# MolecularCloud
# Pioneer Scientist Interview

## The future prospect of biological nanopore technology


***Prof. Shuo Huang***

*School of Chemistry and Chemical Engineering, Nanjing University*


## Introduction

- 2011 Received Doctor's degree at Arizona State University
- 2011-2015 Post-doc fellow at the University of Oxford, UK
- 2015- Lead a research group at Nanjing University, China.

Dr. Huang's research covers a wide range of topics in single molecule biophysics with particular focus on:

- Nanopore based single molecule bio-sensors
- Single molecule diagnosis devices with clinical applications
- An optical multi-modal nanopore platform for single cell studies

Hello everyone! This is Lidan. Welcome to join us in this interview. This is the first episode of MolecularCloud Pioneer Scientist interview series. Our guest today is Prof. Shuo Huang.

Prof. Huang received his doctor's degree at Arizona State University in 2011. From 2011 to 2015, he worked as a post-doc fellow at the University of Oxford, UK. Since 2015, he started to lead a research group in Nanjing University, China.

Dr. Huang's research covers a wide range of topics in single molecule biophysics with particular focus on:
Nanopore based single molecule bio-sensors
Single molecule diagnosis devices with clinical applications
An optical multi-modal nanopore platform for single cell studies

Welcome Dr. Huang!

Thank you, Lidan!

Since 2019, your team has published a number of high-score papers in international renowned journals, such as Nature Communications, Science Advances, Angewandte Chemie International Edition, Chemical Science and iScience. Could you briefly introduce those scientific research achivements to our audience?

Sure. Our research group is really lucky to have a number of important works published during 2019 and 2020.
Those works generally covered three major research topics of our group. Novel nanopore sequencing technology, Nanopore imaging technology and Nanopore single molecule chemistry.

Our innovative work on nanopore sequencing is that we make a series of unmeasurable things measurable. Based on our self-developed NIPSS technology, we successfully sequenced microRNA and xeno-nucleic acid for the first time.

The essence of nanopore technology is a kind of electrochemical method, and electrodes are usually required. However, the DiffusiOptoPhysiology technology we developed is an exception. It’s the first nanopore single molecule detection technique that doesn’t involve electrodes. In fact, the results were even better than expected. We believe that the further development of this technology will open up a new era of low-cost detection chips.

Moreover, we have transformed the conical shaped nanopore into a chemical nano-reactor, which could amplify the signals of single molecule reaction. This work lays the most crucial foundation for the design of multiple novel nanopore sensors.

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Thank you Dr. Huang. As you just mentioned, the main works of your research group in recent years were about nanopore technology, and your team has made so many breakthroughs. So what do you think about the future prospect of biological nanopore technology?

Our research group has accumulated a great amount of experience of biological nanopore technology for many year. It can be said that biological nanopore technology I have seen is sensitive, stable and efficient. The success of nanopore sequencing has made it clear that single-molecule analysis technology can be applied in our daily lives. There will be a large number of low-cost and unique detection methods based on nanopore technology, from my point of view, coming into our life in the future. Maybe, we will see the nanopore technology in a hospital inspection report, or nanopore detection kits that cost as little as a dollar or two. We can even buy products based on the technology from e-commerce platforms and so on.

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Thank you Dr. Huang. Seeing the rapid development of nanopore sequencing technology, we believe that it won’t be too long before the technology comes into our daily life. So, what are the future plans of your research group?

The recent focuses of our research group are on several aspects, including the further exploration of the precise modification of nanopore, and nanopore application.

For the precise modification of nanopore, our work stems from bionics. I often marvel that the nature evolution has built so many biocomponents with exquisite structures and functions. They are so delicate that the most advanced micro-nano processing technology today is no match for a small prokaryotic expression system. We have learned a lot from nature, but that's only a drop in the bucket of the long history of bionic science. And we need to have some development, some creation on the basis of learning.

For the exploration of nanopore application, our research was first developed for a very important one, the nanopore sequencing. At current stage, nucleic acid nanopore sequencing has become a relatively mature scientific research method. Although the technology is still developing rapidly, the main line of technological development has entered into the level of engineering and technology transformation. We also want to explore more applications of nanopore technology, such as single-molecule sequencing of peptides, proteins and polysaccharides. We've already got a lot of exciting preliminary research results in that field, and we hope that we can bring you more surprises in 2020 and 2021.

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Thank you for your sharing. I am looking forward to reading your coming research publication. Any difficulties or interesting things encountered in your research work?

Yes. My students and I have experienced a lot since the establishment of the research group at the end of 2015. There are difficulties as well as interesting things.

For the difficulty, the hardest thing is the cultivation of students. We are working on single-molecule analytical chemistry technology. This research field is highly interdisciplinary, thus chemistry students in our research group also need to learn a lot about biology and physics. Therefore, the cycle period of cultivating an excellent student is relatively prolonged. In the process of study and growth, many students feel that the professor's concept is fresh, but their work is just not efficient enough. They have a certain degree of complaints about the uncatchable innovative points.

Of course, there are also many unintended interesting things. For example, I successively asked four students to do a project, the results of which were published in Nature Communications in 2019. But the former three students were either lacked confidence when in front of difficulties or lacked perseverance due to procrastination. All the reports they gave to me were negative. The reports remained negative until the 4th student really started doing his job, and he opened up the direction of single molecule chemistry for us. I think that persistence, interest, and careful observation of experimental results are essential prerequisites for important scientific discoveries.

Thanks for your sharing. Although you have only said a few words, we can still realize that you have made great efforts to train the students in the past few years. So, do you have any advices for your students to accelerate research work during the COVID-19 pandemic?

Our research group is a typical experiment-based one. The COVID-19 outbreak has hit our scientific research progress very hard. During the non-semester period, my students maintained their scientific research status by sorting out the preliminary research results, reading literatures, conducting innovation research and so on. Those are not long-term solutions for an experimental research group, but as I completely let go of the lab experiments, the process of thought experiments through investigation and research brought me a new kind of fun. That is, demonstrating an experimental program that has never really been carried out through thorough researches. Those thought experiments have also made us find many new ideas.

At the same time, in order to get prepared for returning to the lab, we have also signed a lot of scientific research service orders with many scientific research companies, including GenScript, which can help us make up for some of the lost time. In addition, our research group has also developed comprehensive cooperation with many teams engaged in theoretical chemistry and computer technology to work against the clock through scientific research activities that do not require experimental operations.

Thank you Dr. Huang. Thank you for your support for GenScript and MolecularCloud. You are one of the earliest users of the platform. At the end of the interview, we also want to know if there is anything you'd like to say about MolecularCloud?

I really appreciate the MolecularCloud and similar scientific research sharing platforms. The sharing of scientific research achievements is a big trend all over the world. As far as I am concerned, the sharing of software code, scientific research data and research methods is rapidly spreading in various fields. The sharing of plasmids is a great start, because we can not only share our research work on the platform but also get the research results shared by other teams. In our research field, we often spend a lot of time exploring the plasmid construction completed by other research groups, even though they are not intended to set up those technical obstacles. In that case, why don't we put those resources together so that all interested researchers can benefit from them? As far as I know, many plasmid sharings in our field are still in the inefficient state of mailing samples. I am very glad that the MolecularCloud platform has accelerated the fusion of scientific research and brought scientists closer to each other.

MolecularCloud is already very good at this stage. But in fact, I am a little worried about that the current operation mode of MolecularCloud may bear too much economic pressure during the promotion process. I suggest raising some prices on plasmid requests or increasing profits through advertising. The MolecularCloud team can also screen their requesting or sharing customers based on some sort of scoring criterion to gradually form a good customer environment. The maintenance of a good platform requires costs, I also hope that MolecularCloud can get better and survive for a longer time.

Thank you for your suggestions, we will continue to strive to enhance the value of the platform, form a sustainable operating mode and promote scientific research sharing all over the world.

Thanks again to Dr. Huang for accepting our interview, which has inspired us a lot. Finally, I wish you good health and good luck on your scientific research!

Thanks for the interview.

Thank you very much for listening. We welcome more professors and students to join MolecularCloud to present their researches and publications, express their opinions about hot topics and share biological resources and information!

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Web: http://www.molecularcloud.org

# MolecularCloud
# 先锋科学家采访

## 对话黄硕老师：生物纳米孔技术的前景

**黄硕教授**

南京大学
化学化工学院

## 教育背景

- 2011年于美国亚利桑那州立大学获得生物物理学博士学位
- 2011年至2015年于英国牛津大学化学系从事博士后研究
- 2015年7月应聘南京大学化学化工学院教授

黄硕老师主要科研方向：

- 具有仿生学概念的单分子纳米孔生物传感器的新仪器，新技术的开发
- 基于纳米孔的单分子显微成像技术

大家好，我是丽丹。欢迎收听 MolecularCloud "先锋科学家"系列采访的第一期。今天我们非常荣幸地请到了黄硕老师。

黄硕老师2011年于美国亚利桑那州立大学获得生物物理学博士学位，2011年至2015年于英国牛津大学化学系从事博士后研究，2015年7月应聘南京大学化学化工学院教授。

黄硕老师主要科研方向为具有仿生学概念的单分子纳米孔生物传感器的新仪器，新技术的开发以及基于纳米孔的单分子显微成像技术。黄硕老师2015年入选国家青年千人计划，2017年被评为江苏省"双创人才"。

黄老师，您好！

丽丹，你好！

2019年到现在，您带领的团队连续在国际著名期刊Nature Communications，Science Advances，Angewandte Chemie International Edition，Chemical Science和iScience等发表多篇高分论文。您能简单给大家介绍下这几篇文章的研究成果吗？

好的，我们课题组在2019年至2020年确实很幸运的有多篇重要工作发表。这几篇工作其实总的来说包括了我们课题组近年来的三个主要方向，其中包括1，新型纳米孔测序技术；2，纳米孔成像技术；3，纳米孔单分子化学这三个主要方向。

其中，最具有代表性的工作我想有这几个。纳米孔测序的创新就在于我们将一系列不可测变成可测。通过我们自行开发的“纳米孔错位测序技术”，我们进行了包括非天然核酸、miRNA等短链核酸分子首次单分子测序。

另外，纳米孔技术本质上是一个电化学方法，电极几乎是必须被使用到的。然而，凡事没有必然，我们开发并命名的 DiffusiOptoPhysiology技术很幸运的成为了领域内首个不需要电极的纳米孔单分子检测技术，事实上其应用效果比我们预期的还要好，这项技术的进一步拓展将会为我们开启低成本纳米孔检测芯片的新时代。

此外，我们在纳米孔测序技术开发中所使用的锥形纳米孔道，也被我们改造成了一个化学纳米反应器。将很多无法被观测到的单分子反应过程清晰的放大出来。这个工作为我们设计多种新型纳米孔化学传感器构建了最重要的孔道设计基础。

谢谢黄老师。如您刚刚介绍的，您课题组近年来的主要工作都是围绕纳米孔技术，并且取得了这么多突破性的进展。那么您认为生物纳米孔技术未来的发展前景如何?

的确，我们课题组在生物纳米孔技术研究上有很多年的研究基础。可以说，我所见到的生物纳米孔技术灵敏、稳定且高效。纳米孔测序的成功其实已经让我们非常清晰的看到，单分子分析技术可以走进我们的日常生活。我想未来领域的发展应该会是有一大批成本低廉，功能独特的基于纳米孔技术的检测方法走进我们的生活。我们也许会在医院的检验报告单中看到纳米孔技术的身影，我们也有可能很快看到成本低廉到1-2块钱的纳米孔检测试剂盒，也许我们都能在电商平台上买到基于纳米孔检测技术的商品等等。

谢谢黄老师的介绍，看到纳米孔测序技术的飞速发展，我们相信，纳米孔技术走进生活将不会太遥远。下面，可以请您分享一下您课题组近期研究重点及未来规划吗?

课题组近期的研究重点有这么几个方面，一个是对于孔道精准改造的进一步探索，一个是对于孔道应用的进一步探索。

从孔道精准改造来说，我们的工作源于仿生，我常常惊叹于自然界的进化竟然为我们构建了这么多结构和功能精巧的生物元件。他们如此之精巧，以致于现阶段人类最尖端的微纳加工技术还赶不上一个小小的原核表达体系。我们已经从自然学习了很多，但放在漫长的仿生科学的历史中，我们也仅仅是窥探了一些皮毛。并且要在学习的基础上有所发展，有所创造。

从孔道的应用探索来说，我们的领域最早是面向纳米孔测序这个非常主要的应用在发展的。现阶段，核酸的纳米孔测序已经成为了较为成熟科研方法，技术虽然还在快速发展，但是技术发展的主线问题应该已经进入工程化和技术转化的层面了。我们还希望探索更多的纳米孔技术应用，包括多肽、蛋白质和多糖的单分子测序技术。这些我们已经有了很多非常令人欣喜的前期研究成果，希望能够在2020年至2021年给大家带来新的惊喜。

好的，非常感谢您的分享。我们非常期待您的新成果发表！
接下来，我们想问一下您课题组在研究过程中有没有遇到什么困难或者有趣的事情？

有的，其实课题组从2015年底成立至今，我和我的学生们一起经历了很多。困难有，趣事也有。

从困难来说，我想最难的是对学生的培养。我们从事的方向是单分子分析化学技术，这个研究领域其实本身就具备高度的学科交叉，化学专业的同学在我们课题组还需要学习很多生物学和物理学的知识，这让我们培养一个优秀的同学周期相对拉长了。有不少同学会在这个学习和成长的过程中感到老师讲的概念很新鲜，但自己出活儿不够快，感到创新点难以捕捉，有过不少抱怨。然而之后同学们也慢慢领悟到科学研究中的乐趣，并逐渐收获令他们欣喜的科研成果。

趣事有很多，我这里举一个吧。科学研究中有太多无心插柳的趣事了。比如我们19年发表于Nature Communications的工作，我前后安排了4名同学去做这个项目，但前面的3名同学不是畏难缺少信心，要么就是拖延缺少恒心，给我的汇报都是负面的。直到第4名同学才真正开始做了这个工作，然后就一发不可收拾的为我们开启了单分子化学这个方向。我想，坚持，兴趣和对实验现象的细致观察是能够做出重要科学发现的必要条件。

好的，谢谢黄老师。虽然您只有寥寥数语，但我们能从中体会到这几年来，您为学生培养付出的努力。疫情期间，您建议学生们应该如何在家学习来推进科学研究?

我们课题组是典型的实验型课题组。疫情对我们的科研进度的打击是非常大的。学校未开学期间，我们的同学主要通过整理前期研究成果、文献学习、创新调研等科研活动保持科研状态。虽然这种状态对于实验型课题组也终究不是长久之计，但是完全放下实验，通过调研进行思维实验的过程让我也体会到了一种新的乐趣，即通过深入充分的调研和头脑实验对一个从未真正开展起来的实验方案进行论证，也为我们找到了很多新的思路。

同时，为了即将到来的学期恢复抓紧时间，我们也和很多科研外包公司，包括金斯瑞签了不少科研服务订单，为开学后的科研工作抢回时间。另外，我们课题组现阶段也和很多从事理论化学、计算机技术的团队展开了全面的合作，通过对无需实体实验操作的科研活动为我们抢回进度。

好的，谢谢黄老师的分享！感谢您一直以来对金斯瑞和MolecularCloud 共享平台的支持。您是平台最早的一批用户，在采访的最后，我们也想听听您对MolecularCloud 有什么想说的话吗?

我非常欣赏MolecularCloud平台和类似的科研共享。世界范围内科研成果的共享是个大的趋势。在我所了解的范围内，以软件代码，科研数据和科研手段的共享正在各个领域被快速的推广开来。质粒的共享是个很好的开始，因为我们自己不仅可以共享也同时很需要其它团队的研究成果共享出来。在我们的领域里，我们常常花很多时间去推敲摸索其它课题组的质粒构建方案，而这些本来也不是其它课题组有意设置的技术障碍。既然如此我们为什么不把这些资源放在一起，让所有有兴趣的科研工作者得以从中获益呢。据我所知，现在我们领域内的质粒共享很多还停留在邮寄样品的低效率的状态，我很高兴有分子云平台，加速了领域内的科研融合，让科学家们走的更近。

现阶段MolecularCloud已经非常优秀。但事实上我还多少有点担心分子云现有的运行模式可能会在推广过程中承担了太多的经济压力。我个人是比较建议MolecularCloud可以在质粒索取上提高一些价格或者是通过广告等营收增加收入，亦或是可以通过某种形式给索取客户或者共享客户打分，进行筛选，并逐渐形成一个良好的客户生态。因为好的平台的维持是需要成本的，我本人也是希望MolecularCloud可以越来越好，并长久健康的生存下去。

感谢您的建议，我们也会不断努力提升平台的价值，形成可持续的运营模式，推进世界范围内的科研共享。

再次感谢黄老师接受我们的采访，给我们带来了很多启发。最后祝您身体健康、科研顺利!

谢谢你们的采访！

也非常感谢各位的收听。我们欢迎更多的老师和学生加入MolecularCloud，展示自己的研究成果，参与热点话题的讨论，共享生物资源和信息！