

ThreeBond TECHNICAL NEWS

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For the smooth progression of research and development

Introduction

Congratulations on the publication of the 100th issue of Technical News! The author has convinced that this huge number of publications also reflects the corresponding great achievements in the research and development at ThreeBond. This is an exceedingly amazing accomplishment. The author has been organizing a laboratory at Tokyo Institute of Technology for 26 years, and during this time the author has been carrying out research works on the creation of new polymeric materials with over 150 master course students and 40 PhD-candidate students. The author has kept in touch with the researchers at ThreeBond since the author first set up his laboratory, and the author has fortunately had many occasions to participate in discussion with them while experiencing the difficulties of research and development that differ from those in the university.

The author is a little afraid whether it will be consistent with the purpose of this Technical News, but he would like to share his thoughts obtained from managing the laboratory and having discussion with the researchers at ThreeBond. Although the perspective of this manuscript might be biased towards the university side and reflect a lack of experience in the related area of work, the author hopes this will be a good occasion for us to think together about how we can achieve smoother research and development.

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1. 1. Sharing furthest information through discussion on research works

When researchers are asked about the negative results on their experiments, they often simply reply “it didn’t work well”. This is a very common way of the communication between one party who is actually doing the experiments and the other who is actually doing the experiments and the other who needs to know the results, when the two parties discuss how to proceed based on the results. However, there is a hidden risk that something important could be missed depending on the amount of information that is shared in advance between the two parties and how the communication continues from that point on.

In the case of routine work where the party asking about the progress has an accurate understanding of all of the specific points of the experiment, such as the methods used by the party conducting the experiments and the range of conditions in which they conducted, and properly understands the scope of potentials that needs to be considered, the author believes that it’s possible to proceed to the next step right after sharing the simple information. However if there’s a difference between the scopes that the party conducting the experiments has considered and the scopes that the party asking about the experiments has envisioned, the researchers might miss the chance to take the results of experiment in a fruitful direction. Many factors could play a role, such as each party’s level of knowledge and experience, the nature of the experiment, the relationship between the parties, and people being very busy, but when not enough information is shared and each party fills in the gaps with their subjective view, unexamined areas that should be pursued as possibilities may be missed because each party assumes that they have already been considered.

For example, when comprehensively discussing the results of a series of experiments where parameters such as the temperature axis, time axis, mixing ratio, and type of catalyst can be changed, it might be difficult to accurately discuss the true images if detailed information about those parameters is not shared. Those matters could include what kind of thinking those parameters were based on, which parts were implemented, and what kind of results were obtained after making those considerations. As the party conducting the experiment becomes more experienced, this relationship of trust is something that should be strengthened considerably, which might, however, also cause unfavorable situations.

That is, the party asking about the experiment will be strengthened. This relationship of trust is something that should be strengthened considerably, which might, however, also cause unfavorable situations. That is, the party asking about the experiment takes an overly favorable interpretation for details that haven’t been discussed, assuming that the party conducting the experiment must have already considered them and ruled them out. Even if it takes some time, the author thinks the party conducting the experiment needs to share all the detailed information as accurately as possible, such as the scope they have considered, why they decided that the experiment didn’t work well, and what happened instead of the expected result. Additionally, it might be necessary to devise a way for both parties to take it for granted that all the details regarding the experiments must be shared.

The author assumes. There may not actually be much cause for concern in ThreeBond’s case; research and development at ThreeBond proceeds exceedingly smoothly as the researchers work toward a common goal with the spirit of “creating our future from a single drop”, and things are functioning smoothly enough. But at universities, there is often a reliance on the generosity of each faculty member, and the author is a little concerned that it may be a situation where it is difficult to have smooth discussion in future. For example, research ethics courses have finally been introduced and classroom-based lectures that focus on topics such as health and safety issues, researchers’ social responsibilities and compliance with laws and regulations have begun. However, faculty members must still teach students through their research activities in the lab. It is not just about learning from experience; the author wonders if educational programs can then be set up that steer towards the philosophy “the wise man learns from the mistakes of others.” Now, digressing briefly, the author has a little more to say about universities. Even when one would consider it necessary to take discussion one step further in order to improve the efficiency of the research, faculty members may be conscious of the difference in status between them and students, and may hesitate to start such a discussion if they get the impression that the students do not really want that. Another major point of self-reflection is that most of the professors are involved too much in various tasks that often limit the chance to ask even a simple question about what the results are going on. A certain percentage of students will look for moments between professors’ meetings to discuss even trivial things despite this, and the author is always struck to see many of these

students improve at an amazing speed. Some students can progress through continuous discussion, and there are cases where you say “in that case, how about doing this?” and the student triumphantly answers that they had envisioned being asked that so they tried it already. They’ve thought ahead, by themselves, conducted an experiment and brought their answer to the discussion. Some students will even research various related studies on their own and be able to suggest a new direction to take in order to reach a solution. Those are moments that also excite the author. The author convinces that all of those students have published comprehensive and exceptional theses, and then attained great contributions in various areas including academia and business. This may be one example of harmony between the party who conducts the research and the party who asks about the results.

On the other hand, when students are welcomed to the lab in April every year and they commence research towards their theses, there are some exceedingly rare cases when the author will ask a student about their results and they will only tell him that the research failed, and do not provide any more information no matter how many questions the author asks. In such cases, it is sometimes necessary to make the students to understand that if the only thing being communicated is failure of the research and no details are given at all, it’s impossible to discuss the research any further, and there is a risk that their research itself might not go any further. In some cases, an error in interpretation of analysis data could lead to a misjudgment, so we need to delve into the issue and discuss it, rather than just making a subjective judgement that it didn’t work well. For example, the research often gets on track after the student understands how important it is to communicate as accurately as possible about points like how the reaction mixture looked like (for example, whether the materials dissolved), whether the materials were recovered without undergoing any reactions or unexpected products formed from the analyses of the materials. Then the students become able to discuss what conclusions can be drawn from the results. This is another situation where the author is delighted to watch researchers come into their own by repeating research activities such as subsequent one-on-one discussion, group meetings, conference presentations, and thesis defense presentations.

The author would like to cover one more point about universities. When renowned professor gives a retirement speech, they often say that because it took a rather long time before they were promoted, they had to conduct

experiments by themselves for a long time, which was, however, an irreplaceable asset for them as a researcher. This means that working on experiments themselves led to interesting unforeseen discoveries that can often be missed in the indirect process of listening to student’s reports, and the author assumes that this an expression of university professors’ own feelings about the difficulty of holding discussion with students.

Many new trends in research come from spotting and delving into experimental results that suggest something interesting is happening—so called serendipity—. The author thinks an important point that leads to this is hidden in those unforeseen results that get lumped into the expression “it didn’t work well.” The author himself also encountered unforeseen and interesting things more often during the time that he could carry out his own experiments than he does now, and he feels that those discoveries rapidly broadened his research. Sometimes the author reminisces fondly about that time, and even today he continues to grapple with the issue of how to find useful information together with students the way he did when he conducted his own experiments. The author feels that it is important to share as many opportunities as possible to celebrate the ups and grapple with the downs together, no matter how trivial the results may be, to make sure his students understand that even if they are still unable to find the answer he is very interested in talking about mysterious phenomena that they encounter along the way, and to place the highest priority on maintaining an environment where students can share their unfiltered thoughts on their issues with an experiment at the time they occur. The reality is, however, that many students who work in a lab assume that they should only discuss their results once they are somewhat close to finding an answer, and it takes time and effort to get them to understand the kind of environment the author is trying to create. Additionally, there is an increasing age gap between the author and his students and the time he is able to spend supervising them in the lab is decreasing a little each year, so he feels that it is becoming increasingly difficult to communicate smoothly about things like this without junior staff. The author will now give a few examples of serendipitous experiences he remembers having through discussion with students. In one case, when a new polyaddition reaction was being considered, but the goal of polymerization was not achieved, a highly selective tandem type zipper cyclization reaction was found to proceed quite effectively¹). While the reaction that occurred was very minor, it ended up being applied

in synthesis reactions as Tomita Zipper Cyclization²). In another case, when trying to polymerize a new monomer, it was found that a highly efficient aggregation-induced emission (AIE) pigment happened to be created³). The author thinks an important point here is that all of these discoveries happened when the Ph.D. student who was conducting the research told him that it didn't work well and he was able to thoroughly discuss what was happening with an observant student.

To return to the previous topic, what has been discussed until now applies to informal one-on-one discussion. It can be assumed that later on the results are summarized a little more precisely and more formal discussion is held regularly as a group or with other groups. In addition to the obvious points like the tension of having so many eyes on you and the opportunity to think the results of your experiments over again, the author believes that the discussion is also an effective way to get feedback from people whose position and point of view might differ slightly and find new points to consider.

When a research group begins tackling a new issue, it can be assumed that there are hidden factors that cannot be hypothesized solely with the research method established by the research group. It is also important to have ways of applying outside views, such as academic conferences, documented information, and collaborative research. This is another area where the author feels that ThreeBond has a sufficient structure in place.

Incidentally, once the formal presentation and discussion stage is reached, the author believes that the chance to hear about things that did not work well is mostly lost. As a result, there is a tendency to end up moving in a direction where it is usually difficult to find opportunities to share what didn't work well and to talk with many people about possibilities for achieving one's goals. There may be various hidden issues that need to be overcome in order to create opportunities to present data on research and development that is still in progress in front of a big audience, but the author thinks it could be interesting to create opportunities for formal presentations that enable active discussion of unfinished work that really needs to be discussed and work where things are not going well with the group's knowledge alone and the group thinks they may be coming to a dead end. Obviously, there is a need to make sure the discussion operates properly so that things do not get out of hand and lead to researchers passing on what the author will later refer to as "bugs" to everyone else, but it might be interesting if it functions in

a way that allows researchers to share knowledge about what kind of approaches can be taken when things are not going well and to receive suggestions they had not thought of from people who have different experiences.

2. Positive and negative knowledge accumulated at research organizations

Although trial and error is always part and parcel with research and development, the author believes that in many cases, the rational way to achieve your objectives is to make effective use of knowledge gained by researchers before you and then explore further. It's a process where you're "standing on the shoulders of giants;" applying past knowledge as it enables the party conducting the experiment to make smooth progress in their research and development and achieve their objectives. The author suggests that sharing knowledge that has been accumulated by research organizations about what went well with the whole group and applying it to achieve positive results is a very efficient method. Conversely, the author postulates that even knowledge of what was considered in the past but did not work well is shared within the research and development group as a whole to provide information on methods that should be avoided, and the group then avoids that method as they carry out their research and development work. For example, when it comes to the policy that will be used for future considerations by the party conducting the experiment, what will happen if someone suggests something that someone else considered in the past but did not work well? The author assumes that they will receive the advice that it was considered in the past but it didn't work well so it is best not to do it. Basically, it is effective advice in order to avoid repeating the same mistakes. When it is clear that the person giving the advice has the past experience of things not going well after spending a considerable amount of time considering all of the possibilities and their knowledge that it didn't work well is quite accurate information, it is right to decide to follow that advice in order to avoid failures. However, related to the topic touched on earlier, some doubts about credibility will remain if the person giving the advice omits details on what was considered and how, or if it is found that the judgment that it didn't work well was actually based only on a small consideration under only some of the possible conditions. In those cases, the experiment may have failed due to other factors such as human error or a flaw with the reagent that was used at that time. In any case,

even if the information has not been properly verified and the opinion that it was not successful is presented to many researchers, it might result in everyone believing that it did not work well without considering factors such as the cause. The author thinks that if the opinion is expressed by a particularly trusted researcher or if multiple researchers say something didn't work well, this will deepen other researchers' assumption in one fell swoop.

This process will create misinformation, also known as bugs, throughout the whole research and development team. Once a bug occurs, people will no longer consider any possibilities in that direction, and depending on the situation, the progress of research and development could be hindered. Guarding against bugs like this is a very difficult issue.

The author would like to touch on a topic that is based on experiences at his university and that he feels is slightly relevant. The postgraduate students in the author's lab come from various universities and since they each have a different level of research experience, the first serious issue that is faced is ruling out the possibility that the experiment did not work well due to the skill level of the person conducting. To address this, along with giving students the chance to become familiar with how to conduct experiments and the types of measurement equipment in the lab, the author gets them to perform double-checks by repeating clearly successful experiments that were conducted by more senior researchers and have been reproduced by at least several people before to see whether they can replicate them.

Once the student gets through this process with no issues and it is clear that they are able to replicate the results of their experiments, they can proceed to new research projects. Some students' work goes smoothly as soon as they start working on new projects, but there are also cases where things don't work well at first. In many cases, those students gradually get on track with encouragement from junior staff and senior researchers, but there are also rare instances where the matter is discussed and suggestions are made by the author but nothing they try works. There are times when the author gets students to change their research topic to one with a higher chance of success and they are able to put together a graduation thesis, and through this process of trial and error, the author creates a database in his mind for examples of things that have not gone well. The author also thinks that when highly skilled students whose experiments usually go extremely

well encounter something that doesn't work well, they add it to that database without much further thought.

The author thinks that after a while, those databases are unconsciously used as a guideline for what needs to be avoided when setting a new task or having a discussion with another student. Obviously it can probably be assumed that most of the details in student's databases are accurate information about what does not work well, but there may be some bugs where the method in question actually does work, or would work under slightly different conditions. The author thinks that there are times when we need to carefully consider the veracity of information on things that didn't work well, especially if that information will influence the future direction of research.

Now, the author would like to talk about one of his experiences of discovering a bug. A student of his had said that an experiment hadn't gone well. After that student graduated, the author had the chance to speak with a student who was doing somewhat related research about the very experiment that that student thought did not work well. The author explained as accurately as possible about factors such as the conditions when the experiment was conducted and why it was decided that it hadn't gone well, and told this student that although the author had thought the experiment would work, this was what had ended up happening. This piqued the student's intellectual curiosity and they tried the experiment again, incorporating their own ideas. After a short while, the student came to the author smiling and explained that the experiment had gone well with their improvements. That breakthrough led to new developments in the research.

Additionally, when the author has a research project that he really hopes will progress smoothly and definitely wants to take further, he sometimes takes the very simple method of leaving it for a little while and suggesting that a junior researcher repeat it. The most important thing, and this is something the author's university colleagues feel the same way about and which they have talked about, is that this only works if all of the students who know the details of why the experiment did not work well have graduated, so you need to be patient. Otherwise, the student who has just been assigned the project hears from others who witnessed the negative results about how previous researchers struggled because it didn't work well, and they end up putting on the brakes.

There have been many times when researchers have been talking about a paper that has been published by a different research group and they remark that in the past they

approached the same problem with the same methodology but it didn't work well. They talk about it with a mixture of skepticism and regret. When the author hears these kinds of conversations, he often feels that there must have been a serendipitous element where the successful researchers lucked into the perfect conditions when they conducted their research, but there are also cases where he suspects that the research group remarking that their research did not work well may have had some incorrect assumptions in the database they created, which made it difficult for them to be optimistic about their research.

So eliminating the bugs that have a tendency to accumulate in research groups is also necessary in order to avoid having other research groups and businesses sailing to success with methods that were deemed as something that would not work. It's quite difficult to figure out how to do this. This might be even more true for corporate research and development departments as every moment counts and you can't take your time and use the kind of measures mentioned earlier. Although solutions may be far from reach, when the author has the chance to explain to someone about something that did not work well, he tries to think back and recall as much as he can about how correct that information was, and think a little about whether there are any examples that can explain why it didn't work out. Even when the information that something in the past did not work well is not a bug, he feels that if the reason for why it did not work well can be identified, sometimes hidden signs for new directions of research can be found.

3. To prevent negative knowledge from occurring

Through discussion with researchers of ThreeBond, the author has come to realize on many occasions that there are difficulties you face that do not exist in university research projects. The author will give a few brief examples of difficulties that he feels could lead to "bugs," and try to think of some ways to prevent that from happening.

1. Discussion about the reactivity of one component in a product

In the development of a new product, once the outline of the composition of the product has been settled, the researchers sometimes focus on one component (component A) that most likely contributes to improving performance, and examine the effects of its structure. In this case, they try to keep the weight ratio of component

A to compare the performance after polymerization and curing. However, if the chemical reaction between component A and a different component (component B), proceeds, for example, in a one-to-one molar ratio, it must be important to keep the molar ratio rather than the weight ratio from the viewpoint of chemical reactions. That is to say, when the chemical structure of component A changes, the molar ratio of the functional groups may change if the weight ratio remains the same, which brings about the inappropriate mixing ratio for smooth polymerization and curing. If the researcher did not notice the influence of the imbalanced molar ratio, they might spread misinformation regarding the reactivity of component A.

In such cases, it might be preferable to change both weights of the components A and B so that the functional groups being mixed keep an adequate molar ratio, while keeping the constant total weight of the components A and B in the product.

2. The relationship between the structure and reactivity of epoxy resin

On one occasion, through the discussing the reactivity of epoxy resins, it was explained to the author that epoxy resin A was more reactive than epoxy resin B and the reason for that was discussed together. It didn't have anything to do with the mixing ratio issue mentioned above, so the author tried to figure out the reason from the difference in their chemical structures. Since A and B have almost the same substructure, it was difficult to explain the difference with knowledge of organic chemistry alone, and he was unable to find an answer. Until he happened to come across a review article that comments on the purity issue of the epoxy resin. That is, the difference in purity of epoxy resins available as industrial products often serves as a predominant factor that determines their polymerization and curing activity. This fact might be well-known for researchers who work with epoxy resin all the time, while it was impressive for the author to know the difficulties to carry out R&D with industrial products. Besides, in order to avoid the occurrence of a "bug", the author believes it necessary to indicate clearly that the reactivity difference in this particular case originates from their purity difference but not from the structural difference.

3. The reactivity of catalysts

The author had a chance to discuss the relationship between the structure of the Lewis acid catalyst and the curing speed of a monomer component. In their

experience, a salt of a particular metal exhibits high activity, while that metal is preferably not to use in industrial applications in future. Although they wanted to switch to other catalyst consisting of different metal centers. They were unable to find more active candidates. They were struggling because the activity of catalysts was not predictable solely from their Lewis acidity. The author also felt it reasonable to correlate the catalytic activity with their Lewis acidity, while the relatively higher activity of the catalysts may also lead to their decompositions through hydrolysis, etc. under the reaction conditions. This decomposition is likely to occur, according to some literature mentioning that metal catalysts with a similar structure undergo structural changes due to reactions such as hydrolysis. In cases like this, if you put this information about metal salt structures and variance in catalytic activity straight into your database, you could end up with misinformation in there; you may need to take structural changes in the catalyst into account when ranking the activity of catalysts. Based on this knowledge, the next step may be to explore catalysts that have both somewhat high Lewis acidity and stability not involving any structural changes in use.

4. The possibility of unforeseen reactions with other components

In order to develop products with excellent performance and/or those with added value curing process, multiple components that contain plural functional groups are often mixed in one pot so as to carry out multiple kind of polymerization and curing processes. In this case, there could be unexpected reactions between functional groups other than the ones from which you are expecting. For example, (meth)acrylates could cause a 1,4-conjugate addition reaction with nucleophilic agents such as amines. Thiols may also undergo similar addition reactions if the Lewis base or radical catalysts are present. If peroxide initiators are employed, it is not recommended to mix with components that serve as electron donors such as amines, which lead to any redox reactions.

Obviously, it may not be necessary to consider such possibilities if these reactions are very slow and negligible under the actual storage, polymerization and curing conditions, and/or if the polymerization and curing reactions occur smoother than the unfavorable side reactions. Nevertheless, it might be preferable to carry out any control experiments by picking up some of the components from the product to know whether unexpected reactions happen. While there have been

major advances in analytical methods also for curing reactions, the effective way to discuss reactions involved in the polymerization and curing of the products in detail is to carry out experiments using model compounds possessing a single reactive functional group for each and evaluate their conversion behaviors and structures.

When you're planning to accumulate knowledge on the reactivity and catalytic activity obtained from the experimental results to the database mentioned above as overarching knowledge, it would be preferable to be careful enough when you know that something happens but you don't know why. There might be any limits to the applicability of such information. Besides, if you know the adequate reasons that bring about the difference in reactivity or activity, the information will be more trustworthy. Therefore, the author would like to suggest to the researchers to try to figure out the reason by searching literature, continuing discussion, conducting additional experiments, etc., even though they might be a little time-consuming process.

Closing

When the author was asked to contribute to this issue of Technical News, the author initially intended to describe something more technical, such as an account for the chemical reactions often employed in adhesion processes. However, before touching on the individual technical topics, as introductory remarks, the author just intended to comment on some general matters that can happen if researchers are working as a team on some research and development projects, which consequently covered most part of this manuscript. Although the excellent human network in the research and development divisions in ThreeBond is of an unparalleled caliber and hence it might be possible that some of the issues described here have already been solved or have not been applicable at all to ThreeBond, the author tried to share the author's experiences and thoughts to have an occasion to think together.

The author felt a sense of clarity while writing, probably because the topics covered here were quite new for the author to write. Eventually, the topics turned out to be the main contents of this manuscript. There might be more adequate topics to discuss, such as the importance to look at the organization as a whole and bring a balanced view to your research and development and the importance to stay attuned to issues that you should be tackling.

Since the author has not reached adequate answers to many of the issues mentioned in this manuscript, the author is a little afraid that the contents might be premature. However, the author wishes to share the issues with the readers to start thinking together how to solve them. Last but not least, the author strongly wishes all of you at ThreeBond the very best in your research and development.

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