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Inge Revsbech wins The Journal of Experimental Biology's Outstanding Paper Prize 2013

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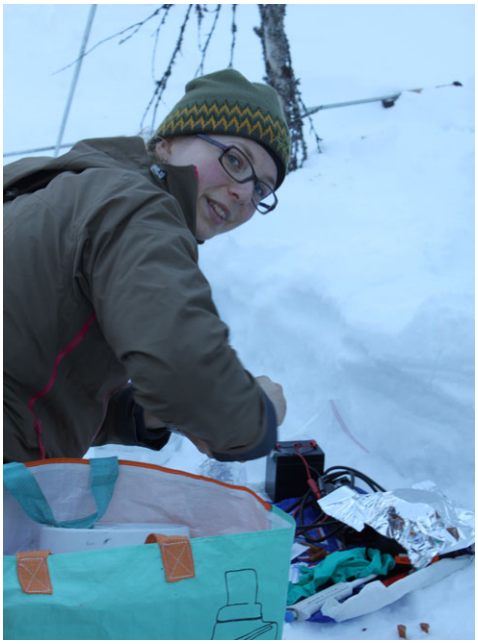
NEWS

Inge Revsbech wins *The Journal of Experimental Biology*'s Outstanding Paper Prize 2013

The Editors of *The Journal of Experimental Biology* are pleased to announce that Inge Revsbech from Aarhus University, Denmark, is the winner of this year's JEB Outstanding paper prize. The prize is awarded in memory of Bob Boutillier (JEB Editor-in-Chief 1994–2003) to a junior author who has made the most significant contribution to an outstanding paper. 'The prize aims to promote and reward the hard work that individual young scientists have put into solving different riddles of any particular species using ingenuity, perseverance and sound technology and methodology', explains Hans Hoppeler, Editor-In-Chief.

Revsbech was the first author on the paper 'Hemoglobin function and allosteric regulation in semi-fossorial rodents (family Sciuridae) with different altitudinal ranges' (Revsbech et al., 2013). Reflecting on the paper, Hoppeler says, 'This year's winner stands out because it integrates mechanistic molecular understanding of a physiological process, in this case the conditions for oxygen transfer in hemoglobin, and relates this understanding to an ecological context. Because of the novel insight provided, this manuscript received top ratings and was therefore shortlisted for the prize, and in the final selection the majority of the editors felt that this particular manuscript represented the kind of research that JEB would like to promote.' (The short list is available at the end of the article.)



Inge Revsbech, the winner of the 2013 JEB Outstanding paper prize. Picture by Andrea Friebe.

Recalling the moment she found out that she had received the prize, Revsbech says, 'My supervisor, Angela [Fago], came into the lab where I was working with a huge smile on her face, saying "You should check your e-mail…now". It was a big surprise and I was very glad – it's a great honour.' Angela Fago's reaction was similar: 'I was very excited; this is a prestigious prize and we were very proud our paper should have such acknowledgement from the JEB.' She adds that 'Inge has spent a lot of energy on the project and it was a wonderful reward after all the effort she has put in.'

The first steps towards this study were taken towards the end of Revsbech's undergraduate degree at Aarhus University, when she realised it was time to think about looking for a supervisor for a PhD or a Master's degree. As she had an interest in comparative physiology, Revsbech went to meet Fago: 'I think we instantly liked each other and I kind of walked out with the startings of a PhD project.' Revsbech goes on to explain that Fago, along with her long-time collaborator Jay Storz at the University of Nebraska–Lincoln, USA, had recently secured funding to look at adaptions to living at high altitude in ground squirrels found throughout the USA. 'Since I was already going to the USA for an exchange to the University of Washington in Seattle for 6 months, I just went straight from there to Jay in Lincoln, Nebraska, and got started on this project.'

Once in Nebraska, Revsbech found herself hitting the ground running: 'The day I arrived in Lincoln, we went out to a cemetery where the largest nearby population [of thirteen-lined ground squirrels] was. It had been drizzling all day and these ground squirrels didn't want to come out. So we hid, and as soon as we saw one come out we'd put out traps with peanut butter, so everything smelt of peanut butter – it was a great start.' After trapping the squirrels, Revsbech and members of Storz's lab took blood samples, storing the samples at –80°C until the team were ready to begin their experiments. Over the course of two summers, the team had collected blood samples from six different species of marmotine ground squirrel living across a range of altitudes from 0 to 4300 m.

Back in Denmark, Revsbech purified the red blood cells in order to measure the hemoglobin's affinity for oxygen and the effect pH has on this affinity. She explains that, 'Normally with high-altitude animals, their blood often has a higher oxygen affinity so it can bind oxygen more easily. But if you have a very high affinity then you might have a problem in actually delivering the blood, and so changes in pH (the Bohr effect) help unload the oxygen.' To her surprise, however, she found that, irrespective of what altitude they inhabited, all the ground squirrels had blood samples with a high affinity for oxygen and an exceptional sensitivity to changes in pH. What's more, when she tested the effect of allosteric effectors, which are known to reduce oxygen affinity in hemoglobin, she found very little or no effect at all.

Meanwhile, in Nebraska, Storz's team had been busy characterising the hemoglobin in more detail by sequencing the hemoglobin genes. Comparing the sequences with those of the human hemoglobin, the team found that residues that are important for binding the allosteric effectors were very conserved, but that residues normally involved in the Bohr effect were not. The data from Nebraska suggested that ground squirrels should be insensitive to pH but sensitive to allosteric inhibitors, which is the opposite of what Revsbech had found. Revsbech was undeterred, as Fago recalls: 'Revsbech has the ability to spend many hours in lab working hard to get good results, but she's also very good at thinking outside of the box, because these results were unexpected by us. She was very keen to understand what

was going on and what kind of solution there could be to our original hypothesis.'

Given that ground squirrels' hemoglobin is both extremely sensitive to pH changes and almost completely insensitive to allosteric effectors, and that amino acid conservation is different compared with the human hemoglobin, Revsbech concludes, 'This supports the growing idea that using human hemoglobin as model for any hemoglobin is not what we should [always] do because it seems that not everyone's [hemoglobin] works like humans' does.' The team are now trying to work out the structure and what residues in the ground squirrel hemoglobin are responsible for the increased sensitivity to pH, but Revsbech jokingly admits that she's 'hooked' on the hibernation field. She explains that as there were no differences amongst ground squirrels in terms of their hemoglobin's affinity for oxygen across the altitudinal range, she became interested by the idea that their hemoglobin might represent an adaptation to hibernation. Revsbech goes on to explain that during hibernation in burrows, oxygen availability may decrease substantially, so having hemoglobin with high affinity might be advantageous. Similarly, during hibernation metabolic rates decrease, and consequently oxygen demand decreases. In this case, releasing too much oxygen to a tissue would be detrimental, and so, again, hemoglobin with high affinity for oxygen might allow the ground squirrels more control over releasing the oxygen. This interest has seen her migrate to a larger and more fearsome animal, the Scandinavian brown bear, and she hopes that after her PhD she may carrying on working with this species, but for now she still has a year left in Fago's lab.

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JEB Outstanding Paper Prize Short List 2013

Anttila, K., Dhillon, R. S., Boulding, E. G., Farrell, A. P., Glebe, B. D., Elliott, J. A. K., Wolters, W. R. and Schulte, P. M. (2013). Variation in temperature tolerance among families of Atlantic salmon (*Salmo salar*) is associated with hypoxia tolerance, ventricle size and myoglobin level. *J. Exp. Biol.* **216**, 1183-1190.

Ashwin, A. B., Zeddies, D. G., Raible, D. W., Rubel, E. W. and Sisneros, J. A. (2013). Auditory sensitivity of larval zebrafish (*Danio rerio*) measured using a behavioural prepulse inhibition assay *J. Exp. Biol.* **216**, 3505-3513.

Callier, V., Shingleton, A. W., Brent, C. S., Ghosh, S. M., Kim, J. and Harrison, J. F. (2013). The role of reduced oxygen in the developmental physiology of growth and metamorphosis initiation in *Drosophila. J. Exp. Biol.* **216**, 4334-4340.

Matsuta, N., Hiryu, S., Fujioka, E., Yamada, Y., Riquimaroux, N. and Watanabe, Y. (2013). Adaptive beam-width control of echolocation sounds by CF–FM bats, *Rhinolophus ferrumequinum nippon*, during prey-capture flight. *J. Exp. Biol.* **216**, 1210-1218.

Nowroozi, B. N. and Brainerd E. L. (2013). X-ray motion analysis of the vertebral column during the startle response in striped bass, *Morone saxatilis*. *J. Exp. Biol.* **216**, 2833-2842.

Revsbech, I. G., Tufts, D. M., Projecto-Garcia, J., Moriyama, H., Weber, R. E., Storz, J. F. and Fago, A. (2013). Hemoglobin function and allosteric regulation in semi-fossorial rodents (family Sciuridae) with different altitudinal ranges. *J. Exp. Biol.* **216**, 4264-4271.

Sensenig, A. T., Kelly, S. P., Lorentz, K. A., Lesher, B. and Blackledge, T. A. (2013). Mechanical performance of spider orb webs is tuned for high-speed prey. *J. Exp. Biol.* **216**, 3388-3394