List of Faculty Mentors
Ph. D. Program in Humanics
Doctoral talent cultivated in this program

The Ph.D. Program in Humanics cultivates leaders equipped with doctoral-level knowledge and skills in the fields of both biomedical sciences and physical sciences/engineering/informatics, together with the scientific expertise to achieve integration of these fields and the capacity to apply them in wider society. The program aims thereby to address challenges to human life and health and enable the sustainable prosperity of all humankind. The leaders fostered in this program are expected to become drivers of science and technology to surmount various challenges facing the world, including the onset of the super-aged society and the associated rise in medical costs and health insecurities, as well as increasing mental health problems. Resolution of these problems will require the capacity to combine the latest knowledge and technology from the field of biomedical science with cutting-edge knowledge and technology from different fields, employ the vocabulary of both fields to engage in dialogue between them, and apply deep insights into them in order to formulate new paradigms. Such paradigms can only be realized through outstanding bi-disciplinary expertise that integrates two different fields of research. Furthermore, it will be essential to seek out real-life applications for research findings on an ongoing basis, utilizing the specific capabilities of problem discovery (the capacity for conceptualization of research topics), breakthrough (the capacity to overcome difficulties sincerely and earnestly), and application (the capacity to communicate solutions to wider society and apply them in practice).
Through such initiatives as the Leading Graduate School Doctoral Program (PhD Program in Human Biology) and the World Premier International Research Center Initiative (WPI) (International Institute for Integrative Sleep Medicine), the University of Tsukuba has worked to develop interdisciplinary education and research in the field of biomedical sciences, and has achieved great progress therein. In the physical sciences/engineering/informatics field, the university has pioneered the field of cybernics, which incorporates insights from neuroscience, kinesiology, robotics, and other fields into cybernetics, leading to the development of revolutionary human assistive technologies such as the HAL robotic suit.

Building on these strengths, this new program defines “humanics” as a discipline that sheds light on the fundamental principles of the physiology and pathology of the “human” as an individual organism, generating new science and technology to achieve a healthy and comfortable life of human beings. Through the development of expertise and applied skills, the program will cultivate individuals capable of independently uncovering basic principles of human life, creating systems to reconstitute and assess the validity of discovered principles, and building new theories of life. The candidates of this program will pursue research, for example, on problems such as decline in cognitive function and sleep disorders in the super-aged society, adding to their previous learning in the field of medicine with studies in engineering and information science, employing fundamental neurological principles to develop artificial neural network devices connectable to the human brain, and using them to advance understanding and control of sensitivity, motivation, ideation, and other mental functions. Others who have previously studied materials chemistry in the engineering field may study medicine and develop molecular robots capable of intervening in cellular functions, enabling understanding and control of the molecular mechanisms of infectious diseases, cancer, and other illnesses.

**Characteristic Features, Excellence, Competitiveness, and Future Potential of the Program**

1. **Combination of biomedical sciences and physical sciences/engineering/informatics**

   The program will build structures for collaboration between the fields of biomedical sciences and physical sciences/engineering/informatics, through a variety of horizontal linkages with university research centers, centering on the internationally competitive and outstanding International Institute for Integrative Sleep Medicine, the Center for Cybernics Research that develops medical/nursing care robots and other cutting-edge human assistive technologies, and the Center for Computational Sciences and the Life Science Center for Survival Dynamics (TARA), both of which are working at the front lines of research internationally. Linkages will also be developed with national research and development corporations within the Tsukuba Science City (National Institute for Materials Science, National Institute of Advanced Industrial Science and Technology), international partner universities, and private companies.
2. Bi-disciplinary educational structure

The program will cultivate students’ bi-disciplinary expertise using a “full double mentor system” in which faculty members from the fields of both biomedical sciences and physical sciences/engineering/informatics provide research guidance to students in their respective laboratories in the course of pursuing joint research projects.

3. Seamlessly integrated curriculum from pre-admission to graduate education

The program will create a seamlessly integrated system for transition to graduate school, whereby prospective students currently studying medicine or physical sciences/engineering/informatics are offered a pre-admission program on physical sciences/engineering/informatics or medicine as applicable. This is one approach to achieving a genuine MD-PhD combined program – something which has proven difficult in Japan thus far. This reform of graduate school admissions has the potential to become a leading model in interdisciplinary education through identification and nurturing of talented prospective candidates for admission, and educational intervention at the pre-admission stage.

4. Procurement of external resources in partnership with business and complete program self-sufficiency in future

During the period of government funding, resources shall be procured through such channels as special joint research projects with business. At the end of the period, complete self-sufficiency will be achieved with the establishment of the CYBERDYNE Ph.D. Program in Humanics (tentative name) through a corporate collaboration.
### Table of Contents

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Solving the mysteries of sleep—Toward new intervention methods for healthy slumber—</td>
<td>Yanagisawa Masashi</td>
</tr>
<tr>
<td>2</td>
<td>Deciphering Neuronal Circuits and Neurotransmitters that play Essential Roles in Behavior and Physiology</td>
<td>Sakurai Takeshi</td>
</tr>
<tr>
<td>3</td>
<td>Molecular Circuits of Sleep and Fear</td>
<td>Liu, Qinguha</td>
</tr>
<tr>
<td>4</td>
<td>Understanding Cortical Slow Waves</td>
<td>Greene, Robert</td>
</tr>
<tr>
<td>5</td>
<td>Addressing the Functional Roles and Evolutionary Origin of Sleep</td>
<td>Hanyashi Yu</td>
</tr>
<tr>
<td>6</td>
<td>Circuits and Functions of the Waking, Sleeping, and Dreaming Brain</td>
<td>Lazarus, Michael</td>
</tr>
<tr>
<td>7</td>
<td>To elucidate functions of sleep - What happens in the sleeping brain</td>
<td>Honjo, Sakiko</td>
</tr>
<tr>
<td>8</td>
<td>Research on Circadian Regulation of Sleep/Wake Cycle</td>
<td>Hirano, Arisa</td>
</tr>
<tr>
<td>9</td>
<td>Cholinergic Regulation of Sleep-Wake Behavior <del>Challenge to Generate Sleepless Mice</del></td>
<td>Niwa, Yasutaka</td>
</tr>
<tr>
<td>10</td>
<td>To elucidate the necessity of sleep with short-sleeping mice</td>
<td>Oishi, Yo</td>
</tr>
<tr>
<td>11</td>
<td>Unlocking the Mystery of Biological Longevity Through Methylation</td>
<td>Fukamizu Akiyoshi</td>
</tr>
<tr>
<td>12</td>
<td>From the Study of Immunoreceptors to Disease Control</td>
<td>Shibuya Akira</td>
</tr>
<tr>
<td>13</td>
<td>Mechanisms Underlying Germ Cell Formation</td>
<td>Kobayashi Satoru</td>
</tr>
<tr>
<td>14</td>
<td>Elucidating the Molecular Mechanism of Mechanotransduction in Blood Vessels and Its Application to Vascular Diseases</td>
<td>Yanagisawa Hiromi</td>
</tr>
<tr>
<td>員名</td>
<td>タイトル</td>
<td></td>
</tr>
<tr>
<td>--------</td>
<td>-------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>佐田亜衣子</td>
<td>幹細胞の不思議を探る:臓器再生と老化のメカニズム</td>
<td></td>
</tr>
<tr>
<td>島田裕子</td>
<td>生物の成熟のタイミングを司る神経内分泌機構の解明</td>
<td></td>
</tr>
<tr>
<td>岩崎憲治</td>
<td>多角的なアプローチによる構造生物学</td>
<td></td>
</tr>
<tr>
<td>北川博之</td>
<td>データ工学と医療・生物データ解析</td>
<td></td>
</tr>
<tr>
<td>天笠俊之</td>
<td>大規模データに対する処理の高速化および知識発見</td>
<td></td>
</tr>
<tr>
<td>北原格</td>
<td>3D-CG Virtual Surgical Navigation</td>
<td></td>
</tr>
<tr>
<td>亀田能成</td>
<td>Designing the future through computational media</td>
<td></td>
</tr>
<tr>
<td>山海嘉之</td>
<td>「サイバニクス」による未来開拓への挑戦</td>
<td></td>
</tr>
<tr>
<td>櫂井鉄也</td>
<td>AI・データ解析・シミュレーションのためのアルゴリズム</td>
<td></td>
</tr>
<tr>
<td>山田悟</td>
<td>安全・安心な人工知能/機械学習の確立を目指して</td>
<td></td>
</tr>
</tbody>
</table>

---

Life Science Center for Survival Dynamics, Tsukuba Advanced Research Alliance (TARA)
<table>
<thead>
<tr>
<th>名称</th>
<th>項目</th>
<th>題目</th>
<th>番号</th>
</tr>
</thead>
<tbody>
<tr>
<td>ヒューマンマシンシステムの安全確保にむけて</td>
<td>Systems and Information Engineering</td>
<td>Towards Safe Human-Machine Systems</td>
<td>29</td>
</tr>
<tr>
<td>人々の行動を計算論的に理解し物理的に支援する</td>
<td>Systems and Information Engineering</td>
<td>Human Technology for Understanding and Shaping Behaviors</td>
<td>30</td>
</tr>
<tr>
<td>人を癒やすAI:人工物の人間らしさとその応用</td>
<td>Systems and Information Engineering</td>
<td>AI cares Human: Utilizing Humanlike Attitude in Artificial System</td>
<td>31</td>
</tr>
<tr>
<td>数値解析を通じた病態解明と治療法の探索</td>
<td>Systems and Information Engineering</td>
<td>Numerical analysis &amp; machine learning based on matrix computations</td>
<td>32</td>
</tr>
<tr>
<td>衝突回避システムの開発とその応用</td>
<td>Systems and Information Engineering</td>
<td>Development and Application of Impact Avoidance Systems</td>
<td>33</td>
</tr>
<tr>
<td>ヒューマンマシンシステムの安全確保にむけて</td>
<td>Systems and Information Engineering</td>
<td>Human Technology for Understanding and Shaping Behaviors</td>
<td>34</td>
</tr>
<tr>
<td>人を癒やすAI:人工物の人間らしさとその応用</td>
<td>Systems and Information Engineering</td>
<td>AI cares Human: Utilizing Humanlike Attitude in Artificial System</td>
<td>35</td>
</tr>
<tr>
<td>数値解析および行列計算を基盤とした機械学習アルゴリズムの開発</td>
<td>Systems and Information Engineering</td>
<td>Numerical analysis &amp; machine learning based on matrix computations</td>
<td>36</td>
</tr>
<tr>
<td>衝突回避システムの開発とその応用</td>
<td>Systems and Information Engineering</td>
<td>Development and Application of Impact Avoidance Systems</td>
<td>37</td>
</tr>
<tr>
<td>数値解析および行列計算を基盤とした機械学習アルゴリズムの開発</td>
<td>Systems and Information Engineering</td>
<td>Numerical analysis &amp; machine learning based on matrix computations</td>
<td>38</td>
</tr>
<tr>
<td>衝突回避システムの開発とその応用</td>
<td>Systems and Information Engineering</td>
<td>Development and Application of Impact Avoidance Systems</td>
<td>39</td>
</tr>
<tr>
<td>数値解析および行列計算を基盤とした機械学習アルゴリズムの開発</td>
<td>Systems and Information Engineering</td>
<td>Numerical analysis &amp; machine learning based on matrix computations</td>
<td>40</td>
</tr>
<tr>
<td>衝突回避システムの開発とその応用</td>
<td>Systems and Information Engineering</td>
<td>Development and Application of Impact Avoidance Systems</td>
<td>41</td>
</tr>
<tr>
<td>衝突回避システムの開発とその応用</td>
<td>Systems and Information Engineering</td>
<td>Development and Application of Impact Avoidance Systems</td>
<td>42</td>
</tr>
<tr>
<td>番号</td>
<td>メンバー名</td>
<td>メンバー名</td>
<td>タイトル</td>
</tr>
<tr>
<td>------</td>
<td>--------------</td>
<td>------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td>44</td>
<td>島野仁</td>
<td>SHIMANO Hitoshi</td>
<td>脂質研究の量と質に視点をもって〜生活習慣病やすべての生命現象、病態に向けた医療応用〜</td>
</tr>
<tr>
<td>45</td>
<td>千葉滋</td>
<td>CHIBA Shigeru</td>
<td>血液がんの克服〜分子メカニズムからベッドサイドへ</td>
</tr>
<tr>
<td>46</td>
<td>松村明</td>
<td>MATSUMURA Akira</td>
<td>脳神経外科疾患の克服、再生をめざして</td>
</tr>
<tr>
<td>47</td>
<td>松村明</td>
<td>MATSUMURA Akira</td>
<td>功能再生治療用ロボットスーツHALの開発</td>
</tr>
<tr>
<td>48</td>
<td>家田真樹</td>
<td>IEDA Masaki</td>
<td>細胞移植をしない新しい心臓再生法の開発</td>
</tr>
<tr>
<td>49</td>
<td>高橋智</td>
<td>TAKAHASHI Satoru</td>
<td>細胞分化におけるLarge Maf転写因子群の機能解析</td>
</tr>
<tr>
<td>50</td>
<td>加藤光保</td>
<td>KATO Mitsuyasu</td>
<td>がん細胞の持続的増殖をもたらす幹細胞誘導の機構</td>
</tr>
<tr>
<td>51</td>
<td>松本正幸</td>
<td>MATSUMOTO Masayuki</td>
<td>心理現象を実現する神経メカニズムの理解を目指して</td>
</tr>
<tr>
<td>52</td>
<td>荒川智</td>
<td>YAMAZAKI Masashi</td>
<td>総合学術における Lipid research in the light of lipid quantity and quality</td>
</tr>
<tr>
<td>53</td>
<td>加藤光保</td>
<td>KATO Mitsuyasu</td>
<td>がん細胞の持続的増殖をもたらす幹細胞誘導の機構</td>
</tr>
<tr>
<td>54</td>
<td>榊本幸一</td>
<td>HASHIMOTO Koichi</td>
<td>粒子線治療のための技術開発</td>
</tr>
<tr>
<td>55</td>
<td>荒川智</td>
<td>YAMAZAKI Masashi</td>
<td>総合学術における Lipid research in the light of lipid quality and quantity</td>
</tr>
<tr>
<td>56</td>
<td>加藤光保</td>
<td>KATO Mitsuyasu</td>
<td>がん細胞の持続的増殖をもたらす幹細胞誘導の機構</td>
</tr>
<tr>
<td>57</td>
<td>加藤光保</td>
<td>KATO Mitsuyasu</td>
<td>がん細胞の持続的増殖をもたらす幹細胞誘導の機構</td>
</tr>
<tr>
<td>58</td>
<td>加藤光保</td>
<td>KATO Mitsuyasu</td>
<td>がん細胞の持続的増殖をもたらす幹細胞誘導の機構</td>
</tr>
</tbody>
</table>
表紙

Faculty of Medicine/Graduate School of Comprehensive Human Sciences

HARA Yuki
Titanium alloy screw coated with the apatite-FGF-2 composit layer

Faculty of Medicine

SANUKI Masaru
1) 行列演算の安定性と多項式演算の効率性の融合
2) e-learningを含むシステム開発と管理、その検証
   1) Combine symbolic and numeric computations
   2) Development and Management of ICT systems, including e-learning

Faculty of Medicine / Center for Artificial Intelligence Research

OZAKI Haruka
コンピュータを通じて医学生物学の問題を変える、解明する
Think and solve the biomedical problems thorough computers

Faculty of Life and Environmental Sciences/Graduate School of Life and Environmental Sciences

SHIGEMORI Hideyuki
不思議な生物現象を化学の力で解明する
Mysterious biological phenomena are elucidated by bioactive substances

Faculty of Life and Environmental Sciences/Graduate School of Life and Environmental Sciences

HARUKA

Faculty of Pure and Applied Sciences/Graduate School of Pure and Applied Sciences

KANO Hideaki
分子の指紋で医工連携〜ラマン散乱を用いたラベルフリー分子イメージング〜
Medical-engineering collaboration with the molecular fingerprint ~ Label-free molecular imaging by Raman scattering ~

Faculty of Library, Information and Media Science/Graduate School of Library, Information and Media Studies

MITSUI Akira
ビッグデータにおける人間とAIの分業最適化
Optimized Division of Labor for Humans and AIs in Big Data

National Institute of Advanced Industrial Science and Technology(AIST)

TATENO Hiroaki
グライコミクスための新技術の開発と細胞一斉解析
Development a novel technology for glycomics and simultaneous cellular analysis

National Institute for Materials Science(NIMS)

NAKAYAMA Tomonobu
ナノ材料を活用する脳型情報処理
Brain-type information processing with nanoscale materials

National Institute for Materials Science(NIMS)

CHEN Guoping
再生医療のための足場材料の開発
Development of Scaffolds for Regenerative Medicine

National Institute for Materials Science(NIMS)

川上亘作
物理化学的アプローチによる医薬品機能の最大化
Physical chemistry for maximizing function of pharmaceuticals

National Institute for Materials Science(NIMS)
<table>
<thead>
<tr>
<th>作者/機関</th>
<th>項目</th>
</tr>
</thead>
<tbody>
<tr>
<td>田村充宏</td>
<td>スマートポリマーで拓く未来医療〜途上国でも利用可能な医療をめざして〜</td>
</tr>
<tr>
<td>清田純</td>
<td>深層学習の健康・医療データへの応用</td>
</tr>
<tr>
<td>髙原勇</td>
<td>モビリティイノベーションの社会応用〜交通均衡の標準理論と新たなモビリティサービス実現〜</td>
</tr>
<tr>
<td>秋山浩</td>
<td>放射線治療の治療予測のためのデータ収集システムの構築と治療効果解析</td>
</tr>
<tr>
<td>佐藤孝明</td>
<td>日本発の1000ドルゲノム解析拠点を目指して</td>
</tr>
<tr>
<td>市橋史行</td>
<td>生理・行動・環境情報に基づく革新的サイバニックシステムの研究開発と社会実装</td>
</tr>
<tr>
<td>Kann, Michael</td>
<td>Intracellular trafficking of subviral structures</td>
</tr>
<tr>
<td>Heldin, Carl-Henrik</td>
<td>Mechanism of signaling via TGF-β receptors</td>
</tr>
<tr>
<td>ten Dijke, Peter</td>
<td>Regulation of TGF-β signaling</td>
</tr>
<tr>
<td>Kim, Seong-Jin</td>
<td>TGF-β とそのシグナル伝達機構</td>
</tr>
<tr>
<td>Chambers, Ian</td>
<td>Transcription Factor Control of Pluripotent Cell Identity</td>
</tr>
<tr>
<td>KAJI Keisuke</td>
<td>Molecular mechanisms of reprogramming</td>
</tr>
<tr>
<td>Fleischmann, Bernd</td>
<td>Mending the Broken Heart</td>
</tr>
<tr>
<td>Lander, Arthur D.</td>
<td>Design principles underlying robust biological systems</td>
</tr>
<tr>
<td>YOKOMORI Kyoko</td>
<td>Mechanism of cell survival in response to DNA damage; Molecular mechanism of epigenetic abnormality disorders Cornelia de Lange syndrome and facioscapulohumeral muscular dystrophy</td>
</tr>
</tbody>
</table>
睡眠医科学（柳沢 正史）
Neuroscience of sleep (YANAGISAWA Masashi)

睡眠というありふれた現象は謎に満ちていて、なぜ我々は眠らなければならないのか、そしてそもそも「睡眠」の実体とは何なのか、まったく明らかになっていません。オレキシンという鍵によってナルコレプシーという睡眠障害の扉を開いた先には、睡眠・覚醒を巡る大きなブラックボックスが待っていました。このブラックボックスをこじ開けるため、柳沢/船戸研究室ではフォワード・ジェネティックス、in vivo カルシウムイメージング、スライスパッチクランプ法等を用いた基礎的研究と、オレキシン受容体を標的とした創薬研究を行っています。最近、フォワード・ジェネティックス研究の進展により睡眠覚醒制御に重要な役割を果たす3つ以上の遺伝子を同定することに成功しました。睡眠の謎を解き、多くの人に還元できる成果が挙げられるよう、日夜実験に取り組んでいます。

Solving the mysteries of sleep  
~Toward new intervention methods for healthy slumber~

Sleep is a quite familiar phenomenon. However, underlying mechanisms of sleep is unknown and even simple questions, why we sleep and what sleepiness is, are unanswered. Thus, sleep is one of the greatest mysteries in today's neuroscience. Our discovery of orexin unlocked the door to the sleep studies, but sleep/wake regulation still remains a challenge for scientists. In order to crack open the black box, Yanagisawa/Funato Lab is engaged in basic research using forward genetic analysis, in vivo calcium imaging, patch-clamp electrophysiology in brain slices with simultaneous multicellular recording and imaging, etc., in addition to drug discovery research targeting the orexin receptor. We have identified three or more causative gene mutations that play important roles in sleep-wake regulation to date, through advances of our forward genetics research. People in our lab are vigorously conducting experiments everyday with the aim of solving the mystery of sleep, and contributing to the reduction of sleep disorders and associated diseases.
分子行動生理学（櫻井 武）
Molecular Behavioral Physiology (SAKURAI Takeshi)

「こころ」はいかにして生まれるのか（講談社ブルーバックス）、睡眠の科学－なぜ眠るのか なぜ目覚めるのか（講談社ブルーバックス）、食欲の科学（ブルーバックス）、＜眠り＞をめぐるミステリー－睡眠の不思議から脳を読み解く（NHK出版新書）など参考にしてください。
Sleep exists in virtually all animals and is essential for viability and normal brain functions. However, the molecular circuit of sleep control is currently unknown. My laboratory will integrate biochemical, genetic and chemical biology approach to identify key genes for sleep-wake regulation. On the other hand, fear is a basic emotion that enhances survival by triggering characteristic physiological and behavioral responses. Whereas learned fear is acquired by experience, innate fear is hardwired and genetically encoded. We developed a forward genetic screen to identify randomly mutagenized mice with abnormal innate fear responses. We hope that this unbiased fear screen will allow us to identify core fear genes, elucidate the molecular mechanism of fear, and reveal the genetic basis of human anxiety disorders.

Molecular Circuits of Sleep and Fear


睡眠時間が2〜3時間ほど短くなるだけで、私たちは不快感を覚え、たとえば運転などの日常的なタスクの作業効率が著しく低下します。幸運なことに、眠ることでその状態から回復することができます。脳の機能を回復させるためには、睡眠ステージの中でも特に深いとされる徐波睡眠が重要であると考えられています。徐波睡眠中には、皮質にある神経細胞群のオン（活動）・オフ（静止）が強く同調し、脳波（EEG）に特徴的なパターンが現れます。このオンの状態における神経活動のパターンは覚醒時とよく似ていますが、じつは重要な違いがあることが、我々の最近の研究からわかってきたのです。私たちの研究グループでは、徐波睡眠中の皮質神経細胞およびそれらが構成するネットワークを詳しく調べることで、特徴的な神経活動パターンにどのような機能があり、どう制御されているのかをつきとめようとしています。

**Sleep and sleep regulation - understanding cortical slow waves**

Missing sleep for even a few hours is unpleasant and normal mental tasks, such as driving, become more and more difficult. Luckily, sleep, especially deep, slow wave sleep will restore the brain’s ability to function. During slow wave sleep neurons in the cortex alternate between silent OFF states and active ON states in a highly synchronous manner - giving rise to characteristic waves in the electro-encephalogram (EEG) from which the state “slow wave sleep” derives its name. The firing rate during the ON states resembles waking, but we are now finding important differences between the pattern of wake activity and slow wave sleep activity. Using quantitative analysis of the organization of the firing we find that sleep is characterized by more disorganized activity between identified neurons that cannot be easily resolved with respect to sleeps role in improved memory. We are currently further characterizing the organization of the activity of neuronal firing with respect to sleep-related learning and of neuronal calcium transients to better understand the function of sleep and in particular of sleep-related neuronal activity.

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Robert Greene, Ph.D. or M.D.
Professor
International Institute for Integrative Sleep Medicine, University of Tsukuba, University of Texas Southwestern Medical Center

E-mail address: RobertW.Greene@UTSouthwestern.edu
URL: https://wpi-iiis.tsukuba.ac.jp/japanese/research/member/detail/robertgreene/
なぜ眠るのか？
～睡眠の生理的意義と進化的起源の解明に挑む～

睡眠は生命に必須です。しかしながら、その具体的な役割はよく分かっていません。睡眠中は意識が低下し、敵に襲われるリスクが上がります。このような一見不利益な生理状態をなぜ動物が有するのか、その進化的背景や意義の解明を目指しています。そのために線虫とマウスを用います。線虫はわずか302個の神経細胞しか持ちませんが、私たちはこのシンプルな動物の睡眠が、哺乳類の睡眠と進化的に保存されたものであることを裏付ける証拠を得ることに成功しました。またマウスでは、夢を生じるレム睡眠の制御に重要な神経細胞を発見し、世界に先駆けて、レム睡眠を遮断できるマウスの開発にも成功しました。これら2種類の動物に注目することで、睡眠の意義を分子レベル・細胞レベルから個体レベルまでのあらゆる階層で解明できると期待しています。

Addressing the functional roles and evolutionary origin of sleep

Sleep is indispensable. However, the function of sleep remains largely unknown. During sleep, the level of consciousness is lowered and the risk of being attacked by predators increases. Yet most animals undergo sleep, suggesting that sleep plays some vital roles. We address the function and evolutionary origin of sleep using the nematode Caenorhabditis elegans and mouse. The nervous system of C. elegans consists of merely 302 neurons. We previously obtained evidence suggesting that sleep in this simple animal and mammalian sleep are evolutionarily conserved. Furthermore, in mice, we successfully identified neurons that are crucial for the regulation of REM sleep, the major source of vivid dreams, and established mice where REM sleep could be efficiently inhibited. Using these two model animals, we aim to elucidate the roles of sleep at multiple levels from molecular and cellular to individual levels.
Circuits and functions of the waking, sleeping and dreaming brain

The investigative focus of our laboratory is the cellular and synaptic basis by which the brain regulates sleep and wakeful consciousness. Our experiments seek to link the activity of defined sets of neurons with neurobehavioral and electroencephalographic outcomes in behaving animals by using innovative genetically or chemically engineered systems (optogenetics, chemogenetics or optopharmacology) in conjunction with recording of the electrical activity produced by the brain or in-vivo imaging (e.g., fiber-optic endomicroscopy). For example, we investigate the control of sleep and wakefulness by the mesolimbic pathway comprising the ventral tegmental area and nucleus accumbens. As the mesolimbic pathway is implicated in motivational and cognitive behaviors, changes in vigilant states are likely associated with the motivational and cognitive responses in animals. Moreover, we are interested in the link between sleep loss and the desire to consume unhealthy foods, i.e. junk foods. We recently found that the loss of REM sleep leads to increased consumption of sucrose and fat and that inhibiting neurons in the medial prefrontal cortex reverses the effect of REM sleep loss on sucrose consumption. We also conduct drug discovery research targeting the adenosine A2A receptor in collaboration with the WPI-IIS Nagase laboratory.

Dr. rer. nat. Michael Lazarus
Associate Professor/Principal Investigator
International Institute for Integrative Sleep Medicine (WPI-IIS),
University of Tsukuba

E-mail address: lazarus.michael.ka@u.tsukuba.ac.jp
URL: https://www.wpiiiislazaruslab.org
私達は日々、睡眠と覚醒を繰り返します。覚醒時には外界を認識し、内なる思考や記憶と外界からの情報を統合し、自らの思考をアップデートして行動を起こします。一方、睡眠時には私達の意識レベルは大きく低下し、外界を認識せず、意図的な動作を起こしません。このようなダイナミックな変化は脳で生み出されると考えられていますが、我々の脳がなぜこのような認知機能の変化を伴う「睡眠」という現象を必要とするのか、未だ明らかではありません。私達は1）睡眠の機能を分子・細胞レベルで理解する事、2）睡眠覚醒サイクルを通じて私達の認知機能が変動するメカニズムの解明を目指します。そのために、自由行動下の動物の神経活動の計測や、神経の性質の基盤となる遺伝子発現解析を行っています。

To elucidate functions of sleep: What happens in the sleeping brain
We repeat the wake-sleep cycle daily. During wake, we recognize the external environment, keep integrating our thoughts, memories, and sensory inputs, then act based on our updated minds. However, during deep sleep, we become unconscious and do not recognize the external environment. It is generally believed that such dynamic changes in our cognition and locomotion derive from the brain, however, the underlying neural mechanisms remain largely elusive. We aim to elucidate 1) the function of sleep, and 2) the neural basis underlying the dramatic changes in our cognition across the wake-sleep cycle. To realize dynamics of neural activity during the wake-sleep cycle, we employ in vivo electrophysiology, opto/chemogenetics, and gene expression analyses.
Research on circadian regulation of sleep/wake cycle

Sleep/wake behavior shows rhythmicity with a period of ~24 hrs and is regulated by the biological clock. The central circadian clock (master clock) resides in the suprachiasmatic nucleus (SCN) of the hypothalamus. It has been well established that the central clock controls the timing of sleep/wake cycle, while the neural mechanism of circadian sleep/wake regulation is largely unclear. We aim to determine the neural network between the central clock and sleep/wake center and uncover its physiological function by using neuroscientific approach in mice.
アセチルコリンによる睡眠覚醒制御機構の解明
〜睡眠はどこまで削れるか〜

私たちは人生の1/3の時間は睡眠に費やすと言われています。そんなに多くの時間をもっと他のことに使うことができればと、どれほど多くの人が願ったことでしょう。例えばその時間がどうして必要なのかを深く知ることができれば、何かヒントが得られるかもしれません。私は遺伝学を用いて、特定の神経や遺伝子に摂動を与え、触らずにマウスの睡眠をどこまで削れるかに挑戦しています。特に100年以上前に発見された神経伝達物質であるアセチルコリンに注目し、20種類以上ある受容体のうち2つを欠失させることで活動期の眠気とレム睡眠を欠失させることに成功しました。現在それらの責任細胞の同定を進めながら、背後にある分子細胞メカニズムの解明に取り組んでいます。“眠くない”マウスや“夢を見ない”マウスに興味のある方、ぜひお声がけください。

Cholinergic regulation of sleep-wake behavior
~Challenge to generate sleepless mice~

We spend 1/3 of our lives for sleep. Many people wish they could use such a long time for something other than sleep. One of the best ways to approach the wish is to understand the underlying mechanism of sleep. To this end, I have been trying to generate sleepless mice by using genetic manipulation, especially in the acetylcholine pathway. So far, I succeeded in generating mutant mice with short sleep and no REM sleep by deleting two subtypes of acetylcholine receptors (Niwa et al. 2018 Cell Reports). I'm now trying to examine these two receptors control of sleep-wake behavior by using genetic approaches.
神経行動生物学（大石 陽）

Neurobehavioral Biology (OISHI Yo)

OISHI Yo, Ph.D.
Assistant Professor/Principal Investigator
International Institute for Integrative Sleep Medicine (WPI-IIIS)
University of Tsukuba

E-mail address: oishi.yo.fu@u.tsukuba.ac.jp
URL: https://www.wpiiiislazaruslab.org/

神経行動生物学（大石 陽）

神経行動生物学（大石 陽）

Short-sleeping mouse exhibit lower amount of sleep.

To elucidate the necessity of sleep with short-sleeping mice

People spend approximately one-third of their life sleeping. Why sleep is compulsory for human life and cannot be avoided, however, remains unclear. It is important to understand why sleep is necessary and how sleep is controlled – not only to elucidate physiological behavior but also to enhance our quality of life.

Recently, we inadvertently created mice that require an extremely low amount of sleep. Surprisingly, these mice do not show an increase in a sleepiness marker. Therefore, the behavior is very similar to that of so-called “short sleepers” – people that can function for long periods of time on little sleep without exhibiting excessive sleepiness. Using multiple “short sleep” models, including this novel mouse model, we study the effect of short sleep on other physiologic functions in the body to understand the necessity of sleep. We also study the neural mechanisms of short sleep to clarify the control mechanisms of sleep.

Recent publications

Unlocking the mystery of biological longevity through methylation

What is longevity? What factors do determine how long we live? We have discovered that methylation (the biological reaction to transfer the methyl group [-CH\_3]) has the key to determine the longevity by investigating the regulation of gene expression. The reaction is deeply involved not only in protein methylation, but also in that of DNA and RNA. To understand the longevity of multicellular organisms, we are approaching the molecular entity of the longevity by applying the techniques of genetics, biochemistry, chemistry, and metabolomics of mouse and C. elegans. Through advances of the longevity research, our laboratory is working on with the aim of knowing how long organisms can live and survive, and feeding back to the increase in the quality of health and life.
SHIBUYA Akira, M.D., Ph.D.
Professor
Life Science Center for Survival Dynamics, TARA
E-mail address: ashibuya@md.tsukuba.ac.jp

SHIBUYA Kazuko, M.D., Ph.D.
Associated Professor, Faculty of Medicine
E-mail address: kazukos@md.tsukuba.ac.jp

TAHARA Satoko, Ph.D.
Lecturer
Life Science Center for Survival Dynamics, TARA
E-mail address: tokothr@md.tsukuba.ac.jp

URL: http://immuno-tsukuba.com/index.html

**From the Study of Immunoreceptors to Disease control**

We challenge for clarification of the basic principle of the immune system through analyses of novel immunoreceptors and their functions at the molecular, cellular and whole body levels. In addition, we develop therapeutics targeting the immunoreceptors for intractable diseases such as cancer, allergy, infection, and autoimmune diseases.

**Immune receptors identified in the Shibuya Lab**

- **DNAM-1 (CD226)**
  - Immunology 1996
  - Immunity 1999
  - J. Exp. Med. 2003
  - J. Exp. Med. 2008
  - PNAS 2010
  - PNAS 2011

- **FcγR (CD351)**
  - J. Exp. Med. 1996
  - J. Exp. Med. 1999
  - Immunity 2003
  - J. Exp. Med. 2008
  - PNAS 2010

- **MAIR-I (CD300a)**
  - PNAS 2009
  - J. Exp. Med. 2011
  - Nat. Commun. 2014

- **MAIR-II (CD300c)**
  - J. Exp. Med. 2003
  - J. Exp. Med. 2008
  - PNAS 2010

- **Allergin-I**
  - Nat. Immunol. 2010

**Development of molecular targeted therapy**

- Cancer
- GVDH
- Transplantation
- Infection
- IBD
- Allergy
- Autoimmunity
- Sepsis
生殖細胞形成機構の解明に挑む

生殖細胞は次代に生命をつなげ、体細胞は個体の生命を支えます。このように運命が大きく異なる生殖細胞と体細胞は、受精卵の分裂により生み出された姉妹同士です。では、どのように生殖細胞への運命が決定されるのでしょうか？ショウジョウバエの産卵直後の卵の後端には、「生殖質」と呼ばれる細胞質があり、それを取り込んだ細胞のみが始原生殖細胞（PGC）となり、生殖細胞に分化することができます。さらに、その生殖質を体細胞に取り込ませると、その細胞は生殖細胞になることがわかりました。このことは、生殖質中には体細胞分化を抑制する分子（母性因子）と、生殖細胞への分化を活性化する母性因子が存在していることを物語っています。私たちは、このような母性因子の同定とともに、PGCの性決定機構の解明に挑んでいます。

Mechanisms underlying Germ Cell Formation

Germ cells are specialized cells that can transmit genetic materials from one generation to the next in sexual reproduction. All of the other cells of the body are somatic cells. This separation of germ and somatic cells is one of the oldest problems in developmental and reproductive biology. In many animal groups, a specialized portion of egg cytoplasm, or germ plasm, is inherited by the cell lineage (germline) which gives rise to germ cells. It has been demonstrated that the germ plasm contains maternal factors required and sufficient for germline development. Our laboratory aims to find the maternal factors for germline segregation, and molecular mechanisms regulating germline sex determination in Drosophila.

The posterior pole of early Drosophila embryo. Green shows primordial germ cells (PGC). Red shows somatic region.
血管メカノトランスダクション機構の解明と疾病への応用

血管は心拍出による機械的刺激に常に晒されています。ではいかに機械的刺激が、血管細胞（内皮細胞、平滑筋細胞、線維芽細胞）に伝搬され、生化学シグナルに変換されるのでしょうか？解剖学的に異なる血管や、老化や炎症で性状が変化した血管では、シグナル伝達はどのように変わるのでしょうか？私たちは、循環器疾患（大動脈瘤や加齢性動脈硬化）のモデルマウスと、ストレッチアッセイ・ラマンイメージング・ゲノムエディティングなどの技術を組み合わせ、メカノトランスダクション機構の解明と診断や治療への応用に取り組んでいます。バイオエンジニアリング・バイオマテリアル・心臓血管外科などの研究室との共同研究も進めています。

Elucidating the molecular mechanism of mechanotransduction in blood vessels and its application to vascular diseases

Blood vessels are constantly exposed to the mechanical stress caused by cyclic pumping of the heart. However, 1) how vascular cells (endothelial cells, smooth muscle cells, and fibroblasts) sense stress and convert to biochemical signals, 2) whether anatomically different vascular systems have distinct signaling pathways, and 3) how damaged/aged extracellular matrix of the vessels affects mechanotransduction, are largely unknown. We utilize mouse models of cardiovascular diseases such as aortic aneurysms and elucidate the molecular mechanism of mechanotransduction in the vessel wall by combining in vitro stretch assays, live imaging, and genome editing. We are currently collaborating with bioengineering, biomaterials, and clinical laboratories.

Recent publications

幹細胞の不思議を探る：臓器再生と老化のメカニズム

幹細胞は、臓器再生に重要な役割を果たすとともに、近年では、老化やがんとの関連性も強く示唆されています。私たちは、そんな不思議な幹細胞の実態を探るべく、マウス皮膚、眼、口腔の3つの組織をモデルに研究を行っています。幹細胞の特性や制御機構の解明は、再生医療への応用や、老化やがんの予防・治療へとつながることが期待されます。

遺伝子改変マウスを用いたアプローチを得意とし、オミクス解析や糖鎖工学、バイオエンジニアリングといった異分野融合にも積極的に取り組んでおります。幹細胞や老化、再生医療、皮膚科学、発生工学に興味のある人、何か新しいことを発見したい人、ぜひ一緒に研究しましょう。

Stem Cells in Tissue Regeneration and Aging

Stem cells have a remarkable ability to regenerate various adult tissues. Our research focuses on elucidating the cellular dynamics and regulatory mechanisms of stem cells, especially using mouse epithelial tissues (skin, eyes and oral) as a model. We identified novel stem cell populations in the mouse skin and established new genetic tools and molecular markers to analyze these cells in vivo (Sada et al., Nat Cell Biol 2016). We are currently studying stem cells in tissue regeneration and aging, by combining cell & molecular biology techniques, genetic-engineering of mice, omics analysis, bioengineering, glycobiology and so on.

Our research goal is to reveal the drivers and effectors of stem cell dysfunction. Targeting these factors may prevent or cure diseases at the stem cell level, with implications for applications in regenerative therapy, and for future treatments of cancer, aging and other disorders.
発生生物学（島田 裕子）
Developmental Biology (SHIMADA Yuko)

SHIMADA Yuko, Ph.D. or M.D.
Assistant Professor
Life Science Center for Survival Dynamics,
Tsukuba Advanced Research Alliance (TARA),
University of Tsukuba

E-mail address: shimada.yuko.gn@u.tsukuba.ac.jp
URL: https://researchmap.jp/yukoshimada

生物の成熟のタイミングを司る神経内分泌機構の解明

生物の各発生段階にはそれぞれ特徴があり、成長と成熟が適切なタイミングで進行することが重要です。私たちは、モデル生物であるキイロショウジョウバエを用いて、幼若期（こども）から成体期（おとな）への成熟過程を司る神経内分泌機構を研究しています。特に、幼い個体が摂取する栄養が、セロトニン産生神経群によって感知されて、ステロイドホルモン生合成のタイミングを調節する分子機構を明らかにしたいと考えています。キイロショウジョウバエの分子遺伝学と細胞生物学を組み合わせることで、様々な栄養環境に応じて成熟のタイミングを変化させる発生プログラムの柔軟性を支える分子基盤の解明に挑戦します。

Neuro-endocrine Mechanisms of Maturation in Drosophila

How do the organisms know their appropriate timing of maturation from the juvenile to the adult? One of the key regulatory mechanisms is steroid hormone biosynthesis in response to various environmental conditions. By using molecular genetics, cell biological analysis, live-imaging system of the fruitfully Drosophila melanogaster, we are trying to understand how the genetic program of organism is flexibly coordinated to accomplish the development from eggs to individuals.

SHIMADA Yuko, Ph.D. or M.D.
Assistant Professor
Life Science Center for Survival Dynamics,
Tsukuba Advanced Research Alliance (TARA),
University of Tsukuba

E-mail address: shimada.yuko.gn@u.tsukuba.ac.jp
URL: https://researchmap.jp/yukoshimada

A relay of hormones controls maturation in human and insects.

Serotonin-producing neurons directly project to the steroid hormone biosynthesis organ.
Structural biology and chemistry by a multifaced approach

We have been studying structure and chemistry of biological molecules mainly using single-particle electron microscopy (EM). The biggest advantages of single-particle EM are as follows. (1) Crystallization is not necessary (2) Large macromolecular complexes can be analyzed (3) A certain amount of sample heterogeneity can be dealt with. Especially single-particle electron cryo-microscopy (cryo-EM) has become a new tool to solve 3D molecular structures at near-atomic resolution. We are planning to study one of fusion gene products that has been thought to cause soft tissue sarcomas using various biochemical methods as well as single-particle EM method.
データ工学（北川 博之）

Data Engineering (KITAGAWA Hiroyuki)

KITAGAWA Hiroyuki, Ph.D.
Professor
Center for Computational Sciences &
Center for Artificial Intelligence Research,
University of Tsukuba

E-mail address: kitagawa@cs.tsukuba.ac.jp
URL: http://kde.cs.tsukuba.ac.jp/~kitagawa/

データ工学と生体・医療ビッグデータ解析

人類がこれまで体験したことのない超大規模なデータを扱うビッグデータ時代が到来しています。データ工学（データベース、データマイニング、機械学習、データ解析等）は、ビッグデータを体系的に扱う学問領域です。我々は、データ工学に立脚したアプローチにより、ビッグデータを活用した新たな科学や社会を切り拓く各種研究開発を推進しています。その一環として、データ工学に基づく生体医療ビッグデータ解析に取り組んでいます。具体的なテーマとしては、脳波、筋電等の生体ビッグデータを用いた自動睡眠分析のための人工知能技術の研究や、健康保険データベースを用いた医療ビッグデータ解析の研究等です。社会にインパクトを与えられる研究を一緒にやりましょう。

Data Engineering and Biomedical Big Data Analysis

Big data era has come to deal with an extremely large amount of data that humanity has never experienced before. Data engineering (database, data mining, machine learning, data analytics, etc.) is an academic field that treats big data systematically. We are conducting various research and development activities involving big data of different domains and applications from data engineering perspectives, which will open up new science and society. In particular, biomedical big data analysis is one of our major research targets. Our current research topics include research on artificial intelligence technology for automatic sleep analysis using a large amount of vital signals such as brain waves, myoelectricity, etc. and research of medical big data analysis using health insurance databases. Let’s do research that has a positive impact on society together.
Efficient processing / knowledge extraction for big data

With the rapid development of computer and network technologies, various kinds of data are being collected and accumulated, which is called "big data," and efficient processing and knowledge extraction from such big data are highly demanded in wide spectrum of domains. We have been engaged in research/development on techniques of efficient processing and knowledge extraction for big data exploiting database and data engineering technologies. Research topics: efficient processing of big data using GPU/FPGA/many-core processors, data mining and knowledge extraction from big data exploiting techniques, such as NMF (non-negative matrix factorization), search and knowledge extraction from semi-structured data, such as Linked Open Data (LOD) and graphs, management and knowledge extraction for scientific domains, such as biology and astronomy.

GPU Acceleration of Label Propagation

- Basic idea
  - Express the algorithm by only operations suitable for GPUs

- Data layout
  - The CSR format

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Experimental Evaluation

- Observation
  - GPU-WOP (without partitioning) is the fastest
  - Load balancing is important

![Processing Time (ms)](chart)

(a) amazon  (b) dblp  (c) youtube

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-Yusuke Kozawa, Toshiyuki Amagasa, Hiroyuki Kitagawa:
GPU-Accelerated Graph Clustering via Parallel Label Propagation, CIKM 2017, pp. 567-576, 2017-
ハイパフォーマンスコンピューティングとビッグデータ解析

スーパコンピュータにより応用分野の支配方程式をシミュレーションする計算科学は、理論科学、実験科学と並ぶ学問分野です。計算科学を高度に行うことをハイパフォーマンスコンピューティングといいます。また、大規模な実験データや計算データを解析するビッグデータ解析もスーパコンピュータの重要な応用です。シミュレーション、ビッグデータ解析を効率的に行うためのスーパコンピュータの設計、またスーパコンピュータを十二分に活用するためのソフトウェアの研究開発を行っています。

High Performance Computing and Big Data Analysis

Computational science that simulates governing equations in science, is a major study like theoretical science and experimental science. High performance computing enables computational sciences using supercomputers. Big data analysis that processes large-scale experimental data and computing data is also an important application for supercomputers. Our laboratory designs supercomputers to efficiently process scientific simulation and big data analysis, and develops software to fully utilize the supercomputers.

情報科学（建部 修見）

Computer Science (TATEBE Osamu)

TATEBE Osamu, Ph.D.
Professor
Center for Computational Sciences, University of Tsukuba

E-mail address: tatebe@cs.tsukuba.ac.jp
URL: http://www.hpcs.cs.tsukuba.ac.jp/~tatebe/

Oakforst-PACS supercomputer
Storage system of Oakforest-PACS
Designing the future through computational media

I belong to the computational media group at the division of computational informatics, center for computational sciences. I am an advisor of the department of intelligent interaction technologies at graduate school of systems and information engineering and the Ph.D program in empowerment informatics too. My mission is to open frontier humanics based on the state of the art technologies of computational research and information science. Computer vision, video analysis, mixed reality, augmented reality are of the key components to shape our future society.

Computer vision and advanced computer-human interface based on image and video media are powerful enough to change the future of our society. Below are some snapshots of our students’ works.
3-Dimensional Virtual Surgical Navigation

With the lack of surgeons and drastic improvement of medical technology, attention has focused on VR surgery using ICT technology. As the results, some achievements such as “tailor-made human body CG model”, “preoperative planning, intraoperative guidance, postoperative confirmation using CG data”, are realized. On the other hand, the realization of “surgical navigation” to properly guide the surgeons in accordance with the progress of surgical operation is still on the development. Our laboratory conducts on researches of surgical navigation aiming to realize (1) 3D sensing for surgical situation, (2) visualization of surgical information using sensing results, (3) accurate AR (Augmented Reality) navigation according to the surgical situation, (4) constructing practical navigation system.

3D-CG Virtual Surgical Navigation aims for...

- Improving Instruction Level: Integration of 3D simulation and onsite navigation.
- Elimination of Surgeon Shortage: VR/AR remote treatment, advanced skill passing.
- Doctor’s Education: Evaluation of surgical procedures and proficiency by 3D sensing.

**KITAHARA Itaru, Ph.D.**
Associate Professor
Center for Computational Sciences,
University of Tsukuba

E-mail address: kitahara@ccs.tsukuba.ac.jp
URL: http://www.image.iit.tsukuba.ac.jp/
高速なデータベース技術の実現を目指して

データを効率的に管理・処理するためには、それらを支えるデータベースシステムが非常に重要な技術要素となっています。しかしながら、既存のデータベースシステムやデータ処理技術の性能を十分に発揮させることは容易ではありません。我々の研究チームでは、大量のデータを超高速に処理するためのデータベースシステムおよびデータ処理アルゴリズムの研究開発を行っています。具体的には、近年様々な分野で利用が広がっているグラフデータを対象とした、超高速なデータ処理アルゴリズムならびに検索システムの開発を中心とした研究を推進しています。

Toward Efficient Database Systems

The database systems are now one of the essential and fundamental tools for managing and processing large-scale data generated by various applications. However, it is not a trivial work to ensure high performance data processing on existing database systems and algorithms. In order to overcome the performance limitations, we are now developing high performance database systems and fast data processing algorithms to cope with the large-scale data. Especially in the recent few years, we are currently studying efficient processing/search algorithms that are focused on graph structured data.

Graph Clustering

- Find dense components from a graph
  - Community detection over social networks
  - Event detection from microblogging services
  - and more...

Efficiency

- Our algorithm runs x500 faster than SCAN
  - It computes 1.4 billion edges within 6.4 sec.

Deep Learning Approach to Automated Sleep Stage Scoring

For the diagnosis of sleep disorders, the ratio and the transition of patient’s sleep states (stages) will be one of the most effective evidences. However, the sleep stage scoring is very time-consuming, because it is conducted by visually inspecting biological signals. To address this problem, we are developing an automated sleep stage scoring method using deep learning algorithms. In this research, we attach great importance to collaboration with sleep medicine doctors and expert. By using their knowledge about sleep and its stages, our proposed method achieved the scoring with high accuracy.
サイバニクス（山海 嘉之）
Cybernics (SANKAI Yoshiyuki)

SANKAI Yoshiyuki, Ph.D
Professor/Research Director
Faculty of Engineering, Information and Systems,
Center for Cybernics Research,
University of Tsukuba

E-mail address: office@ccr.tsukuba.ac.jp
URL: https://ccr.tsukuba.ac.jp

【サイバニクス】による未来開拓への挑戦
人・ロボット・情報系の融合複合新領域【サイバニクス】を駆使し、超高齢社会における課題解決のための「革新技術の研究開発」、医療・福祉・生活の分野における「新産業創出」、未来開拓型の「人材育成」を同時展開し、好循環の医療イノベーションの創出に挑戦しています。

世界初のロボット治療機器「医療用HAL®」は、欧州での医療機器承認に続き、日本や米国でも治療効果のある医療機器として承認されという快挙を達成しています。「サイバニクス革命」、人とテクノロジーが共生する未来社会「Society5.0/5.1」、「重介護ゼロ®社会」の実現に向けた研究開発に挑戦しています。

Challenging the Future based on “Cybernics”
In order to solve social problems in super aging society and to realize medical innovation, we are simultaneously promoting "Research & Development of Innovative Technology", "Creation of New Industry" in the fields of medical, welfare and life, and "Human Resource Development". As an example of the outcome, the world's first Cybernic treatment device "Medical HAL®" was approved as a medical device for neurological disorders in Japan and the United States, after the approval of medical devices in Europe. We are challenging to realize the "Cybernics Revolution", "Society 5.0 / 5.1" and "ZERO Burdening-Care Society".
Mathematical Algorithms for AI, Data Analysis and Simulation

Computers play an important role in various fields of science and engineering. By representing phenomena in the real world (Physical space) on a computer (Cyber space), we can utilize computers to understand and predict various systems and phenomena in the real world. In our research group, we develop mathematical algorithms and their software implementations for artificial intelligence (AI), data analysis, physical simulations, etc. We also research and implement high performance computing methods to exploit the computing power of supercomputers.
Research on Medical Imaging and Image Processing

My research fields are medical imaging and image processing. I am mainly working on the following four research subjects. The first subject is the research on image processing, which aims at generating cross-sectional images in CT and PET imaging modalities. The second subject is the research on Computer-Aided-Diagnosis, which aims at supporting the diagnosis by MD using medical image processing techniques. The third subject is the research on Computational Anatomy, which aims at generating 3-D digital model of human atlas together with applying it to, for example, simulation and navigation of surgeries. The last one is the research on newest image processing and computer vision, aiming at applying them to medicine. In particular, I am believing that I am one of top runners in the field of image reconstruction in CT and PET.
AIセキュリティ・プライバシー（佐久間 淳）
AI Security and Privacy (SAKUMA Jun)

SAKUMA Jun, Ph.D.
Professor
Dept. of Computer Science,
Graduate school of SIE,
University of Tsukuba

E-mail address: jun@cs.tsukuba.ac.jp
URL: www.mdl.cs.tsukuba.ac.jp

安全・安心な人工知能/機械学習技術の確立を目指して
機械学習技術の急速な発展に伴い、画像や音声などの認識精度が人間の認識能力を超える程度にまで改善しました。機械学習が優れた予測・認識能力を発揮するためには、大量のデータが必要となります。当研究室では、データが個人情報を含む場合に、プライバシ保護と機械学習における活用を両立させるための暗号理論や統計的プライバシ保護技術を研究開発しています。今後は機械学習が人間や社会にとって重要な判断や意思決定の一部を担うようになることが予想されます。研究室レベルでは良好に動作する機械学習も、社会実際に利用される場面においては、その悪用を企む者の存在のために、安定的に期待した動作をすることは限りません。当研究室では、AIを安定に動作させるためのAIセキュリティ技術を研究しています。

Safety and Security of AI/Machine learning
Large amounts of data are required for machine learning to demonstrate excellent prediction and recognition ability. We study cryptographic theory and statistical privacy protection technology that achieve both privacy protection and machine learning when data contains personal information. Machine learning is expected to support important decision-making performed by experts. Machine learning is expected to support important decision-making for humans performed by experts. Machine learning that works well at the laboratory level while it does not necessarily produce the expected behavior because of the existence of those who are planning to misuse it. Our laboratory is studying AI security technology to make AI operate stably.

AI-人間系における脅威

- 機械が善手(だが人間の方が得意)だと思われていたタスクも機械のほうが優秀になりつつある
- これからの機械学習研究
  - より賢いAIを作る
  - AIと人間の上手な協調
  - 倫理観をもった「やりすぎない」AI

人間、データの接点を通じて、MLに悪影響を及ぼす
ヒューマンファクター（伊藤 誠）
Human Factors (ITOH Makoto)

Towards Safe Human-Machine Systems

Introduction of automation for safety may cause troubles/accidents. Actually serious accidents occurred in highly automated systems such as aviation and nuclear power plants. Human factors/cognitive systems engineering have been developed in order to establish safe human-machine systems. Today’s vital issue in human factors is to design safe automated driving systems. Human factors is not just a psychology but an engineering based on deep understanding of humans.

ヒューマニクスの学生へのメッセージ

自動車の自動運転などでは、ユーザの特性を適切に踏まえてシステムをデザインしないと、かえって不安全なことになりかねません。真に有用なシステムをデザインできるためには、センサ、制御則、ハードウェアなどのいわゆる工学的な知識・技術と、人間の生体的、心理的機能・特性を広く・深く理解することが必要です。ヒューマンファクターのエンジニアは、言ってみれば、オーケストラの指揮者のように、個々の要素技術（楽器）を理解したうえで、全体の調和を図ることができなければなりません。「ヒューマンファクターのエンジニアはコンダクターたれ」が私のモットーです。
社会工学（大澤 義明）
Socio-Economic Planning (OHSAWA Yoshiaki)

OHSAWA Yoshiaki, Ph.D.
Dean, Graduate School of Systems and Information Engineering
Professor, Institute of Policy and Planning Sciences
University of Tsukuba

E-mail address: osawa.yoshiaki.fu@u.tsukuba.ac.jp
URL: http://infoshako.sk.tsukuba.ac.jp/~tj330/Labo/koshizuka

移動革命と都市計画
都市・地域・環境の課題を計量的アプローチにより分析することで地域課題解決に取り組みます。既存の理論や汎用的分析手法にとらわれることなく、地域性や課題特性を踏まえ理論的手法を選択し（場合によっては開発し）、理論と実践を両輪とする学際研究を目指します。研究テーマは、都市計画に関する全般であり、最近では、移動革命、インフラ維持管理、地域間税競争、住民投票の効率性、都市景観の計量分析、自治体間広域連携、IoTを用いた都市計画、持続可能な自治体制度に力点を置いております。

Mobility Innovation and City Planning
In order to solve urban and regional problems, qualitative and interdisciplinary approaches are utilized. Regardless of existing academic theory or general analysis methods, theoretical methods (in some cases, we create them) are chosen based on characteristics of the region and the problem from practical and theoretical. Although research theme is general about city planning, recently, the followings topics are studied: mobile innovation and urban planning, civil infrastructure management and maintenance, tax competition and harmonization, efficiency of referendum, quantitative analysis of cityscape, wide-area cooperation among local governments, city planning with IoT, and sustainable system of local government.

コープレーションプログラムと高専
Research on H₂ Energy
LEGO model on Tsukuba Science City
Alliance with Kashima Antlers

Joso–City 2019 Symposium
Football with Teshio Residents

30
人々の行動を計算論的に理解し物理的に支援する

人々の残存機能や、本来有する能力を引き出すための技術であるサイバニクス、および人による脳神経系を通じた情報と機械系の機能を融合する人工知能の研究を行っています。装着型ロボットにより人の動作を支援するロボット工学、人々の行動を顕在化し学習を支援するとともに、意思や感情の理解を深化するセンシング技術、個人のビッグデータを予防や行動変容に活かすIoH/IoT技術を中心とする人間拡張やインタラクションの技術を、医工融合分野や発達支援分野へ応用する研究を行っています。人の物理・生理／病理・心理学的な深い理解に基づき、工学及び情報学的な手法により人々の機能改善や行動形成を支援する新しい学問分野や新産業の開拓に挑戦しています。

Human Technology for Understanding and Shaping Behaviors

The research of our team includes artificial intelligence, Cybernics, wearable robotics and devices, affective computing, social robotics and assistive robotics with a particular emphasis on machine learning, pattern classification and dynamical modeling approaches. A special emphasis is laid on the design of empowering people, particularly for elderly, adults and children with special needs. Cybernics technology brings out latent human capabilities and potential abilities of people. AI for bridging between human neural systems and machine. Robotics, sensing, and IoH (Internet of Human)/IoT technology to support human actions are applied to in medicine and special education.

車椅子のライフスタイルを変革するテクノロジー
Standing Mobility Unlimited
Changing the life style of people forced to be seated

ロボットにより歩行を支援するヒューマン・ロボティクス
Human Robotics
Science & technology behind Robot-assisted locomotion

人工知機能体下を測る：個人のビッグデータを予防医学へ
AI measures swallowing
AI/IoH wearable health tech to prevent aspiration pneumonia

表情から情動を推定するウェアラブルデバイスの開発
Science of smiles
Wearable affective computing for understanding social interaction

人間拡張技術やインタラクション技術を、医工融合分野や発達支援分野へ応用する
Challenge to transfer technologies to society in engineering, medicine and developmental support
人と機械の一体化技術

人的身体機能の獲得・補助・改善するロボット/デバイスの開発に焦点をあて、基礎研究から、実現場での研究開発、臨床・実証研究へと社会実装までを視野に入れて研究開発を推進し、広く社会へ貢献していく人支援機器/デバイスの開発を目標としています。人の身体機能・構造・生理特性、人を取り巻く実環境を十分に理解と、ロボット技術、情報技術を駆使し、生体情報センシング、バイオフィードバック、人-機械系のインタラクションを活用した親和性の高い人-機械一体化システムの構築を目指します。研究フィールドとして、身体機能の獲得・改善・補助に関する医療・ヘルスケア分野、重作業・ストレスの軽減などの介護・労働分野、アスリートに対する運動・感覚提示などの競技・障がい者スポーツ分野など、様々な分野への展開を進めて行きます。

Integration between Human and Machine

We are developing human support system and technology focused on medical and health care field for physical function improvement or physiologic function examination, labor and care field for reducing heavy works, and sports field to present motion and sensation to various athletes. It includes human-machine integration system, biological motor control system, biological/physiological system analysis, robot treatment technology, motion and skill learning support system, robot safety technology. We conduct research and development of the human support systems to contribute to real social world by integrally implementing fundamental researches related with proof of concept, applied researches for actual use and safety, and empirical study to investigate the effectivity in actual environment.
Application of image processing technology to medical and welfare fields

In our laboratory, we are focusing on creating medical image processing systems and sensor-based welfare systems as follows:

1) Analysis of swallowing and elucidation of dysphagia based on videofluorography (Fig.1)
2) Development of assistive systems for the visually impaired based on RGB-D sensors and smartphones (Fig.2)

Please contact us, if you are interested in these research themes.
生物模倣モデルの実社会システムへの応用

社会システムの構造を知るために様々な数理的手法（モデル化、シミュレーション、理論解析）を駆使して研究しています。特に、生物の巧済な仕組みに着目し、それらを参考にした理論やモデルの構築と、その実社会システム（交通、エネルギーマネジメントなど）への応用可能性を検討しています。具体的には、脳や循環器などを複雑なネットワークシステムとしてとらえ、その生理学的知見をもとに、IT、交通インフラ、次世代パワーエレクトロニクス、革新的疾病治療法などの幅広い分野へ応用可能な理論の構築を目指しています。近年の人工知能技術は、神経回路網の工学的応用から生まれた技術といえます。

Application of bio-inspired model to real world systems

In our laboratory, various mathematical approaches such as modelling, numerical simulation, theoretical analysis are focused in order to understand the mechanism and structure of real world systems. Specifically, bio-inspired or bio-mimetic model is a key concept of our research group so that we are aiming to propose basic theory and models of real world systems, e.g. traffic systems, energy management systems, and so on. For example, we consider the brain and cardiovascular systems as a complex network system and based on the physiological knowledge on those systems, we try to invent a theory applicable to a wide variety of field ranging from engineering to medicine, namely IT, traffic infrastructure, next generation power electronics, innovative disease treatment. Recent development of artificial intelligence technologies is derived from neural networks applied to engineering systems.

Neural Networks for phase reconstruction of magnitude spectrograms

1. Adversarial loss

2. Similarity metric measured in hidden layer of D
計算知能学とマルチメディア処理
〜世の中を快適にするためのマルチメディアのスーパーインフラをつくりあげる〜

が大局的な研究戦略になります。この目標の下、日夜研究に取り組んでいます。より具体的には、インターネット上を流れる膨大で様々なメディア（テキスト、画像、音）やデータ（医療、公共サービス、金融）、それを生み出すデバイス、消費するデバイスを含め、計算知能学（AIを含むより広義なインテリジェンス）を使って、いかに人々の生活を「本質的」によりよいものにしてゆくのかを、産業としての視点、また実用から基礎理論の視点で、幅広く研究しています。さらに多様な分野を、アセットからデータ連携、倫理・法的ハードルの解消、ルール策定などのデータアーキテクチャにも興味を持って取り組んでいます。

Computational Intelligence and Multimedia Processing

"A comprehensive research strategy is to create a super multimedia infrastructure to make the world a better place."

Under this goal, we are engaged in research day and night. More specifically, we use computational intelligence (broader intelligence including AI) to study how to make people's lives better "essential" from an industrial point of view and from a practical to basic theoretical point of view, including the enormous variety of media (text, images, and sounds) and data (healthcare, public services, and finance) flowing on the Internet, the devices that produce them, and the devices that consume them. We are also involved in a wide range of areas with interest in data architecture, including asset, data collaboration, elimination of ethical and legal hurdles, and rulemaking.
HUMAN-AGENT INTERACTION (OSAWA HIROTAKA)

OSAWA Hirotaka, PhD in Engineering.
Assistant Professor/Researcher
Faculty of Engineering, Information, and Systems/Center for Artificial Intelligence Research
University of Tsukuba

E-mail address: osawa@iit.tsukuba.ac.jp
URL: http://hailab.net/

Al cares Human: Utilizing Humanlike Attitude in Artificial System

Human-agent interaction (HAI) has become an important field in the field of human-computer interaction (HCI). The agent in HAI behaves with users as if it has its own intentions. It triggers users' social responses, and instructs users through social channels. The use of HAI is widespread from the field of entertainment to medical purposes. For example, several agents have tried to solve dementia and autism through their behaviors. We defined an agent as an artificial social actor that is accepted by users through her/his intentional stance, based on Dennett's Intentional Stance, whether users are conscious or unconscious of the fact.

The goal of our lab is to proposing several usage of agent and agency to the society. Human-agent interaction is on the intersection of artificial intelligence, human interface, cognitive science and other related studies. Everything related to the HAI is our target. For example, what kind of expression evoke a user as an agent (like shape, motion, behavior, and auditory and visual changes), how to create credible agent, and the mutual behaviors of agents and effect for users.
我々の研究グループでは、数値解析および行列計算を基盤とした機械学習アルゴリズムの開発を進めています。大規模シミュレーションの計算時間の大部分は巨大な行列の線形方程式や固有値問題などの基本的な問題の求解に費やされており、我々のグループではこれらの大規模行列計算に対する並列数値計算法の開発を行っています。また近年では、これらの行列計算を基盤とした機械学習アルゴリズムやディープニューラルネットワーク計算法を独自に開発しており、医療データを始めとして様々なデータ解析への応用を進めています。

Numerical analysis & machine learning based on matrix computations

Our research group has been developing numerical analysis and machine learning algorithms based on matrix computations. One of the most time-consuming parts of large-scale simulations is matrix computation including solutions of linear systems and eigenvalue problems. We have been investigating efficient and parallel numerical algorithms for computing such large-scale matrix computations. Recently, we have also been developing original machine learning and deep neural network algorithms based on matrix computations and applying some real-world problems including medical data.
Numerical Methods for Matrix Problems

My studies have involved matrices (arrays of numbers, symbols, expressions, arranged in rows and columns) and include linear least squares problems, linear ill-posed problems, linear systems of equations, optimization problems, and eigenvalue problems. My main interests are on the design of numerical algorithms for these problems, their convergence and error analyses, and their applications. The underlying fundamentals are linear algebra, matrix analysis, and numerical computations. In particular, I’m interested in solving the singular cases which are regarded as difficult in theory and practice.

Selected publications


Fig. CPU time [second] versus relative residual
細胞の恒常性維持の分子メカニズム

細胞に、温度・pHなどの環境変化や栄養源飢餓などのストレスが生じると、それに対応する細胞応答が起こることで、細胞の恒常性が維持される。私たちの研究室では、単細胞真核生物である出芽酵母(\textit{Saccharomyces cerevisiae})を用いて、「遺伝子発現の転写後制御」と「細胞内シグナル伝達系」の観点から、細胞の恒常性維持の分子メカニズムの研究を行っています。具体的には、(1)酵母と動物細胞におけるRNA結合タンパク質による遺伝子発現の転写後調節機構、(2)RNA局在と局所的翻訳の制御機構、(3)小胞体ストレス応答の制御機構、(4)小胞輸送による前胞子膜形成の分子機構について、研究を行っています。

Molecular Mechanism of Cellular Homeostasis

In our laboratory, we are focusing on understanding the molecular mechanisms and the physiological functions of the following processes. (1) Post-transcriptional regulation of gene expression by RNA-binding proteins. (2) Molecular mechanism of mRNA localization and local translation regulating cell polarity, asymmetric cell division, and cell-fate. (3) Regulation of the endoplasmic reticulum stress response by protein kinases. (4) Prospore membrane formation by vesicle docking.

ヒューマニクスの学生へのメッセージ

酵母は、医学・生命科学の様々な研究領域で、真核細胞のモデル生物として利用されています。酵母とヒトの共通性を外見から見いだすのは難しいですが、生命現象の基本的な分子機構は驚くほど保存されています。酵母を研究することにより、真核細胞の基本的な性質について知ることができます。大隈良典先生のオートファジーの分子機構の発見（2017年ノーベル医学生理学賞）は有名な酵母研究の成果です。酵母の実験系は、生物初心者にもハードルが低く、実験に入ることができます。また、酵母はゲノムレベルの解析が容易なことから、システムバイオロジーの実験材料にも使われています。

Message to Humanics students

Yeast is known for its commercial and industrial applications (fermentation and compound synthesis). Also, many biological processes are evolutionarily conserved from yeast to human, making it an ideal model organism for research. It is affordable and grows rapidly, making systems approach and high-throughput studies possible.
再生幹細胞生物学（大根田 修）
Regenerative Medicine and Stem Cell Biology (OHNEDA Osamu)

私たちの研究室では、治療効果の高い組織幹細胞の臨床応用を目標に再生医学研究を行っています。組織幹細胞は生体内に存在し、再生能力や多様な細胞に分化する能力を有しています。当研究室では主に間葉系幹細胞（MSC）と血管内皮前駆細胞（EPC）を用いて研究を行っています。しかしながら、幹細胞移植の治療効果は、年齢・病状・薬物治療歴等の様々な患者背景に左右されます。よって当研究室では、組織幹細胞のポテンシャルを最大限引き出すことを目的として、患者背景の違いが組織幹細胞に及ぼす影響および加齢による影響について詳細な分子メカニズムの解明を行っています。

Analysis of Tissue Stem Cells derived from Patients

Our laboratory mainly focus on the development of tissue stem cells for clinical application. Tissue stem cells are undifferentiated cells found in variety of tissues, which bear immense potential in the form of a long-time rejuvenation ability, and differentiation potency to several type of cells under the right induction. However, in clinical setting, the success of stem cell re-transplantation depends on the donor's background; factors such as age, pathological condition or drug consumption. Driven to harness the best potential of tissue stem cells, our laboratory aim to deciphering molecular mechanism on either how tissue stem cells could function or deteriorate depends on their backgrounds.
Molecular Neurobiology (MASU Masayuki)

MASU Masayuki, M.D. & Ph.D.
Professor
Laboratory of Molecular Neurobiology,
Faculty of Medicine,
University of Tsukuba

E-mail address: mmasu@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/basic-med/molneurobiol/

Molecular Mechanism of Neural Circuit Formation

The nervous system regulates perception, cognition, and behavior through the complex network in which an enormous number of neurons are connected via synapses. Our research group is interested in the molecular mechanisms that regulate the formation of the neural network and acquisition of brain functions. We study the roles of axon guidance molecules and sugar chains in neural network formation by using genetically modified mice. We take a multidisciplinary approach involving molecular biology, biochemistry, genetic engineering, neuroanatomy and neurobehavioral methods.
遺伝医学（野口 恵美子）
Medical Genetics (NOGUCHI Emiko)

NOGUCHI Emiko, Ph.D. M.D.
Professor
Faculty of Medicine
University of Tsukuba

Email address: enoguchi@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/basic-med/m-genetics/

ゲノム解析を通じた病態解明と治療法の探索

ヒトのゲノム配列の多様性は私たちの顔かたの違いや病気のなりやすさ、薬の効きやすさ等、様々な影響を与えています。私たちの研究室では特にアレルギーなどの免疫関連疾患を中心として病気のなりやすさ、なりにくさにつながるような遺伝子の変化についての研究を行っています。近年の次世代シークエンサーの開発などのゲノム解析技術の進歩により多くのゲノムデータが日々産出されています。それらのデータを利用してアレルギー疾患などのいわゆる“ありふれた疾患”についても疾患発症の予測精度を高めたり、新たな治療薬の開発などにつなげることを目指しています。

Differences in our DNA sequence are responsible for the differences in our appearance, susceptibility to diseases, and variability to drug response. The focus of our research was to identify novel genetic variants associated with allergic diseases/immune-related diseases and to elucidate the associated pathways by genome analysis. Big genetic data has been generated by next generation sequencing and array-based genotyping technique in recent years. Using this big data, we aim to improve our ability to predict common diseases and new treatments.

Genome-wide association analysis

HLA-peptide binding assay
(diseases treatment)

Polygenic risk score
(disease prediction)
橋渡し・臨床研究学 (荒川 義弘)

Translational and Clinical Research (ARAKAWA Yoshihiro)

ARAKAWA Yoshihiro, Ph.D.
Professor and Director
Tsukuba Clinical Research and Development Organization (T-CReDO),
Advisor to the Director of Tsukuba University Hospital,
University of Tsukuba

E-mail address: arakawa-tky@umin.ac.jp
URL: http://www.s.hosp.tsukuba.ac.jp/t-credo/

時代に即した橋渡し・臨床研究のあり方を探る

基礎研究の成果を患者に応用できるようにするには、多くのステップと多数の専門家の協力が必要であり、臨床研究の段階では法律に則った開発が必要である。また、疾病構造は国ごとに異なり、医療技術の進歩とともに急速に変化を遂げており、開発品目のモダリティも低分子医薬品から抗体医薬、再生医療、遺伝子治療と多様になっている。さらに、最近は難病や希少疾患を標的に、ゲノム医学やビッグデータを応用した研究開発も活発になっている。T-CReDOは国の審査承認機関である医薬品医療機器総合機構（PMDA）と連携大学院協定ならびに包括連携協定を結び、時代に即した開発のあり方を探索し、研究者に対し出口戦略の支援や起業家育成プログラム等の人材育成を行っている。また、我々自身でもゲノム医療やロボットの開発に係る研究などいくつかの臨床研究を実施している。

Exploring the New approach in Clinical and Translational Research

In order to apply the basic research achievements to patients, the development according to the regulation is required. It takes long time and requires huge resources. In addition, the disease structure varies from country to country, and is rapidly changing with advances in medical technology. The modalities of development items are varied from small molecule drugs to antibody drugs, regenerative medicine, and gene therapy. Furthermore, recently, research and development using genomic medicine and big data has been activated, targeting incurable diseases and rare diseases. T-CReDO establishes a agreement for joint graduate course and a comprehensive cooperation agreement with Pharmaceutical and Medical Devices Agency (PMDA), which is a Japanese review and approval agency, and is searching for the ideal way of development. Taking such advantages, we provide the support of researchers in development and many training programs including the one for entrepreneurs. In parallel, we are conducting some clinical research by ourselves such as the development of robots and genome medicine.

The principle is to set up Target Product Profile (TPP) by identifying the Clinical Needs, and to promote the Technology Transfer as early as possible by promoting Open Innovation.

According to the modalities, standard strategies are different.
Lipid research in the light of lipid quantity and quality
~ medical strategy towards biological events and pathologies~

Metabolism is one of the fundamental biological events at the level of cells, tissues, and body. Recently, more attention is being individually gained in the light of metaflammation, immunometabolism, cancer metabolism, and brain science. We have studied lipid metabolism, and through SREBP, CREBH, and Elovl6 similarly experienced our own extensions in different areas. Especially, Elovl6, identified as a novel long fatty acid elongase regulates fatty acid composition. Lessons from the KO mice implicate that this "lipid quality" regulates insulin resistance, life-related diseases, and furthermore, a wide variety of biological phenomenon, which tempts us to extend a novel medical strategy with elovl6, fatty acid chain length, and potentially food fatty acid composition as targets. Another target of concept is energy sensing system. Recent data suggest that energy sensor molecules including CtBP2 sense hub metabolite and regulate energy metabolism inside the cells and potentially connecting inter-organ metabolism. In Humanics, we attempt to understand molecular structure and mechanism through fusion with new areas.

2. Transcriptome network analysis identifies protective role of the LXR/SREBP-1c axis in murine pulmonary fibrosis. JCI Insight. 2019
4. SREBP1 Contributes to Resolution of Pro-inflammatory TLR4 Signaling by Reprogramming Fatty Acid Metabolism. Cell Metab. 2017
血液内科（千葉 滋）
Hematology (CHIBA Shigeru)

CHIBA Shigeru, Ph.D. or M.D.
Professor/Chair
Department of Hematology,
Faculty of Medicine,
University of Tsukuba

E-mail address: schiba-tky@umin.net
URL: www.ketsunai.com

血液がんの克服
〜分子メカニズムからベッドサイドへ

造血器腫瘍（白血病や悪性リンパ腫など）のゲノム異常の解析や、腫瘍の微小環境の解析を通じ、細胞や分子レベルでの病態の解明に基づく治療法開発を目指す。化学療法や造血幹細胞移植でダメージを受ける正常造血とその再生、あるいは骨髄微小環境に関する研究も含まれる。材料としては、患者から得られた血液、骨髄、生検組織などの生体材料の他、培養細胞や遺伝子改変マウスなどを用い、細胞生物学解析、DNA、RNA、タンパク質の解析、免疫染色など様々な技術を駆使して研究を行う。

Getting over blood cancers
〜 From molecules to bedside 〜

Our research ultimately aims at developing new treatment methods for hematologic malignancies such as leukemias and lymphomas, based on the understanding of cellular and molecular pathophysiology of these diseases through the analyses of genetics and tumor microenvironment. Notably, the blood production system is damaged by chemotherapy and hematopoietic stem cell transplantation for the treatment of hematologic malignancies. Our research scope includes regeneration of hematopoiesis, focusing on the bone marrow microenvironment. To these ends, clinical materials obtained from patients, such as blood, bone marrow, and biopsied tumor, and cultured cells and genetically engineered mice will be used for the cell biological and immunological analyses and analyses of DNA, RNA, and protein.

Materials from patients
DNA sequencing, etc.

Identification of genetic abnormalities
Characterization of cells
Clinical trial
Drug evaluation
Modeling diseases in mice
脳神経外科疾患の克服、再生をめざして

脳神経外科研究グループでは脳腫瘍、脳卒中、機能的脳神経外科疾患、神経画像に関する基礎研究、臨床研究、医工連携研究を行っています。悪性脳腫瘍に対する自家腫瘍ワクチン、不活化ウイルスの研究、悪性脳腫瘍に対する中性子捕捉療法の研究、各種脳腫瘍における遺伝子解析と治療応用の研究を行っています。脳卒中に対しては歯髄幹細胞を用いた再生医療、ナノ粒子の研究、ロボットスーツHALを用いた脳機能再生の研究、嚥下モニター装置(GOKURI)を用いた嚥下機能の評価と治療への応用、新規ステントの臨床研究、スポーツ頭部外傷の治療研究、などを行っています。その他、神経画像を用いた脳機能の評価と治療応用の研究を行っています。

Aiming overcome of Neurosurgical Disease

In Neurosurgical Research group, various clinical and basic research projects in Neuro-oncology, Neurovascular disease, Functional neurosurgical disease have been performed. Neuro-oncology; Autologous tumor vaccine therapy and virus therapy, Boron neutron capture therapy, genetic analysis and its application Neurovascular disease; regenerative therapy using dental pulp stem cells and nanoparticles, robotic suits HAL, swallowing device (GOKURI), clinical research of new stent devices. Clinical research for Sports concussion

Ref.
ロボットスーツHALを用いた機能再生治療

ロボットスーツHAL（Hybrid assistive limb）は、筑波大学システム情報系で開発された外骨格型の動作訓練支援ロボットです。筑波大学附属病院では、HALを用いた機能再生治療の安全性・有効性を検証するため、様々な疾患に対してHALを用いた臨床研究を行ってきました。

現在、われわれの施設で進めている整形外科関連の臨床試験の対象は下記のごとくです。①脊髄症術後の急性期、②脊髄症術後の慢性増悪（脊髄萎縮）、③脊髄損傷・障害（急性期・慢性期）、④頚椎術後の上肢（C5等）麻痺、⑤腕神経叢損傷（神経移行術後）、⑥脳性麻痺、⑦姿勢異常（首下がり）、⑧人工膝関節・高位脛骨骨切り術（術後）、⑨肩関節機能障害。加えて、腰HAL、足関節HAL、手関節HALの研究も行っています。今後とも医工連携での研究を進め、脊椎・関節患者の病態に合わせて、最適なロボット治療を選択して、新たな治療法の開発を進めて行きたいと考えております。

Functional regeneration therapy using robot suits HAL

HAL is a new wearable exoskeletal robot suit that interactively provides motion according to the wearer’s voluntary drive. Various types of HAL, including for lower limbs, for single joints, and for lumbar support, have been developed. In the Tsukuba University Hospital, under tight medicine and engineering cooperation, we have progressed several clinical trials and researches of functional regeneration therapy using HAL for intractable musculoskeletal diseases including spinal cord injury/lesion, cerebral palsy and joint diseases.
心臓再生（家田 真樹）
Cardiac regeneration (IEDA Masaki)

IEDA Masaki, Ph.D. or M.D.
Professor and Chair
Department of Cardiology, Faculty of Medicine,
University of Tsukuba

E-mail address: mieda@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/clinical-med/cardiology/

我々は世界で初めて、マウス非心筋細胞（線維芽細胞）を拍動する心筋細胞に直接転換できる心筋リプログラミング遺伝子群（Gata4, Mef2c, Tbx5）を発見しました（Ieda et al., Cell 2010）。その後、ヒトでも同様の遺伝子群の同定に成功し、さらに心筋リプログラミング遺伝子による治療で、心筋梗塞マウスの梗塞巣が縮小して心機能が改善することを発表しました(Miyamoto et al., Cell Stem Cell 2018)。またこの細胞リプログラミングという新しい研究手法を応用して、心臓の発生に関わる新規遺伝子Tbx6を同定し、同遺伝子が心筋のみならず血管の形成や、さらに循環器疾患にも関与する可能性などを明らかにしました(Sadahiro et al., Cell Stem Cell 2018)。このように細胞移植を必要としない新しい心臓再生法の開発や、循環器疾患の病態解明を目指して、独創的な研究を展開しております。

We first discovered that a combination of cardiac-specific transcription factors—Gata4, Mef2c, and Tbx5—directly reprogrammed cardiac fibroblasts into induced cardiomyocyte-like cells (iCMs) in vitro without reverting to a pluripotent stem cell state (Ieda et al, Cell, 2010). The same combination of cardiac transcription factors could also directly reprogram resident cardiac fibroblasts into iCMs in situ and improve cardiac function after myocardial infarction in mice. Thus, cardiac reprogramming can be a potential approach for cardiac regeneration in heart failure patients.
細胞分化におけるLarge Maf転写因子群の機能解析

Large Maf転写因子群は、遺伝子の発現を調節する転写調節因子ですが、ヒトおよびマウスではMafA、MafB、c-MafおよびNrlの4種類が知られています。これらの因子は、目、内耳などの感覚器、副甲状腺、膵臓などの内分泌器、骨、軟骨、筋肉などの運動器、腎臓など泌尿器系に発現しており、それらの臓器の細胞分化と機能維持に重要な働きをしていることが明らかとなっています。またこれらの遺伝子異常により、ヒト疾患が発症することも報告されています。ゲノム編集を用いた遺伝子改変マウスを用いて、Large Maf転写因子群の細胞分化と機能維持、疾患発症における機能解析を行なっています。

Functional Analysis of Large Maf Transcription Factors in Cell Differentiation

Large Maf transcription factors are transcriptional regulators that control the expression of target genes. Four factors, MafA, MafB, c-Maf and Nrl are known in both human and mouse. These factors are expressed in sensory organs such as the eyes, inner ear, endocrine organs such as parathyroid, pancreas, exercisers such as bones, cartilage and muscles, urinary system such as kidney, and are used for cell differentiation and function maintenance of these organs. It is also reported that human diseases develop due to these genetic abnormalities. Using genetically modified mice by genome editing, we are performing functional analysis of Large Maf transcription factors in cell differentiation, function maintenance and disease onset.
がん細胞の持続的増殖をもたらす幹細胞性誘導の機構

がんの最も重要な特徴は、細胞数が増え続けることにある。正常組織でも、骨髄の造血細胞や腸粘膜上皮などは、持続的に分裂増殖を行なっていますが、これらの組織では、細胞分裂によって増える細胞の数と細胞死によって失われる細胞の数が一致してバランスがとられ、総細胞数の動的平衡が保たれます。私は、がん組織では、幹細胞性誘導という現象によって細胞数が持続的に増え続けるようになることを見い出し、その分子メカニズムを明らかにしてきた。幹細胞性誘導に関わるGPNMBやTMEPAIという分子を標的としたがん幹細胞標的治療を開発して、再発のないがん治療を実現することを目指しています。

Stemness Induction as a Mechanism of Autonomous and Tumorigenic Cancer Cell Proliferation

Cancer is characterized by autonomous and tumorigenic cell proliferation. Even in normal tissue, such as bone marrow hematopoietic cells and intestinal epithelial cells continue cell division but these normal tissues make dynamic balance between cell division and cell death to keep stable total cell numbers. We have identified stemness induction observed in cancer cells is a mechanism that makes autonomous and tumorigenic cell proliferation of cancer cells and trying to elucidate the molecular mechanism of this phenomenon and to develop a cancer stem cell targeting therapy in order to achieve a relapse-free cancer treatment.
The goal of our research is to understand neural mechanisms underlying cognition such as attention, memory, prediction, learning and decision making. In particular, we are investigating the role of monoamine systems, such as dopamine and serotonin, in cognitive functions. Experiments in our laboratory center on the brain of awake behaving monkeys as a model for similar systems in the human brain. Using electrophysiological, pharmacological and optogenetic techniques, we examine what signals monoamine neurons convey while monkeys are performing cognitive tasks and how the signals, released monoamine, work in targeted brain areas to achieve the tasks. These studies will provide more mechanistic accounts of cognitive disorders.
粒子線治療のための技術開発

粒子線治療は世界的な注目を集めており、世界で多くのプロジェクトが開始されています。筑波大学は陽子線治療で35年の経験があり、高度な治療技術の研究実績があります。また、この分野の専門家の教育を行ってきました。陽子線、重イオン線、中性子捕捉療法を含む粒子線治療のために、癌治療の新技術開発を目指します。

Development of new techniques for particle therapy

Particle therapy has been getting worldwide attention, and many projects are started in the world. University of Tsukuba has 35 years experience in proton beam therapy, has been investigating advanced treatment techniques and has performed education of specialists of this field. For the particle therapy including proton, heavy ion and neutron capture therapy, we are developing new techniques to perform the cancer treatment.
Face `all-time-phase of radiation disasters'

In the event of radiation disasters, the necessary knowledge and skills are different depending on the time phase: (1) `emergency medical care' and `radiation protection' after the occurrence of radiation disasters, (2) `radiation measurement', `radiation protection', `radiation emergency medicine' and `crisis communication' in the subsequent phase, (3) `epidemiology', `statistics', `decontamination', `risk communication' and `mental health' in the recovery period, and (4) `disaster training' in the pre-preparation stage. Our group is working on education of the specialist of radiation disasters with the `all-time-phase of radiation disasters' as a key word. Research themes are radiation measurement, radiation protection, radiation control, health risk management, etc., aiming for developments of new technologies and research aiming at the establishment of new evidence.
地域産業活性化を目指す橋渡し研究
機能性食品・先端技術を応用した医療機器などの開発

橋渡し研究、臨床研究に取り組むことにより、より質の高い医療や健康支援活動を実現し、地域住民の健康な生活に貢献します。また、地域発の機能性食品、AIなどの先端技術を応用した医療機器などのシーズ開発を推進し、地域産業の活性化を目指しています。近年、倫理的・科学的に妥当な方法で実施する、高品質の臨床研究の社会的ニーズはますます高まっていますが、人材が不足しています。そのため本研究室では、臨床研究に関わる人材をOJT教育にて養成し、社会に供給する教育活動にも積極的に貢献しています。

Translational research for activation of region’s industry
Development of functional foods and cutting-edge medical devices

Major activities of our group are,
1. Development of effective prevention treatments such as functional foods for lifestyle-related diseases,
2. Construction of a seamless platform for clinical translational research in Tsukuba Clinical Research and Development Organization (T-CReDO),
3. Education of experts of integrative celerity research process for clinical translational research.

Our major scientific interests are,
1. Effective and practical management of technology in clinical trials field,
2. Effective prevention treatments for lifestyle related diseases.

The following are examples of projects for students in doctoral or master’s programs.
1. Study on amelioration of process for reliable clinical translational research
2. Extraction of problematic points in specific clinical trials and proposition of solution
Development of Healthcare Innovation Ecosystem

Nevertheless a number of research achievements by talented scientists with tremendous efforts, the productivity of medical products including pharmaceuticals, medical devices, and regenerative medicine products are decreasing. Manufacturers are seeking innovative scientific achievements to be their flagship products from academia. We provide an educational course of translational research for scientists and business managers, who will eventually form a startup team to bridge the gap between the scientific achievement to the product development. The program is named "Research Studio powered by SPARK", which will be a platform as a startup accelerator to be a part of innovation ecosystem from Tsukuba area in alliance with Boston, San Diego and SF Bayarea. Join us to take your science into the real market for medical innovation!
医学医療系 人間総合科学研究科
Faculty of Medicine/Graduate School of Comprehensive Human Sciences

血液腫瘍学分野（坂田（柳元）麻実子）
Hematology-Oncology (SAKATA-YANAGIMOTO Mamiko)

SAKATA-YANAGIMOTO Mamiko, Ph.D. or M.D.
Associate Professor,
Department of Hematology,
Faculty of Medicine,
University of Tsukuba

E-mail address: sakatama-tky@umin.net
URL: http://www.ketsunai.com/english/

血液細胞と免疫の出会い
～造血システムを制御して、疾病の制御を目指しませんか～
造血システムに由来する血液細胞は、からだの“炎症”や“免疫”を司る中心的な役割を果たしています。血液細胞はときにゲノム/エピジェノム異常を獲得することで、“白血病”や“悪性リンパ腫”といった様々な血液がんを発症します。さらには、血液がん以外のさまざまな固形がん、自己免疫疾患、アレルギー、感染症といった多くの疾病において、血液細胞は炎症細胞へと最終分化（≒変身）して疾病の中心部位へと遊走し、免疫を司ることで疾病を誘発/悪化させると考えられています。私たちの研究室では、臨床サンプルや独自に樹立したマウス白血病/リンパ腫等の実験モデルを材料とし、次世代シークエンスを用いた体細胞変異解析やシングルセルシークエンス解析等の技術を駆使することにより、血液がんの仕組みについて明らかにしています。さらには、血液細胞を制御することで、免疫システムの変調を促し、多様ながんを制御する方法を開発しています。

Crosstalk between blood cells and immunity
Blood cells derived from the hematopoietic system play a central role in controlling the “inflammation” and “immunity” of the body. Blood cells acquiring genetic/epigenetic events eventually develop various types of blood cancers such as “leukemias” and “malignant lymphomas”. Furthermore, in many diseases other than blood cancers, such as solid cancers, autoimmune diseases, allergy and infectious diseases, blood cells are terminally differentiated into inflammatory cells, migrate to the central part of diseases, and finally control the local immunity. Our laboratory has been clarifying the mechanisms of blood cancers using the next generation sequencing technologies: somatic mutation analysis and single cell sequencing. Furthermore, by controlling blood cells and their immune response, we are trying to establish novel methods to control various cancers.

Blood system

Discovery of novel mutations
Next-generation sequencing
Understanding of immune environments

Blood cancers “Leukemia/lymphoma”

Cancers
Autoimmunity
Infection
Migration

Hematopoietic stem cells
Self renewal
Terminal differentiation into inflammatory cells

Hematopoietic progenitors

56
感染生物学（川口 敦史）
Infection Biology (KAWAGUCHI Atsushi)

新型インフルエンザの出現と病原性発現の分子基盤
A型インフルエンザウイルスは、自然界ではカモなどの水禽類で維持され、水禽類から陸生の鳥や哺乳動物へウイルスは伝播します。しかし、鳥由来のウイルスが種の壁を超えて、ヒトで病気を引き起こすメカニズムは明らかにされていません。我々は、従来のウイルス学だけでなく、構造生物学や膨大な疫学情報を背景にしたバイオインフォマティクスを活用して、新型インフルエンザの出現予測や病原性発現機構の解明をめざしています。また、得られた成果をもとに、抗インフルエンザ薬の開発も展開しています。

Molecular basis of emergence and pathogenicity of pandemic influenza
Aquatic birds are the reservoir of influenza A viruses in nature and the source for transmission of influenza A viruses to other animal species. However, the avian influenza A viruses hardly replicate in humans, the molecular mechanism how avian influenza overcomes the species barrier is also unknown. The aim of our study is to clarify the molecular mechanism of species barrier and pathogenesis of influenza virus through multidisciplinary studies between classical virology, structural biology, and bioinformatics using epidemiological data. We also try to develop an anti-viral compound that can block the viral infection.
ゲノム生物学（村谷 匡史）
Genome Biology (MURATANI Masafumi)

MURATANI Masafumi, Ph.D.
Professor
Department of Genome Biology,
Faculty of Medicine,
University of Tsukuba

E-mail address: muratani@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/tmrc/

微量検体のゲノム・エピゲノム統合解析技術の開発と応用
システムレベルでの生命現象の理解に不可欠な定量的・網羅的な情報を収集・解析する上で、ゲノミクスは生命科学研究に必須の手法となりました。私たちのグループでは、宇宙医学・生物学研究とバイオバンク臨床検体のゲノム・エピゲノム解析を主なテーマながら、これらの研究を進める過程で開発された微量検体解析技術とインフォマティクス手法、および運用ノウハウを、様々な共同研究や企業への技術移転など*を通じて応用しています。ゲノム医療、ラボドロイドによる実験の自動化、臨床検査・研究への機械学習の導入をはじめ、社会的に必要とされている課題に対応しながら研究分野を定義し、解析手技や科学的な考え方を実戦で磨きたい方にも面白い環境です。

Technology development for genomics analysis of limited samples
Quantitative data acquisition by genomics technologies and informatics analysis are essential parts of life science. The main research interests in our group is genomics and epigenomics in space medicine and clinical research, with particular focus on development of technologies for limited sample analysis. We also collaborate with clinicians and industry partners* to implement our methods to personalized medicine and automated laboratory testing using AI and robotics. These collaborative projects provide our group members with opportunities to learn real-world technological demands and to shape unique research programs fitting to individual career aspiration.

*MM is Senior Research Fellow of Genome Science Research Center, LSI Medience Corporation through cross-appointment system, and Research Advisor of Robotic Biology Institute Inc.
Implants coated with fibroblast growth factor-2 (FGF-2)-apatite composite layers show enhanced soft-tissue formation, bone formation, and angiogenesis owing to the biological activity of FGF-2.
1) Combine symbolic and numeric computations

Formula manipulation (symbolic computation) is used to analyze continuous modeling and emphasizes exact computation faster. Numerical computation is used to analyze discrete modeling, and emphasizes approximate computation accurately. Concept of symbolic-numeric computation is to treat perturbation input such as polynomial, rational function with floating-point numbers and matrix without distinction. Developing and implementation of algorithm can be studies from mathematical approach using medical data and other actual data.

2) Development and Management of ICT systems, including e-learning

Use of computers/ICT system is indispensable for promoting research. Not only implementation and computation described in above, development of system (including e-learning system) and of contents can be also learned and researched pathing practical work experiments.

(Collaboration: Office of Educational Cloud, University of Tsukuba)
Think and solve the biomedical problems thorough computers

Now the massive measurement technologies convert diversities of life, such as genome, into biological big data. However, we human are ‘ill-equipped’ to extract latent biological meanings from the massive data and solve the biomedical problems. Therefore, our lab is developing methods to think the biomedical problems through the informatics point of view and interpret massive data with the help of computers and AI: (1) AI-based prediction and interpretation of functions of genome sequences, (2) Integrative analyses of massive biological data sets, (3) Single-cell informatics (informatics for single-cell omics data), (4) Evolution of genomes and epigenomes. In addition, we apply informatics and statistics to biological and disease research.
Mysterious biological phenomena are elucidated by bioactive substances

Organic compounds concerning with life and biological phenomena are called "natural products". The investigation of bioactive natural products from plants, animals, and microorganisms is very important to understand the molecular mechanisms for their life and biological phenomena. On the other hand, natural products play an important role in lead compounds for new drug development. My research interests are isolation and structure elucidation of new bioactive substances from plants, animals, and microorganisms and determination of the molecular mechanisms for interesting and mysterious biological phenomena and discovering bioactive substances useful for development of new drugs and providing new biological molecular tools. These research works are essentially required in isolation and structure elucidation of bioactive substances using current chromatographic techniques, spectroscopic analyses, and chemical syntheses.
選択的タンパク質分解はなぜ大事か
細胞内のタンパク質は時空間特性的な制御を受けて選択的に分解されており、その分解制御が細胞周期、ストレス応答など広範な生命現象において必要です。この選択的タンパク質分解を主に担っているのがユビキチン・プロテアソームシステム(UPS)です。私たちの研究室ではUPSがどのように制御されているのかを解明し、様々な生命現象を“タンパク質分解”という側面から捉えようとしています。

The Regulation of Selective Protein Degradation
The proteins in our cells are selectively degraded in a spatiotemporal manner, and such degradation is essential for the regulation of a wide range of cellular events, such as cell cycle progression, stress response, and so on. The major pathway that mediates the selective protein degradation is the Ubiquitin and Proteasome System (UPS). Our laboratory is analyzing the regulatory mechanism of the UPS to understand the physiology of ‘regulated protein degradation’.
Microbial communities demonstrate a wealth of behavior in response to environmental stimuli due to the variety of and interactions between microbes in these communities. Furthermore, they have a significant impact on human life and well-being, highlighting the need for innovative technologies to control microbial community development. We aim to elucidate the behavior of individual bacteria within communities and interactions between communities and to clarify community adaptation to the environment and microbial interactions with other environmental organisms. To achieve this, we will develop novel technologies to image and analyze microbial communities from the individual to the community level. We will clarify the role of heterogeneity and cell-cell interactions within these communities.
生理遺伝学（丹羽 隆介）
Physiological genetics (NIWA Ryusuke)

NIWA Ryusuke, Ph.D.
Associate Professor
Faculty of Life and Environmental Sciences,
University of Tsukuba

E-mail address: niwa.ryusuke.fw@u.tsukuba.ac.jp
URL: https://sites.google.com/view/niwa-lab-tsukuba

幹細胞・生殖・老化・寄生を制御する臓器連関システムの研究
ホルモンと神経は、多くの臓器の機能を連動させながら、個体内外の状態・環境に応答して生命体の生理状態を調節しています。私たちは、この臓器連関システムが生殖や老化、そして寄生にどのような役割を担うのかに関心を持ち、キイロショウジョウバエと寄生蜂を主材料にして研究しています。研究アプローチとしては、遺伝学、生理学、生化学、そしてイメージングの手法を用いています。

また、得られた基礎的知見に基づき、X線結晶構造解析やハイスループットスクリーニング系などを援用した応用指向の研究（創農薬研究）にも着手しています。

Interorgan communication system
to regulate stem cells, reproduction, longevity, and parasitism

The neuroendocrine system coordinates communication between multiple organs to regulate organismal physiology in response to intra- and extra-environmental conditions. Our group has been studying the role of neuroendocrine-dependent interorgan communications in regulating stem cells, reproduction, longevity, and parasitism mainly by using the fruit fly Drosophila melanogaster and its parasitoid wasps. We pursue a combined approach with genetics, physiology, biochemistry, and bioimaging.

Based on the basic scientific data obtained above, we also employ application-oriented research to identify and develop new insecticides by high-throughput screen system and X-ray crystallography.
Mitochondrial biology

Mitochondria are “energy plants” of the cell, producing large amount of ATP from nutrients of foods we eat. Mitochondria contain their own genome, called as mitochondrial DNA (mtDNA). Accumulation of pathogenic mutations in mtDNA decreases produced ATP by mitochondria and induces various abnormalities in whole body. These symptoms are called as mitochondrial diseases. The detailed expression mechanisms of diverse disease phenotypes are not well known, and effective treatments for mitochondrial diseases have not been established. We are investigating the influences of mutations of mtDNA and/or mitochondria-related nuclear coded genes on cellular or biological functions by using animal models or cell models.

Representative pathogenic point mutations

Large-scale deletion

Analyses of
- Mitochondrial functions
- Histopathology
- Disease phenotypes
- Gene expressions
- Protein functions
Medical-engineering collaboration with the molecular fingerprint
~ Label-free molecular imaging by Raman scattering ~

Nonlinear Raman scattering is one of the powerful techniques to visualize living cells and tissues without staining or molecular tagging. In our laboratory, we are aiming at developing a novel molecular imaging method using the nonlinear Raman scattering in order to establish molecular-based diagnosis of cancer, digestive and heart diseases without the need for any exogenous contrast agent.
Human-in-the-loop Big Data & AI (MORISHIMA Atsuyuki)

Optimized Division of Labor for Humans and AIs in Big Data

Disaster prevention, healthcare, education, environments, hunger and poverty – we need to gather and integrate the powers of humans and machines to solve difficult problems we face in our society. Morishima and Matsubara Lab are conducting research toward establishing science and technologies for the fused intelligence, which is achieved by combining the network of billions of humans and AIs and BigData. We aim at not only publishing papers, but also making our society a better place with our research results; we develop platforms based on our research results and work with experts in a variety of domains. So far, we developed optimized solutions that combines humans and AIs in domains such as natural disaster responses, libraries and local governments. We will take this approach in the target domains of the Ph.D. Program in Humanics as well.
Development a novel technology for glycomics and simultaneous cellular analysis

From the microorganisms to the mammals, the outermost cell surfaces of all organisms are covered with glycans, acting as an intermediary role over the conversation between cells and cells. In addition, glycans are called "cell features" because they change with the type and state of cells (differentiation, tumorigenesis etc.) and are also expected as targets of drug discovery. In this way, glycans are attractive molecules, but due to the complex structure, understanding the functions and application of glycans is not sufficient.

In my laboratory, we have been developing technologies to quantitatively and comprehensively analyze the glycome of various cells with extreme precision and resolution by fusing various technologies such as glycan engineering, protein engineering, cell biology, and chemical biology. We have been developing innovative technologies that contribute to society by analyzing glycans of various cells such as stem cells, cancer cells, and microorganisms. If you are interested in research on glycans from basics to applications, let's study together!
ナノ材料科学（中山 知信）
Nanomaterials Science (NAKAYAMA Tomonobu)

NAKAYAMA Tomonobu, Ph.D.
Professor
Grad. School of Pure and Applied Sciences, University of Tsukuba
Deputy & Administrative Director and PI, WPI-MANA, NIMS
Deputy Director, ICYS, NIMS

E-mail address: NAKAYAMA.Tomonobu@nims.go.jp
URL: www.nims.go.jp/NanoFIG/index-j.html

ナノ材料を活用する脳型情報処理
過去数十年に渡るナノスケールの物質・材料の研究は、多くの興味深いナノ材料を生み出しました。今、我々はナノ材料を連結したナノシステムを作り上げ、新しい機能を生み出す段階に来ています。ナノシステムが目指す方向の一つに、脳型の情報処理をこなす材料システムの開発があります。これは、生物の脳に発現する学習・記憶・連想といった高度な機能を、非生体材料から成るナノシステムに持たせようというもので、生体材料を使わずに、生物物性を再現する代表的なシステムはロボット、すなわち機械システムでしょう。最近、シナプスの動作を模倣するデバイスも現れ、ソフトウェアの助けを借りずに思考するシステムの実現は、着実に近づいています。当研究室では、ナノ材料の物性やナノシステムの挙動作をナノテクノロジーを駆使して計測し、その生物機能類似性に着目します。機械システムに人間性を与え、脳科学の進展にも貢献する脳型ナノシステムを一緒に開発しましょう。

Brain-type information processing with nanoscale materials
The research of nanoscale materials over the past few decades has yielded many interesting materials and structures. We are now at the stage of creating nanosystems for emerging new functions by linking such nanomaterials. One of the directions that nanosystems aim for is the development of materials systems that handle brain-type information processing. This is to give high-level functions, such as learning, memorization and associative thinking realized by the biological brains, to nanosystems made of non-biological materials. A typical system that reproduces biological properties without using biomaterials is a robot, namely mechanical system. Recently, devices that mimic synaptic plasticity have also appeared, and the realization of systems that think without software assistance is steadily approaching. In our laboratory, we measure physical properties of materials at the nanoscale and behavior of nanosystems at macroscopic scales with a help of the state-of-the-art nanotechnology and focus on their similarities to biological functions. Let’s develop brain-like nanosystems that gives humanity to mechanical systems and also contributes to the advancement of brain science.
再生医療のための足場材料の開発

けがや病気などで失われた生体組織の再生に重要な細胞足場材料と細胞機能制御材料の研究開発を行っています。細胞足場材料として、生体吸収性合成高分子および天然高分子を用いて多孔質構造や力学強度などを制御した高分子多孔質材料および複合多孔質材料、細胞によって産生される細胞外マトリックスで構成され、ナノ・マイクロ構造をもつ生体親和性材料について研究しています。また、生体組織の再生に重要な幹細胞の機能を制御するため、機能性分子をマイクロパターン化した材料や、生体内の微小環境を模倣した細胞培養材料にも取り組んでいます。

Development of Scaffolds for Regenerative Medicine

We are devoted to the research of biodegradable scaffolds and functional biomaterials for tissue engineering of lost or damaged tissues and organs and for manipulation of cell functions. Porous scaffolds with well controlled pore structures, hybrid scaffolds of biodegradable synthetic polymers and naturally derived polymers and highly biocompatible matrix biomaterials with nano- and microstructures constructed from cultured cells are designed and prepared. Biomaterials that mimic the in vivo nano- and microenvironment surrounding cells and micro-patterned surfaces are created to manipulate cell functions, particularly stem cell functions.

Preparation of porous scaffolds and their applications for regenerated medicine

Hybrid scaffold

Collagen microspone

Synthetic polymer skeleton

Funnel-like porous scaffold

Tissue engineering

Regenerated skin

Regenerated cartilage
物理薬剤学 (川上 亘作)
Physical Pharmacy (KAWAKAMI Kohsaku)

KAWAKAMI Kohsaku, Ph.D.
Professor/Group Leader
Medical Soft Matter Group,
International Center for Materials Nanoarchitectonics,
National Institute for Materials Science
Graduate School of Pure and Applied Sciences, University of Tsukuba

E-mail address: kawakami.kohsaku@nims.go.jp

物理化学的アプローチによる医薬品機能の最大化

物理薬剤学において、活性物質が単独で体内に投与されるのはほとんどなく、その効果を最大に発揮するためには製剤化が行われます。巧みな製剤化によって、医薬品化合物を所望のタイミングで所望の部位に送達し、効果を最大化しつつ副作用を抑えることができます。我々は一連の製剤研究を行っていますが、近年は特に非晶質状態の利用に注力しています。医薬品化合物はその構造多様性から様々な非平衡状態をとることが可能で、物理化学の観点からも魅力的な材料です。我々は医薬品化合物が形成する非晶質状態の構造変化およびその溶解過程の制御を行い、物理化学の基礎に迫るとともに、その知見で治療効果を高める実務的視点も持って研究を進めています。

Physical chemistry for maximizing function of pharmaceuticals

Pharmaceutical compounds are not administered to human body only by themselves but after being formulated for maximizing their function. Sophisticated formulation technologies enable delivery of pharmaceutical compounds to desired sites at desired timing, which can maximize their functions and minimize side-effects. We are conducting series of formulation studies with focus on utilization of amorphous state, as pharmaceutical compounds are attractive for designing glass materials because of their structural diversity. We are investigating non-equilibrium dynamics of pharmaceutical glasses to make progress in basic science of physical chemistry as well as to make contribution to effective drug delivery.
スマートポリマー（荏原 充宏）
Smart polymers (EBARA Mitsuhiro)

EBARA Mitsuhiro, Ph.D.
Associate Professor/Group Leader
Graduate School of Pure & Applied Science,
University of Tsukuba
International Center for Materials Nanoarchitectonics (WPI-MANA),
National Institute for Materials Science (NIMS)

E-mail address: EBARA.Mitsuhiro@nims.go.jp
URL: https://www.nims.go.jp/bmc/group/smartbiomaterials/index.html

スマートポリマーで拓く未来医療
～途上国でも利用可能な医療をめざして～

みなさん、スマートポリマー（スマポ）ってご存知でしょうか？ポリマーとはプラスチックのことです。そのプラスチックの中でも、周りの環境の変化に敏感に応答して（空気を読んで？）自ら性質を変えるとても賢いプラスチックのことをスマポと呼んでおります。私たちは、このような新素材を利用して、未来の医療材料（バイオマテリアル）の研究に取り組んでおります。特に、電気や水などのライフラインが不十分な途上国、被災地、宇宙などでも病気を治せるような医療機器をつくるべく、日々、創造と開発を行っております。

Smart polymer technologies for global health

Most of my research interests focus on developing ‘smart’ biotechnologies using stimuli-responsive polymers that respond to small changes in external stimuli (e.g., Temperature, pH, light, magnetic field, piezoelectric etc.) with large discontinuous changes in their physical properties. These ‘smart’ biomaterials are designed to act as an ‘on-off’ switch for not only newest biomedical applications in developed countries such as drug delivery technologies, gene therapy, affinity separations, chromatography, diagnostics, but also public health in developing countries diagnostics for Malaria, Influenza, and HIV etc.
当研究室では深層学習の健康・医療データへの応用を研究します。健康・医療データには様々な特性のパラメーターが存在することから、高精度で効率の良い深層学習にはデータの標準化が鍵となります。当研究室では健康・医療データの生成・プライバシー保護・標準化・正規化・深層学習、そして結果の視覚化などによる理解の各ステップを研究対象とし統合することにより、高精度の予測による個別化医療の実現を目指します。

Deep Learning on Health and Medical Data

We study deep learning on health and medical data. Each variable in health and medical data has different characteristic, thus data standardization plays critical role for accuracy and efficiency of deep learning. We investigate data generation, data privacy protection, data standardization, deep learning, and data visualization, to achieve personalized preventive medicine based on precise predictions.
The future mobility society is full of possibility. The freedom of the movement is the essential desire that we can share with the world as well as Japan being on the way to a aging society. Applying the Mobility Innovation (CASE*) to society should be near at hand, but we face various problems. We expect the equilibrium of transportation network to solve Traffic problems (ex. traffic accident zero, traffic clearing up and improvement of the convenience), so that future Mobility as a Service will be implemented. We study the equilibrium of transportation network theory such as transport analysis of the traffic flow information obtained from the measurement of LASAR, LIDAR and camera, the machine learning of traffic congestion data, and optimization of the spatial order with CASE. The next-generation Mobility Platform (Tsukuba model) that we proposed is adopted in Council on Competitiveness-Nippon by results of research, and the project is in progress.

The future Mobility as a Service

Traffic flow information by LASAR and LIDER

Spatial distribution of IoT vehicle information
放射線治療の治療予測のためのデータ収集システムの構築と治療効果解析

私は、特別共同研究の枠組みで株式会社日立製作所ヘルスケアビジネスユニットより筑波大学に2018年に参りました。日立では、粒子線治療に関連した装置やソフトウェアの研究・開発を長年担当しておりました。近年、様々な分野で大規模なデータを扱うビッグデータ解析が盛んに研究されています。放射線治療においても、過去の症例をもとに治療効果や治療品質を高めるための症例解析の研究が徐々に進められています。筑波大学では陽子線治療のパイオニアであり、1983年に治療を開始してから36年年にわたり五千を超える症例データを蓄積しています。これらのデータを整備し、各疾患における特徴をもとに治療効果を予測するモデルを作ることは今後の治療の効果を高めるために重要です。一方、日常の診療の中で研究のためのデータを収集するのは容易ではありません。日常の診療の中で入力した治療の情報を自動的に収集し、治療効果予測の研究をしやすいように整理するシステムの構築が必須です。米国では大病院を中心にこのようなシステムの構築が進んでいますが、日本ではまだ普及しているとは言えません。筑波大学附属病院の放射線腫瘍科に効率的なデータ収集システムを構築し、日本のモデルケースとしていきたいと考えています。

Data collection and analysis for outcome prediction of radiation therapy

I was transferred from Hitachi, Ltd. for special collaborative research in 2018. I have worked for research and development of the system and software for particle therapy for years. Recently, research with big data is becoming popular in various fields. Clinical analysis for radiation therapy is proceeding to predict clinical outcome and improve quality of life based on past clinical case. Tsukuba university is one of the pioneer of proton therapy and accumulate over 5,000 clinical cases of proton therapy since starting proton therapy in 1983. It is very important to establish the model for prediction of clinical outcome with analysis of these clinical cases based on the features in each disease for improvement of treatment quality. On the other hand, it is not easy to collect data for research in daily practice. In order to facilitate research on prediction of treatment effectiveness, it is essential to construct a system that automatically collects and organizes information on treatments entered in routine practice. In the United States, such systems have been developed mainly in large hospitals. However it can not be said that it is still popular in Japan. I hope to build an efficient data collection system in the radiation oncology department of University of Tsukuba Hospital and to make it a model case in Japan.
With the aim of the first 1000 dollar genome analysis for Japan

The Research and Development Center for Precision Medicine (PMC) was established as Japan’s first omics analysis center aiming to develop a $1000 genome sequencing technology. Using state-of-the-art technologies in genome sequencing and mass spectrometry, the Center aims to provide analytic and translational approaches to provide precise diagnosis of cancers and various diseases in a data-driven/evidence-based approach.

The Center has been working with the Tsukuba Preventive Medicine Research Center, which offers a comprehensive medical examination utilizing the function of initiative prevention of medical research. In order to promote collaborations with leading domestic and international research institutions, the PMC is also active in cross-border multidisciplinary networking.

The Center aims to establish a research infrastructure for the implementation and realization of Precision Medicine, to improve/determine the best course of treatment for each individual.
生理・行動・環境情報に基づく
革新的サイバニックシステムの研究開発と社会実装

当該研究グループでは、IoH (Internet of Humans)/IoT、ロボット、AIによるサイバニック技術で医療、福祉、生活・職場、生産を繋ぎ、社会が直面する課題解決を実現するサイバニック産業の創出にチャレンジしています。当該研究グループの先端技術の特徴として、人の外的情報（行動情報・生活情報など）に加えて、人の内的情報（脳神経情報・生理情報など）をサイバニックインタフェース・デバイスで扱い、これらをサイバニックシステムと連動させることで、脳神経系、生理系、身体系、行動系、生活系、環境系からスーパーコンピュータまでを一体的に扱うことができる「革新的サイバニックシステム」の研究開発と社会実装に取り組んでいます。

Development and Social Implementation of Innovative Cybernic System based on Human-Related Information

CYBERDYNE Inc. group develops and socially implements a Cybernic Technology powered by Internet of Humans/Internet of Things (“IoH/IoT”), Robots, and AI, to create a Cybernic Industry that will connect medical filed, welfare field, Living support field (at home and in work environments) and manufacturing field in order to solve the various problems that a hyper-aging society must tackle. This technology has a unique advantage in its ability to access and integrate information within the human body (e.g. Brain-nerve and vital information) and information outside the human body (behavior, life and environmental information) treated by Cybernic interfaces and devices. “Innovative Cybernic System” enables information of the brain-nerve, vital, physiological, behavioral, life and environmental systems to be integrated and connected to a super computer.
Intracellular trafficking of subviral structures

We are interested in the intracytoplasmic transport of different viral components that are involved in nuclear delivery of viral genomes. The main focus is the human hepatitis B virus (HBV) and adeno-associated viruses (AAV). While HBV exhibits an extreme efficiency and is a major human pathogen, counting for 600,000 deaths per year, AAVs do not cause any human disease, are inefficient but they are a major platform for gene transfer. We like to understand the reasons of efficacy of both viruses, which are largely based on their intracellular transport and in particular on their interaction with the cell nucleus. For HBV, we aim to decrease efficiency for cure, while for AAV we like to increase efficiency for a better use in therapy. Being at the interphase between virology and cell biology our research targets the molecular interactions with cellular partners mainly by using real-time microscopy.

Our aim is to elucidate molecular mechanisms involved in TGFβ signaling in normal and malignant cells. TGFβ has both tumor suppressor (inhibits growth and induces apoptosis) and tumor promoting (stimulates invasiveness and metastasis) effects in cancer cells. In addition, TGFβ exerts pro-tumorigenic effects in the tumor micro-environment, since it stimulates angiogenesis and the development of cancer associated fibroblasts, and inhibits immune surveillance. TGFβ binding to type I and type II receptors (TβRI and TβRII, respectively), induces signaling via Smad transcription factors which affects the transcription of specific genes, as well as via non-Smad pathways, including MAP-kinases, PI3-kinase, the tyrosine kinase Src, and liberation of its own intracellular domain (ICD). We are interested in elucidating the mechanism by which TGFβ induces pro-tumorigenic and tumor suppressive pathways. Our goal is to develop selective TGFβ inhibitors which inhibits the pro-tumorigenic pathways, while leaving the tumor suppressive pathways unperturbed.
Regulation of TGF-β signaling

Transforming Growth Factor-β (TGF-β) signaling is an important component in human development and normal cellular function. Aberrant TGF-β signaling, however, is implicated in various human diseases, including cancer. Our group focuses on 1) elucidation of yet unresolved aberrant TGF-β signaling mechanisms and 2) control of misregulated TGF-β signaling for the restoration of homeostasis. In our Cancer Signaling Laboratory at the University of Tsukuba, we are exploring the use of novel in vitro selected ligands against TGF-β signaling proteins, which could be used as experimental tools or a potential therapeutics. We are currently establishing various selection platforms to identify macrocyclic peptide-, protein-, and aptamer-based ligands (Figure 1). All communication in our lab is conducted in English.

Figure 1. Schematic depicting an in vitro selection platform known as the Random non-standard Peptide Integrated Discovery (RaPID) system used for the identification of macrocyclic peptide ligands against TGF-β signaling protein targets.

TGF-β and its signaling pathway in tumorigenesis

Recent advances emphasize the importance of TGF-β and its signaling pathway in tumorigenesis and metastasis. TGF-β signaling inhibitors have shown promise in blocking the TGF-β-mediated tumor progression and metastasis, and enhancing antitumor immunity. Our Lab is trying to define important in vivo properties of TGF-β, with the intent to better understand how these activities participate in the processes of malignant transformation and tumor progression. Efforts are focused toward translational research, particularly the identification of therapeutic interventions based on successful application of either TGF-β agonists or antagonists in malignancy and in immune disorders. Our Lab is also focusing on identification of novel genes and novel genetic alterations involved in the invasive human cancers by the RNA-based NGS sequencing in cancer patients.
Transcription Factor Control of Pluripotent Cell Identity

Our work on pluripotent stem cells focuses on three strands: (i) how transcription factors (TFs) interact with partner proteins and chromatin to direct efficient self-renewal, (ii) how changes in TF interactions drive commitment to differentiate, (iii) how the pluripotency TF network is reconfigured to enable entry to the germline. (i) To understand how TFs control cell identity we use mass spectrometry to identify partner proteins (Gagliardi et al., *The EMBO J.*, 2013). Repeating this with mutant proteins focussed attention on 6 NANOG interacting proteins. We are using biochemical and advanced microscopic approaches to determine how these partners deliver NANOG function. (ii) To assess how TFs act on chromatin we analyse RNA-seq and ChiP-seq data. Coupling ChIP with FACS to dissect distinct sub-populations of pluripotent cells tells us about TF interdependencies at individual loci before, and at the earliest stages of commitment to differentiation (Festuccia et al. *The EMBO J.*, 2018). Coupling ChIP with a technique for genome-wide analysis of enhancer activity (ChIP-STARR-seq) enables us to find novel active enhancers, genome-wide in distinct pluripotent populations (Barakat et al. *Cell Stem Cell*, 2018). (iii) We have recently shown that OTX2 restricts entry of cells into the germline and that in the absence of OTX2, germline differentiation exhibits aspects of a default differentiation (Zhang et al, *Nature*, 2018). These results suggest that OTX2 acts like a traffic warden, to restrict access to the germline and to usher cells towards the soma.
Molecular mechanisms of reprogramming

In 2006, a technology to generate induced pluripotent stem (iPS) cells from differentiated somatic cells using only 4 factors has been developed. iPS cells can be derived from any individuals and differentiate into various cell types, they have already been used for disease modelling, drug discovery, toxicology tests, and regenerative medicine. However, only 1 in 100-1,000 somatic cells can give rise to iPS cells and why the efficiency is so low, how the 4 factors induce pluripotency has not been elucidated. Our group aims to understand the molecular mechanism of the reprogramming, improve the technology and also generate fully functional other cell types useful for medicine, via cellular reprogramming based on the knowledge.
Mending the Broken Heart

Our primary interest is to explore different strategies to repair the heart after myocardial infarction (MI) either by using cell replacement approaches (exogenous repair) or by trying to redirect terminally differentiated cardiomyocytes (CMs) into cytokinesis (endogenous repair). We could show in mouse that embryonic- or ES cell-derived CMs engraft in infarcted hearts, improve function and lower the incidence of post-infarct arrhythmias. We have also demonstrated that engraftment is strongly enhanced by magnet-driven positioning of nanoparticle-loaded CMs. While the adult heart does not display repair upon MI, the neonatal mouse heart can partially regenerate due to remaining cell cycle activity and cytokinesis of some resident CMs. We have therefore generated transgenic systems to unequivocally identify CMs in cytokinesis and to screen molecules for their potential to bring adult CMs back into the cell cycle and make them divide. Thus, our long term goal is to at least partially repair the heart post-MI and to treat its long term sequelae such as heart failure and arrhythmias.
Design principles underlying robust biological systems

Systems biology fuses experimental biology with mathematics, physics, engineering and computer science, in a search for fundamental design principles that explain the complexity of life. We investigate how cells accurately know their locations in space; how tissues and organs stop growing at precisely-determined sizes; and how selection for control of these processes opens the door to combinatorial fragility, wherein combinations of small changes (e.g. in gene expression) can lead to catastrophic failures (e.g. birth defects). We work with mice, fruit flies, zebrafish, and frequently combine genetic experiments with mathematical modeling. We also study the influences of such control processes on how cancer arise and grow.
Mechanism of cell survival in response to DNA damage; Molecular mechanism of epigenetic abnormality disorders Cornelia de Lange syndrome and facioscapulohumeral muscular dystrophy

The Yokomori laboratory studies the mechanisms of higher-order chromatin structural organization and how they influence genome integrity and functions, such as DNA repair and gene transcription, with special focus on chromatin structural organizers cohesins and condensins, and human epigenetic abnormality disorders, Cornelia de Lange syndrome and FSHD muscular dystrophy, using genome-wide pooled and single cell/nucleus sequencing analyses. In addition, the role of PARP signaling in epigenetic DNA damage response and its relationship to cellular metabolism are being investigated using laser microirradiation and real-time fluorescence dynamics techniques.

Epigenetic regulation of gene expression and DNA damage response in human disorders

YOKOMORI Kyoko, Ph.D.
Professor
University of California, Irvine, U.S.A.
School of Integrative and Global Majors,
University of Tsukuba

E-mail address: kyokomor@uci.edu
URL: https://www.faculty.uci.edu/profile.cfm?faculty_id=4476
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<td>我々は大規模な前向き遺伝的スクリーニングを個別化したマウス集団に適用し、睡眠障害を引き起こす神経細胞のネットワークを明らかにしました。</td>
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<td>The investigative focus of our laboratory is the cellular and synaptic basis by which the brain regulates sleep and wakeful consciousness. Our studies seek to link the activity of defined sets of neurons with neurobehavioral and electrophysiological outcomes in behaving animals by using innovative genetically or chemically engineered systems (optogenetics, chemogenetics, or optopharmacology) in conjunction with recording of the electrical activity produced by the brain or in-vivo imaging (fiber-optic endomicroscopy).</td>
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<td>SHIOKAWA Hiroaki</td>
<td>計測科学研究所センター/システム情報工学研究科</td>
<td>Center for Computational Sciences/Graduate School of Systems and Information Engineering</td>
<td>応用数学</td>
<td>Data engineering</td>
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<td>坂崎和正</td>
<td>HORII Kazumasa</td>
<td>計測科学研究所センター/システム情報工学研究科</td>
<td>Center for Computational Sciences/Graduate School of Systems and Information Engineering</td>
<td>応用数学</td>
<td>Intelligent informatics</td>
<td><a href="http://kdec.cs.tsukuba.ac.jp">http://kdec.cs.tsukuba.ac.jp</a></td>
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<td>SANKAI Yoshiyuki</td>
<td>計測科学研究所センター/システム情報工学研究科</td>
<td>Faculty of Engineering, Information and System/Graduate School of Systems and Information Engineering Center for Cybernics Research</td>
<td>応用数学</td>
<td>Cybernics: fusion of Humans, Robots and Information Systems</td>
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<td>SAKURAI Tetsuya</td>
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<td>Faculty of Engineering, Information and System/Graduate School of Systems and Information Engineering</td>
<td>数理科学</td>
<td>Numerical Analysis</td>
<td><a href="http://www.cs.tsukuba.ac.jp/~sakurai/index.jhtml">http://www.cs.tsukuba.ac.jp/~sakurai/index.jhtml</a></td>
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<td>Faculty of Engineering, Information and System/Graduate School of Systems and Information Engineering</td>
<td>医薬画像科学</td>
<td>Medical imaging technology</td>
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<td>佐久間淳</td>
<td>SAKUMA Jun</td>
<td>計測科学研究所センター/システム情報工学研究科</td>
<td>Faculty of Engineering, Information and System/Graduate School of Systems and Information Engineering</td>
<td>医薬画像科学</td>
<td>Medical imaging technology</td>
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<td>Faculty of Engineering, Information and System/Graduate School of Systems and Information Engineering</td>
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<td>MAKINO Shoji</td>
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<td>Faculty of Engineering, Information and System/Graduate School of Systems and Information Engineering</td>
<td>医薬情報科学</td>
<td>Media information processing</td>
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<td>Faculty of Engineering, Information and System/Graduate School of Systems and Information Engineering</td>
<td>医薬情報科学</td>
<td>Policy and planning sciences</td>
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<td>Faculty of Engineering, Information and System/Graduate School of Systems and Information Engineering Center for Cybernics Research</td>
<td>医薬情報科学</td>
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<td>氏名 Name</td>
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<td>研究内容 Research subject</td>
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<td>KAWAMOTO Hiroaki</td>
<td>システム情報系システム情報工学研究科 サイバニクス研究センター</td>
<td>Faculty of Engineering, Information and Systems/Graduate School of Systems and Information Engineering/Center for System Analysis</td>
<td>Intelligent mechanics/Mechanical systems</td>
<td>知能情報学</td>
<td>Intelligent informatics</td>
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<td>TAKIZAWA Hotaka</td>
<td>システム情報系システム情報工学研究科</td>
<td>Faculty of Engineering, Information and Systems/Graduate School of Systems and Information Engineering</td>
<td>Medical image processing, videofluoroscopy, Elucidation of dysphagia, Assistive system for visually impaired people</td>
<td>医学薬剤学</td>
<td>Medical imaging technology</td>
<td><a href="http://www.pr.cs.tsukuba.ac.jp/">http://www.pr.cs.tsukuba.ac.jp/</a></td>
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<td>BABA Yukino</td>
<td>システム情報系システム情報工学研究科</td>
<td>Faculty of Engineering, Information and Systems/Graduate School of Systems and Information Engineering</td>
<td>Human Computation, Machine learning, Data mining, Crowdsourcing, Collective intelligence, Human-AI collaboration</td>
<td>知能情報学</td>
<td>Intelligent informatics</td>
<td><a href="http://yukinobaba.jp/">http://yukinobaba.jp/</a></td>
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<td>安藤弘春</td>
<td>ANDO Hiroyasu</td>
<td>Faculty of Engineering, Information and Systems/Graduate School of Systems and Information Engineering</td>
<td>A study on mathematical models of biological systems based on complex dynamics and their applications for engineering</td>
<td>理学情報学</td>
<td>Mathematical engineering</td>
<td><a href="http://www.tinos.tsukuba.ac.jp/researcher/0000005543">http://www.tinos.tsukuba.ac.jp/researcher/0000005543</a></td>
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<td>延原肇</td>
<td>NOBUHARA Hajime</td>
<td>Faculty of Engineering, Information and Systems/Graduate School of Systems and Information Engineering</td>
<td>Computational Intelligence Multi-Media Processing Image Processing Smart Interaction Web Science Web Intelligence Multi-Agent Bio-informatics Information Visualization</td>
<td>計算知能</td>
<td>Computational intelligence</td>
<td><a href="http://mobuharanen.com/">http://mobuharanen.com/</a></td>
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<td>大澤博隆</td>
<td>OSAWA Hironao</td>
<td>Faculty of Engineering, Information and Systems/Graduate School of Systems and Information Engineering</td>
<td>Human-agent interaction (HAI) has become an important field in the field of human-computer interaction. The agent in HAI behaves with users as if it has its own intentions. It triggers users' social responses, and instructs users through social channels. The use of HAI is widespread from the field of entertainment to medical purposes. The key factor in agent design through HAI is whether it has necessary and sufficient triggering expressions to evoke users' social behaviors. If we mistake the selection of appropriate expressions for users and tasks, we could create exaggerated agents that would impose greater cognitive loads on users. Our laboratory proposes to use HAI method in the field of HCI, where all expressions that evoke a user as an agent (like shape, motion, behavior, and auditory and visual changes) are called agential triggers.</td>
<td>ヒューマンエージェントインタラクション</td>
<td>Human-Agent Interaction</td>
<td><a href="http://hlab.net/">http://hlab.net/</a></td>
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<td>今倉徹</td>
<td>MAKURA Akira</td>
<td>Faculty of Engineering, Information and Systems/Graduate School of Systems and Information Engineering</td>
<td>Numerical analysis, matrix computations and their parallel algorithms: Machine learning and AI algorithms based on matrix computations</td>
<td>理数解析・機械学習</td>
<td>Numerical Analysis・Machine learning</td>
<td><a href="http://www.cs.tsukuba.ac.jp/~emakura/">http://www.cs.tsukuba.ac.jp/~emakura/</a></td>
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<td>保園信一</td>
<td>MORIKUNI Keichi</td>
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<td>入江貴則</td>
<td>NAIKU Mineki</td>
<td>Faculty of Engineering, Information and Systems</td>
<td>Numerical linear algebra, matrix analysis, numerical algorithm</td>
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<td>大橋修</td>
<td>OHIKIDA Osamu</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Post-transcriptional regulation of gene expression, endoplasmic reticulum stress response, molecular basis of membrane structure formation by vesicle fusion</td>
<td>分子細胞生物学</td>
<td>Molecular and Cellular biology</td>
<td><a href="http://www.md.tsukuba.ac.jp/basic-med/molcellbio/">http://www.md.tsukuba.ac.jp/basic-med/molcellbio/</a></td>
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<td>鈴木哲也</td>
<td>MASUMOTO Masayuki</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Cell biology</td>
<td>生物情報学</td>
<td>Stem cell biology</td>
<td><a href="http://www.md.tsukuba.ac.jp/stemcell/">http://www.md.tsukuba.ac.jp/stemcell/</a></td>
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<td>鳥口真実子</td>
<td>NOGUCHI Eiko</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Our research goal is to elucidate the molecular mechanisms that control neural circuit formation and neural functions.</td>
<td>免疫学</td>
<td>Neuroscience</td>
<td><a href="http://www.md.tsukuba.ac.jp/basic-med/neuroscience/">http://www.md.tsukuba.ac.jp/basic-med/neuroscience/</a></td>
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<td>荒川義弘</td>
<td>ARAKAWA Yoshhiro</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Human Genetics, Allergic diseases, Pediatric diseases</td>
<td>遺伝医学</td>
<td>Genetic medicine</td>
<td><a href="http://www.md.tsukuba.ac.jp/basic-med/r-m-genetics/index.html">http://www.md.tsukuba.ac.jp/basic-med/r-m-genetics/index.html</a></td>
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<td>岳野剛</td>
<td>SHIMANO Hisashi</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Clinical Research Methodology, Regulatory Science</td>
<td>臨床薬理学、医薬品規制科学</td>
<td>Clinical Pharmacology, Pharmaceutical Regulatory Science</td>
<td><a href="http://www.ishopt.tsukuba.ac.jp/t-credo/index.html">http://www.ishopt.tsukuba.ac.jp/t-credo/index.html</a></td>
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<td>前田寛史</td>
<td>ICHIBA Shinji</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Lipid metabolism and various in vivo organ pathologies(obesity, diabetes, inflammation, cancer, brain, neurogen, and regenerative medicine), understanding and visualization of pathology/mechanism at organella and molecular levels</td>
<td>代謝内分野学</td>
<td>Metabolism and Endocrinology</td>
<td><a href="http://www.s.u.tsukuba-endocrinology.jp/">http://www.s.u.tsukuba-endocrinology.jp/</a></td>
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<td>千葉真</td>
<td>MATSUMURA Akira</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Using both parent-derived samples and mouse models, the mechanism of blood cancers will be unravelled at the molecular levels. Based on the discovery, new methods to treat the patients will be intended. Physiologic mechanisms of blood production in the bone marrow is also within our scope.</td>
<td>血液内科学</td>
<td>Hematology</td>
<td><a href="http://www.ketsunami.com/">http://www.ketsunami.com/</a></td>
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<td>山形正幸</td>
<td>YAMAZAKI Masashi</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
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<td>山崎正義</td>
<td>YAMAZAKI Masashi</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Robot rehabilitation, regenerative medicine</td>
<td>難病外科、放射線科学</td>
<td>Neurosurgery, Radiation Oncology</td>
<td><a href="https://neurosurgery-tsukuba.com/">https://neurosurgery-tsukuba.com/</a></td>
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<td>山口正幸</td>
<td>YAMAZAKI Masashi</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
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<td>山本充</td>
<td>MATSUDA Hiroshi</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Medical image processing, videofluoroscopy, Elucidation of dysphagia, Assistive system for visually impaired people</td>
<td>医学薬剤学</td>
<td>Medical imaging technology</td>
<td><a href="http://www.pr.cs.tsukuba.ac.jp/">http://www.pr.cs.tsukuba.ac.jp/</a></td>
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<td>山本充</td>
<td>MATSUDA Hiroshi</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Human Computation, Machine learning, Data mining, Crowdsourcing, Collective intelligence, Human-AI collaboration</td>
<td>知能情報学</td>
<td>Intelligent informatics</td>
<td><a href="http://yukinobaba.jp/">http://yukinobaba.jp/</a></td>
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<td>山本充</td>
<td>MATSUDA Hiroshi</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>A study on mathematical models of biological systems based on complex dynamics and their applications for engineering</td>
<td>理学情報学</td>
<td>Mathematical engineering</td>
<td><a href="http://www.tinos.tsukuba.ac.jp/researcher/0000005543">http://www.tinos.tsukuba.ac.jp/researcher/0000005543</a></td>
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<td>山本充</td>
<td>MATSUDA Hiroshi</td>
<td>Faculty of Engineering, Information and Systems/Graduate School of Systems and Information Engineering</td>
<td>Computational Intelligence Multi-Media Processing Image Processing Smart Interaction Web Science Web Intelligence Multi-Agent Bio-informatics Information Visualization</td>
<td>計算知能</td>
<td>Computational intelligence</td>
<td><a href="http://mobuharanen.com/">http://mobuharanen.com/</a></td>
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<td>山本充</td>
<td>MATSUDA Hiroshi</td>
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<td>ヒューマンエージェントインタラクション</td>
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<td><a href="http://hlab.net/">http://hlab.net/</a></td>
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<td>山本充</td>
<td>MATSUDA Hiroshi</td>
<td>Faculty of Engineering, Information and Systems/Graduate School of Systems and Information Engineering</td>
<td>Numerical analysis, matrix computations and their parallel algorithms: Machine learning and AI algorithms based on matrix computations</td>
<td>理数解析・機械学習</td>
<td>Numerical Analysis・Machine learning</td>
<td><a href="http://www.cs.tsukuba.ac.jp/~emakura/">http://www.cs.tsukuba.ac.jp/~emakura/</a></td>
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<td>山本充</td>
<td>MATSUDA Hiroshi</td>
<td>Faculty of Engineering, Information and Systems</td>
<td>Numerical linear algebra, matrix analysis, numerical algorithm</td>
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<td>研究内容</td>
<td>専門分野</td>
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<td>織田見真司</td>
<td>KIDA Masaki</td>
<td>医学医療系</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Cardiac regeneration, heart failure, cardiovascular disease</td>
<td>病理学</td>
<td>Cardiovascular medicine</td>
<td><a href="http://www.md.tsukuba.ac.jp/cardiomed/cardiology/">http://www.md.tsukuba.ac.jp/cardiomed/cardiology/</a></td>
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<td>長谷川哲郎</td>
<td>OSHIKA Tetsuro</td>
<td>医学医療系</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Optophysiological optics, lens disorder, corneal disorder, quality of vision</td>
<td>眼科学</td>
<td>Ophthalmology</td>
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<td>高橋智樹</td>
<td>TAKAHASHI Satoshi</td>
<td>医学医療系</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Functional analysis of large Maf transcription factor family, Mouse Space experiments, Functional analysis of sugar chains</td>
<td>発生工学・分子生物学</td>
<td>Developmental technology, Molecular biology</td>
<td><a href="http://www.md.tsukuba.ac.jp/basic-med/anatomy/embryology/">http://www.md.tsukuba.ac.jp/basic-med/anatomy/embryology/</a></td>
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<td>加藤光保</td>
<td>KATO Mitsuyasu</td>
<td>医学医療系</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Cell division kinetics of cancer stem cells and its targeting therapy</td>
<td>癌学・腫瘍学</td>
<td>Pathology, Oncology</td>
<td><a href="http://www.md.tsukuba.ac.jp/epatho/">http://www.md.tsukuba.ac.jp/epatho/</a></td>
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<td>松本正幸</td>
<td>MATSUMOTO Masayuki</td>
<td>医学医療系</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>The goal of our research is to understand neural mechanisms underlying cognition such as attention, memory, prediction, learning and decision making. Experiments in our laboratory center on the brain of awake behaving monkeys as a model for similar systems in the human brain.</td>
<td>神経科学</td>
<td>Cognitive and Behavioral Neuroscience</td>
<td><a href="http://www.md.tsukuba.ac.jp/basic-med/cog-neurosci/index.html">http://www.md.tsukuba.ac.jp/basic-med/cog-neurosci/index.html</a></td>
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<td>藤原二</td>
<td>ISOBE Takeji</td>
<td>医学医療系</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Development of equipments for particle beam therapy</td>
<td>医学物理学</td>
<td>Medical Physics</td>
<td><a href="http://www.pmc.trsukuba.ac.jp/research/index.html">http://www.pmc.trsukuba.ac.jp/research/index.html</a></td>
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<tr>
<td>藤原智也</td>
<td>1960年6月9日生</td>
<td>医学医療系</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Radiation science</td>
<td>放射線科学</td>
<td>Radiation science</td>
<td><a href="http://ramsep.md.tsukuba.ac.jp/">http://ramsep.md.tsukuba.ac.jp/</a></td>
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<td>井本泰幸</td>
<td>HASHIMOTO Koichi</td>
<td>人間総合科学研究科</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>1. Development of effective prevention treatments such as functional foods for lifestyle-related diseases. 2. Construction of a seamless platform for clinical translational research in T-CRedO.</td>
<td>人間総合科学研究科</td>
<td>Clinical and Translational research</td>
<td><a href="http://www.md.tsukuba.ac.jp/basic-med/cog-neurosci/index.html">http://www.md.tsukuba.ac.jp/basic-med/cog-neurosci/index.html</a></td>
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<td>小野寺雅志</td>
<td>KOYANAGI Tomoyoshi</td>
<td>医学医療系</td>
<td>Faculty of Medicine</td>
<td>Focusing on the development of business models of start-up companies for pharmaceuticals, medical devices and regenerative medicine products in early stage, which is called “Translational Research”. Performing investigational research of “ecosystem” of startup community in the Biotech/Medtech field in U.S. and Japan.</td>
<td>人間総合科学研究科</td>
<td>Clinical and Translational research</td>
<td><a href="http://www.md.tsukuba.ac.jp/cog-neurosci/index.html">http://www.md.tsukuba.ac.jp/cog-neurosci/index.html</a></td>
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<td>安野晃典</td>
<td>ASANO Yoichi</td>
<td>医学医療系</td>
<td>Faculty of Medicine/Graduate School of Pure and Applied Sciences</td>
<td>Optical engineering, Photon science</td>
<td>光工学</td>
<td>Optical engineering</td>
<td><a href="http://oeg-news.blogspot.com">http://oeg-news.blogspot.com</a></td>
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<tr>
<td>山崎真利</td>
<td>SATO Makoto</td>
<td>医学医療系</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Inflammation, Lymphoma, cancer genome, cancer immunology, cancer microenvironment</td>
<td>生物学</td>
<td>Hematology</td>
<td><a href="http://www.ketsuaini.com/english/">http://www.ketsuaini.com/english/</a></td>
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<td>流川和子</td>
<td>SHIBUYA Kazuko</td>
<td>医学医療系</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Basic Immunology, Clinical Immunology, Immunotherapy, Drug development, Allergy, Cancer Immunology, Autoimmune diseases, Infectious Immunology, Inflammation</td>
<td>眼科学</td>
<td>Immunology</td>
<td><a href="http://immuno-tsukuba.com/">http://immuno-tsukuba.com/</a></td>
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<tr>
<td>川口浩史</td>
<td>KAWAGUCHI Atsushi</td>
<td>医学医療系</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Study of virus pathogenesis and host immune responses to control emerging infectious diseases including influenza</td>
<td>生物学</td>
<td>Infection biology</td>
<td><a href="http://www.md.tsukuba.ac.jp/basic-med/infectionbiology/virology/">http://www.md.tsukuba.ac.jp/basic-med/infectionbiology/virology/</a></td>
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<td>村上英明</td>
<td>MURATAI Shinji</td>
<td>医学医療系</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Genomics and epigenomics analysis of limited samples</td>
<td>眼科学</td>
<td>Genome biology</td>
<td><a href="http://www.md.tsukuba.ac.jp/hmnc/">http://www.md.tsukuba.ac.jp/hmnc/</a></td>
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<td>原住友子</td>
<td>HIROTA Yuki</td>
<td>医学医療系</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Development of Combination medical instruments: Growth factor composite bone screw</td>
<td>口腔外科学</td>
<td>Orthopaedic surgery</td>
<td><a href="http://tsukuba-tekiji.jp/">http://tsukuba-tekiji.jp/</a></td>
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<td>野坂勝</td>
<td>SATO Shigeki</td>
<td>医学医療系</td>
<td>Faculty of Medicine</td>
<td>1) fast and efficient computation via symbolic computation and high-precision computation via numerical computation, and both collaboration. 2) educational informatics pathing e-learning for inter-disciplinary area</td>
<td>人間総合科学研究科</td>
<td>Computational biology</td>
<td><a href="http://www.utsukuba.ac.jp/~satocts/">http://www.utsukuba.ac.jp/~satocts/</a></td>
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<td>尾崎健</td>
<td>Ozaki Haruka</td>
<td>医学医療系 / 人工知能科学センター</td>
<td>Faculty of Medicine / Center for Artificial Intelligence Research</td>
<td>AI-based genome analyses, Massive biological data analyses, Single-cell informatics</td>
<td>人工知能科学</td>
<td>Artificial Intelligence Research</td>
<td><a href="https://sites.google.com/view/ozaklab">https://sites.google.com/view/ozaklab</a></td>
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<td>武田隆</td>
<td>MAEDA Naoki</td>
<td>医学医療系</td>
<td>Faculty of Medicine/Graduate School of Comprehensive Human Sciences</td>
<td>Development of Combination medical instruments: Growth factor composite bone screw</td>
<td>人工知能科学</td>
<td>Artificial Intelligence Research</td>
<td><a href="http://www.utsukuba.ac.jp/~satocts/">http://www.utsukuba.ac.jp/~satocts/</a></td>
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<tr>
<td>筒井満年</td>
<td>SHIGEMORI Hideyuki</td>
<td>生命環境科学</td>
<td>Faculty of Life and Environmental Sciences/Graduate School of Life and Environmental Sciences</td>
<td>Elucidation of the Mechanism of Bioactive Substances involved in Mysterious Biological Phenomena</td>
<td>生命環境科学</td>
<td>Natural products chemistry</td>
<td><a href="http://www.utsukuba.ac.jp/~sanuki.masaru/">http://www.utsukuba.ac.jp/~sanuki.masaru/</a></td>
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<tr>
<td>両宮潤</td>
<td>TANAKA Jun</td>
<td>生命環境科学</td>
<td>Faculty of Life and Environmental Sciences/Graduate School of Life and Environmental Sciences</td>
<td>Molecular biology, Cell biology</td>
<td>高分子化学</td>
<td>Molecular and Cellular biology</td>
<td><a href="http://tchibalab.org/">http://tchibalab.org/</a></td>
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<td>Name</td>
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<td>Research subject</td>
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<tr>
<td>NOMURA Nobuhiko</td>
<td>Faculty of Life and Environmental Sciences/Graduate School of Life and Environmental Sciences</td>
<td>Bioconversion, Cell-cell interaction, Biofilm</td>
<td>Applied microbiology</td>
<td><a href="http://www.envr.tsukuba.ac.jp/~microbio/index.html">http://www.envr.tsukuba.ac.jp/~microbio/index.html</a></td>
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<td>Li, Tsai-Kun</td>
<td>National Taiwan University</td>
<td>Topoisomerase-targeting drugs, DNA damage and repair, DNA topology and its biological implications</td>
<td>Molecular and Cellular biology</td>
<td><a href="http://www.imbim.tsu.se">http://www.imbim.tsu.se</a></td>
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<tr>
<td>Akio Takahashi</td>
<td>Toyota Motor Corporation (R&amp;D Center for Strategic Frontiers in Social Planning, University of Tsukuba)</td>
<td>Advanced mobility, Hydrogen society, Intelligent transportation system</td>
<td>Advanced mobility</td>
<td><a href="https://www.toyota.co.jp/">https://www.toyota.co.jp/</a></td>
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<td>Hikaru Itoh</td>
<td>National Institute of Advanced Industrial Science and Technology (AGT)</td>
<td>Computational science, Chemical biology, Life/Health/Medical Informatics, Drug development chemistry</td>
<td>N/A</td>
<td><a href="https://www.molfop.jp/research/ddt1.html">https://www.molfop.jp/research/ddt1.html</a></td>
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<td>Kiyoshi Abe</td>
<td>National Institute of Materials Science (NIMS)</td>
<td>Study of scaffolds and biomaterials for cell function manipulation and regenerative medicine</td>
<td>N/A</td>
<td><a href="https://www.nims.go.jp/gradient/index.html">https://www.nims.go.jp/gradient/index.html</a></td>
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<tr>
<td>Nobuyuki Seta</td>
<td>RIKEN</td>
<td>We study deep learning on health and medical data. Each variable in health and medical data has different characteristic, thus data standardization plays critical role for accuracy and efficiency of deep learning. We investigate data generation, data privacy protection, data standardization, deep learning, and data visualization, to achieve personalized preventive medicine based on precise predictions.</td>
<td>Deep Learning for Medical Information</td>
<td><a href="http://www.riken.jp/en/research/labs/mih/">http://www.riken.jp/en/research/labs/mih/</a></td>
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<tr>
<td>Takanori Fujita</td>
<td>Uppsala University</td>
<td>The research interest of C-H. Heldin is related to the mechanisms of signal transduction by growth regulatory factors, as well as their normal function and role in disease. In particular, platelet-derived growth factor (PDGF), a major mitogen for connective tissue cells, and transforming growth factor β (TGF-β), which inhibits the growth of most cell types, are studied. An important goal is to explore the possible clinical utility of signal transduction antagonists.</td>
<td>Wound Healing Research, Oncology</td>
<td><a href="http://www.imbim.tsu.se">http://www.imbim.tsu.se</a></td>
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### Research Institutions and Programs

- **Data Collection and Analysis for Outcome Prediction of Radiation Therapy**
  - Programme: Medical Informatics
  - University: University of Tsukuba
  - Website: [http://www.pmrc.tsukuba.ac.jp/radioncology/](http://www.pmrc.tsukuba.ac.jp/radioncology/)

- **Computational chemistry on pharmaceutical formulations**
  - Programme: Computational chemistry
  - Institution: University of Tsukuba
  - Website: [https://www.cyberdyne.jp/](https://www.cyberdyne.jp/)
  - Additional Information: *Cybernics: Life system · artificial heart system · security · network system · big data*

- **Identification of a new biomarker specific for human diseases in cancer, congenital diseases, and chronic diseases.**
  - Programme: Drug Discovery Research and Development
  - Institution: University of Tsukuba
  - Website: [https://www.mentra.com/jp/](https://www.mentra.com/jp/)
  - Additional Information: *Mentra* · *Mentraomics* · *MentraWiki* · *MentraMart* · *MentraPortal* · *MentraLab*

- **We have been developing new medical devices using smart polymers.**
  - Programme: Smart Biomaterials
  - Institution: University of Tsukuba
  - Website: [https://www.mentor.com/](https://www.mentor.com/)
  - Additional Information: *Mentra* · *Mentraomics* · *MentraWiki* · *MentraMart* · *MentraPortal* · *MentraLab*

- **We are studying deep learning on health and medical data. Each variable in health and medical data has different characteristic, thus data standardization plays critical role for accuracy and efficiency of deep learning. We investigate data generation, data privacy protection, data standardization, deep learning, and data visualization, to achieve personalized preventive medicine based on precise predictions.**
  - Programme: Deep Learning for Medical Information
  - Institution: RIKEN

- **We have been developing new medical devices using smart polymers.**
  - Programme: Drug Discovery Research and Development
  - Institution: University of Tsukuba
  - Website: [https://www.mentra.com/jp/](https://www.mentra.com/jp/)
  - Additional Information: *Mentra* · *Mentraomics* · *MentraWiki* · *MentraMart* · *MentraPortal* · *MentraLab*
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<tr>
<th>名前</th>
<th>Name</th>
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<th>Affiliation</th>
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<th>Research subject</th>
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<td>ten Dijke, Peter</td>
<td>ライデン大学</td>
<td>Leiden University</td>
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<td>Kim, Seong-Jin</td>
<td>ソウル大学校</td>
<td>Seoul National University</td>
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<td>Fleischmann, Bernd</td>
<td>ボン大学</td>
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<td>Lander, Arthur D.</td>
<td>カリフォルニア大学アーバイン校</td>
<td>University of California, Irvine</td>
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<td>横森馨子</td>
<td>カリフォルニア大学アーバイン校</td>
<td>University of California, Irvine</td>
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**Research Content (Research subject):**
- TGF-β is a multifunctional cytokine involved in diverse cellular functions, including cell growth/handimmune response. TGF-β signaling has emerged as a key architect of stroma-receptor poor-progression in cancer. Disseminated tumors show a strong dependency on TGF-β1-activated stroma during the establishment and subsequent expansion of metastasis. TGF-β also has a positive role on the cancer stem cell (CSC) population promoting or sustaining stemness of the pool of CSCs in diverse types of malignancy. Since TGF-β1 signaling is dysregulated in most of human cancers, thus affecting the overall progression to malignancy, TGF-β signaling has been considered a potentially novel therapeutic target for treating various cancers acquired by EMT. In the TGF-β1 signaling pathway, TGF-β receptor I kinase inhibitors have shown promise in blocking the TGF-β1-mediated tumor progression and metastasis, and enhancing anti-tumor immunity in nonclinical animal models. Vactosertib, a TGF-β1 receptor I kinase inhibitor, has shown significant preclinical antitumor efficacy in a range of in vivo metastatic and orthotopic xenograft models and has completed phase 1 clinical trials in USA. Recent molecular classification of gastrointestinal cancer has identified a poor-progression transcriptional subtype associated with mesenchymal traits and genes upregulated by TGF-β1 in stromal cells are robust predictors of cancer recurrence and metastasis. This observation warrants the development of anti-TGF-β therapies for the treatment of poor-progression cancers with TGF-β1response signature.

**Specialty:**
- Molecular and Cellular Biology
- Oncology

**Research Interests:***
- Molecular Biology
- Cell Biology
- Developmental Biology
- Stem Cell Biology
- Systems Biology
- Computational Biology
- Glycobiology
- Neurobiology
- Cancer Biology and Evolution
- Systems Biology
- Cancer Biology and Engineering
- Developmental Biology
- Stem Cell Biology
- Systems Biology
- Cancer Biology and Evolution
- Developmental Biology
- Stem Cell Biology
- Systems Biology
- Cancer Biology and Engineering

**Affiliations:**
- University of California, Irvine
- The University of Edinburgh
- Leiden University
- Seoul National University
- The University of Bonn
- The University of Edinburgh
- University of California, Irvine
- University of California, Irvine

**Web Sites:**
- http://faculty.sites.uci.edu/landerlab
- http://ccb.lumc.nl/about-the-ten-dijke-lab-34
- http://www.crm.ed.ac.uk/research/group/biology-reprogramming
- http://www.physiologie.uni-bonn.de/
- http://faculty.sites.uci.edu/landerlab
- https://ccb.lumc.nl/about-the-ten-dijke-lab-34
- http://faculty.sites.uci.edu/profile/clf/faculty_id=447687
ヒューマニクス学位プログラムホームページ
http://www.phd-humanics.tsukuba.ac.jp/

卓越大学院プログラム（WISE Program(Doctoral Program for World-leading Innovative & Smart Education)）
http://www.mext.go.jp/a_menu/koutou/kaikaku/takuetudaigakuin/index.htm

事務局
ヒューマニクス学位プログラム グローバル教育院 事務室
〒305-8577 茨城県つくば市天王台1-1-1 総合研究棟A703 グローバル教育院 事務室
TEL. 029-853-7085
Ⓒ Ph. D. Program in Humanics, University of Tsukuba.

School of Integrative and Global Majors (SIGMA) Office
School of Integrative and Global Majors (SIGMA), the University of Tsukuba 1-1-1 Tennodai, Tsukuba, Ibaraki 305-8577 JAPAN
TEL. +81-29-853-7085
Ⓒ Ph. D. Program in Humanics, University of Tsukuba.