

Proposal: In-situ production of self propelled microparticles

IVAR DIJCK - S2306301
Rijksuniversiteit Groningen
June, 2017

I. APPLICANT

Name: Ivar Dijck
Initials: ILD
Mobile: +31627270899
Email: I.dijck@hotmail.com

II. INSTITUTE

Rijksuniversiteit Groningen (RUG)
Nijenborgh 4
9747 AG Groningen
The Netherlands

III. ABSTRACT

Self propelled particles are particles that expend chemical energy to move, this is also called chemotaxis. In this context self propelled particles generate their own chemical gradient which propels them forward. This uses up the chemicals in question until the system reaches equilibrium and any powered motion must stop. For this research a living polymerization reaction will be used to create a chemical gradient in the concentration of the monomer in solution.

The mechanism for self propelled particles is thought to be used much in the workings of the cell. Furthermore many potential applications for self propelled particles exist in medicine, where the particles may be able to better deliver drugs to specific areas. The effect is not yet widely known and only recently have more papers been coming up with it.



**rijksuniversiteit
 groningen**

More fundamental research to this effect is needed to understand it fully. Thus far self propelled particles (SPPs) have only been created in very controlled conditions. The purpose of this research is to create self propelled particles in an in-situ way through self assembly of the components to break the symmetry of the micro particles.

Keywords:

Self propelled particles, self assembly, diffusion, micro particles, living polymerization

IV. RESEARCH PROGRAMME

Chemical gradients are ubiquitous in nature and chemistry as a whole, and they can propel particles. I propose to make self propelled particles in-situ. In most previous attempts the system was always highly ordered before hand and special Janus particles were used.[4] In this research, although the parts are naturally still prepared before hand, the final step is done in-situ. Just like how I imagine it would happen in nature, catalytic agents coupling with a micro particle and thereby propelling. These particles are in some sense positive feedback given their reaction rate will increase as its diffusion goes up, increasing the potential reaction rate it can achieve. At this scale Brownian motion dominates meaning the particles do not fly around like little rockets, but the extra motion shows up as a higher diffusion coefficient instead.



Figure 1: Shows typical Brownian motion tracks for two particles, red having a much lower diffusion coefficient compared to blue. Taken from 40nm particles in a cell.

The effect of SPP comes about when theres a chemical gradient. This chemical gradient wants to be canceled by nearby solution as always, this is related to the mechanism for osmotic pressure. The net effect of this osmotic pressure/chemical gradient is to propel the particle in the direction of the lower monomer concentration.

Currently artificial self propelled particles are usually made from so-called Janus particles, particles with 2 different sides.[6] This breaks the symmetry to facilitate having one direction as preferred direction of motion. The propulsion mechanism here is often thought to be what is called self-electrophoresis instead of self-diffusiophoresis, but the effect is the same.[9] Janus particles are clearly rather rare given the specific circumstances to make them. This research will show a plausible way in which self propelled particles can come about with minimal ordering.

All that is needed for self propelled particles to exist is a symmetry breaking and a high catalytic activity. Using spontaneous symmetry breaking through the use of low concentration, high activity catalyst has not been done before. This research will show that self propelled particles can easily form in almost any chemical system. To study the effect that these SPPs have on a system we will use a very strong catalyst, but you can imagine it working to a lesser extend with any other catalyst as well.

The idea of this research is to make the micro particles link with the initiator in the solution and start the SPP phase at the same time. The concentration of the initiator will be such that on average only 1 should be available per microparticle. This means that the otherwise symmetrical particles gain a specific direction by having the initiator on one side. This solution will then be studied under the microscope and the motion of the particles tracked to determine the diffusion coefficient from the MSD graph (mean square displacement).

The effect of having close to one initiator on average is that I would expect to observe a stochastic distribution of particles that do or do not have the catalyst. Particles with more than one will show a diffusion dependant on the angle between the two catalysts on its surface. Living polymerization initiators have a very high rate of activation, making many active chains at once.

Living Polymerization

Living polymerization means that there is no mechanism for terminating the chain propagation and the initiation step is much faster than the chain propagating step.

Living polymerization has many attractive properties, but most importantly is that the initiator is as reactive as possible, given their low concentration in the sample. Further properties like reactivity scaling linearly with the number of growing chain ends is also very useful. Low poly dispersion will mean a fairly steady rate of polymerization should be reached as quickly as possible.

Initiator Catalyst

In previous work a first generation Grubbs catalyst[2] was used in combination with norbornene.[1] For the polymerization to be considered living, a 3rd generation Grubbs catalyst[3] with oxo-norbornene is a good candidate, given its fast rate of initiation and aggressive ROMP rate. Additionally an easy to follow process for linking this catalyst to silica particles is described that could be adapted for our purposes. All generations of Grubbs catalysts are commercially available.

Norbornene also has the advantage of having a high optical transparency when in solution.

Micro Particles

The micro particles also do not have to be made out of a specific material, any will do. Obvious choices would include dyed poly styrene particles (such as from Thermo Fisher) or Silica micro particles. Size will have a definite effect upon the strength of the self propelled effect, but the range in literature is around $1\mu\text{m}$. [5] Different materials here obviously also mean a different coupling method between the catalyst and particles is needed, though many of such different methods are known. Silica appears to be the best choice here because of the excellent mono dispersivity it can be commercially bought in.

Silica micro particles tend to aggregate less than polymeric particles or gold. Aggregation should be less of a big problem given the low concentrations we will be working at in general.

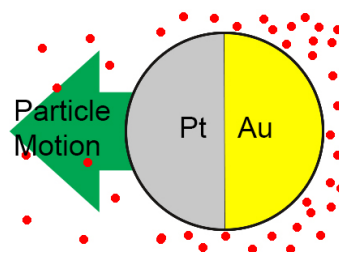


Figure 2: Janus particle showing how it moves down a chemical gradient created by itself.

Linker

A linker is needed between the catalyst and the particle. Such a linker would preferably first react with the catalyst, then put into the mix. The reason for this order is the low concentration of linker and particles in the solution, binding the catalyst to the link maximizes the chances of binding to a particle quickly. During this phase the particle should bond in a fairly quick way else all the monomer will have been polymerized already before the particles are propelled anywhere. There are many silane based linkers commercially available for linking with silica. Especially 3-aminopropyl trimethoxy silane (APS) and 3-(chloro)propyl trimethoxy silane look to be promising in that regard.[1] These could be linked to the imidazole part of the Grubb's catalyst before hand.[13] Low efficiency here is not such a problem since any non working catalysts should simply give the same result as no catalyst at all. The imidazole group stays attached to the Ruthenium during the catalytic cycle.[14]

Hardware

Most important piece of hardware will be a microscope with which to track the particles. This can be a normal light microscope since the particles are of micrometer size. One micron is on the edge of what our eyes can distinguish. Frames will be taken every fraction of a second and from that movie, the position of individual particles can be traced through time. By having a low concentration of particles there will be as little visual clutter as possible in the frames, making it easier to track them.

Software

Tracking particles can be done in ImageJ open source software, with the Fiji module. The Fiji module is designed specifically for tracking particles from microscope data. This data can be analyzed easily by an Excel macro I wrote previously to obtain averages of exponents and MSD graphs. The slope of mean squared displacement graphs is then the experimental diffusion coefficient.

Challenges The biggest challenges are linking the catalyst with the particles quick enough, and making sure the micro particles don't aggregate too much. If such problems crop up there are many ways of adjusting, such as using different linkers or changing solvent respectively. Since the effect is not very dependent on the specific chemicals used, these problems shouldn't be blockers for the project as a whole.

V. APPLICATION PERSPECTIVE

Research into self propelled particle is still in its infancy so direct applications are not yet known. However there are a great many potential applications, especially in fundamental research as models or in medicine for drug delivery.

The vast majority of people in the world will at some point in their lives take drugs for medical reasons. Most drugs that are on the market today are not targeted and very inefficient. The solution to this has been to simply increase the dosage and spread the

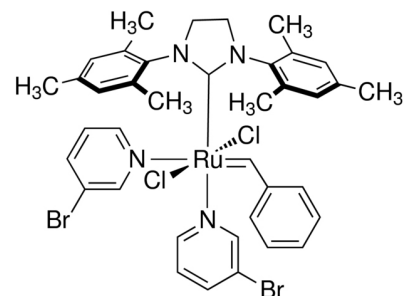


Figure 3: The 3rd generation Grubb's catalyst chemical structure.

payload throughout the body. Drugs can have negative effects on the body where it is not needed, most of the administered drugs have no effect since they do not end up where they are needed and simply get broken down by the body at some point. Making drugs targetable through the usage of self propelled particles could greatly increase medicine effectiveness. An obvious way to do this in a practical sense is to have them "swim upstream" of some chemical gradient naturally occurring in the body to where the drugs are needed. The molecules stored inside the micro particles would then be released, or the particles as a whole taken up by the cell (if they are small enough).

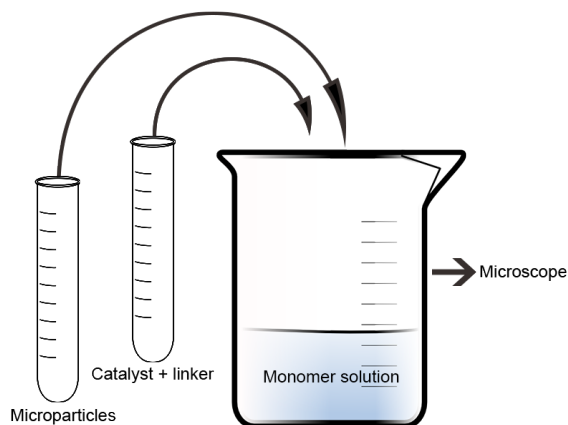


Figure 4: Overall scheme for the project. Linking the catalyst will require some organic synthesis. The effects that the self propelled particles have on the system can be studied by analysis of the data from the microscope.

Potentially more complicated control mechanisms can be made onto the particles to direct them where to go, for example light activated polymerization.[8] In this scenario anywhere the light shines the polymerization reaction would take place, increasing the diffusion of those particles and thus steering them towards darker areas. Such controls can be used to actively and reversibly target the particles to certain areas, in the body or otherwise. This also shows another rare life like behaviour of (negative) phototaxis.[10]

Given the physical nature of the effect, any sufficiently active, unsymmetrical particle would be self propelled. Since this effect is not described accurately yet such effects are glossed over still. In

molecular biology many large protein complexes may have a self propelled component contributing to their activity.[11] This may also, in part, explain the often non-diffusive motion of many cell components seen in living cells (combining with crowding and active transport effects). Similarly large complexes in chemistry in general can have a self propelled character.[12] This will show up as a larger than expected diffusion coefficient leading to a higher activity. Diffusion coefficients are still notoriously difficult to predict given a particle in solution.

VI. INFRASTRUCTURE

This work will be carried out in a laboratory at the Otto group in the Stratingh Institute for Chemistry, this institute was recently awarded with a Nobel prize (Feringa). This would be a new direction for the group, adding to the diverse chemistry being studied there. Plenty of lab equipment already exists in this group such as UPLC's and glove boxes. Microscopes could be made available in a different group nearby (Poolman group). If needed a new light microscope could be purchased (equipment budget of 10K).

VII. BUDGET

Materials costs mostly for miscellaneous chemicals and the micro particles. Equipment budget for a microscope if needed (see also above).

	Costs
PhD costs	208K
Materials	20K
Equipment	10K
Total	238K

REFERENCES

- [1] Ryan A. Pavlick, Ayusman Sen, "A Polymerization-Powered Motor" (Angew Chem Int Edit 40 (2011) 9374-9377)
- [2] Robert H. Grubbs. et al., "Living ring-opening metathesis polymerization" (Prog. Polym. Sci. 32 (2007) 1-29)
- [3] Robert H. Grubbs. et al., "Controlled Living Ring-Opening-Metathesis Polymerization by a Fast-Initiating Ruthenium Catalyst" (Angew Chem Int Edit 42 (2003) 1743-1746)
- [4] Peter J Butler, Ayusman Sen, "Impulsive Enzymes: A New Force in Mechanobiology" (Biomed Eng 8 (2014) 106)
- [5] Tung-Chun Lee, Peer Fischer, "Self-Propelling Nanomotors in the Presence of Strong Brownian Forces" (Nano Lett 14 (2014) 2407-2412)
- [6] Jing Zhang, Zhanhua Silber-Li, "The Self-Propulsion of the Spherical Pt-SiO₂ Janus Micro-Motor" (Micromachines-basel 8 (2017) 123)
- [7] Hila Elimelech, David Avnir, "Cross-linked polyethylene@silica: the first full interpenetrating network hybrid particles" (J Mater Sci 43 (2010) 9613-9619)
- [8] Mao Chen, Jeremiah A. Johnson, "Light-Controlled Radical Polymerization: Mechanisms, Methods, and Applications" (Chem Rev 138 (2016) 15535-15538)
- [9] Liu Ran, Sen Ayusman "Autonomous Nanomotor Based on Copper-Platinum Segmented Nanobattery" (J Am Chem Soc 137 (2011) 2140-2154)
- [10] J. Palacci, P. M. Chaikin "Light-activated self-propelled colloids" (Philos T Roy Soc A 372 (2014) 20130372)
- [11] Hari S. Muddana, Ayusman Sen, Peter J. Butler, "Substrate Catalysis Enhances Single-Enzyme Diffusion" (Am Chem Soc 132 (2010) 2110-2111)
- [12] Samudra Sengupta, Ayusman Sen "DNA Polymerase as a Molecular Motor and Pump" (Am Chem Soc 8 (2014) 2410-2418)

-
- [13] Soon Hyeok Hong, Robert H. Grubbs "Highly Active Water-Soluble Olefin Metathesis Catalyst" (J Am Chem Soc 128 (2006) 3508â€”3509)
- [14] Jeniffer A Love, Robert Grubb "A Practical and Highly Active Ruthenium-Based Catalyst that Effects the Cross Metathesis of Acrylonitrileâ€”" (Angew Chem Int Edit 41 (2002) 4035â€”4037)