2018, organised by IPHYS; 13 participants, 38 % from abroad
- Mitochondria apoptosis and cancer 2019, Vestec, Czech Republic, 17-20/9/2019, organised by the Institute of Biotechnology of the CAS, co-organised by IPHYS; 100 participants, 40 % from abroad

IPHYS has also organised national meetings attended predominantly by Czech nationals but also by foreign participants such as Czech Lipidomic Conferences (2016, 2019), Biomedical Signal Analysis and Processing for Diagnostics Workshops (2016, 2018, 2019), 11th Congress of the Czech Society for Neurosciences (2017, 2019), Bioenergetics Conference (2019), and 45th Conference of Experimental Cardiology of the Czech Physiological Society (2017). In addition, IPHYS has organised regular PhD Student Conferences to give students the opportunity to interact with younger and older colleagues through active participation (presentation of their results) and discussions. The Institute also supports IPHYS researchers to attend congresses, conferences, and workshops abroad.