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Solid Phase Synthesis of DNA Nanostructures in Heavy Liquid

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Introduction of the solid phase method to synthesize biopolymers has revolutionized the field of biological research by enabling efficient production of peptides and oligonucleotides. One of the advantages of this method is the ease of removal of excess production materials from the desired product, as it is immobilized on solid substrate. The DNA origami method utilizes the nature of nucleotide base-pairing to construct well-defined objects at the nanoscale, and has become a potent tool for manipulating matter in the fields of chemistry, physics, and biology. Here, the development of an approach to synthesize DNA nanostructures directly on magnetic beads, where the reaction is performed in heavy liquid to maintain the beads in suspension is reported. It is demonstrated that the method can achieve high folding yields of up to 90% for various DNA shapes, comparable to standard folding. At the same time, this establishes an easy, fast, and efficient way to further functionalize the DNA origami in one-pot, as well as providing a built-in purification method for easy removal of excess by-products such as non-integrated DNA strands and residual functionalization molecules.

1. Introduction

DNA origami is a powerful tool that enables nanoscale control of matter properties and shape. DNA nanotechnology was introduced by Nadrian Seeman[1] and then further revolutionized when scaffolded DNA origami technique was used to form 2D[2] and 3D[3] shapes. DNA origami utilizes the ability of short DNA strands (called staples) to base pair with a long single strand scaffold at desired positions, to form designed shapes. The software caDNAno is widely used to easily design DNA origami from DNA helices constrained to a honeycomb or square lattice.[4,5] Later, alternative ways of folding and designing DNA origami were introduced, such as twisting and bending via base deletions or insertions,[6] or wireframe polygonal origami.[7,8]

Successful folding of DNA origami requires excess of DNA staple strands, which often need to be eliminated for downstream applications. Several methods have been used for this purpose since the beginning of the DNA origami technique. Purification with physical extraction from agarose gel electrophoresis enables purification of a specific band but it results in a low yield, agarose contaminated and diluted product.[3,9] Ultrafiltration is also used to separate DNA origami from excess of folding material through molecular weight cut-off membrane filters with high recovery yields.[10] PEG precipitation can also be used to separate folded origami from excess of staples but residual PEG molecules can remain in the samples.[11] Moreover, size exclusion chromatography with FPLC[12] or HPLC[13] can effectively separate DNA origami not only from excess of staples but also separate monomeric products from dimers and multimers. Although generally giving good purification results, the method has drawbacks, such as being time consuming and often resulting in diluted samples with lower overall yields.

Various applications of DNA origami require additional modifications with functional elements, where it is crucial to remove the excess of the functional groups from the modified DNA origami. Such functional elements can be proteins,[14] ligands that are often used to study spatial arrangement of receptors,[10,15–17] antibodies,[18,19] or quantum dots.[20] Our previous systematic study about the effective separation of DNA origami from excess of functional groups showed that the optimal method depends on the type of functional group.[12] Overall, a good candidate is size exclusion chromatography but it requires expensive equipment, is time consuming and results in diluted sample. Magnetic beads were also tested, and revealed effective separation between 30 to 70% depending on the functionalization molecule.[12,21]

Solid phase synthesis is a method in which molecules covalently bound on a solid support are synthesized in a single serial reaction, often providing high yield and pure sample with increased simplicity and speed. It was originally used to synthesize peptides[22] but nowadays is widely used in the production of DNA, and RNA oligomers. Often, the solid support is a bead which is linked to the production molecule by

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DOI: 10.1002/smll.202204513

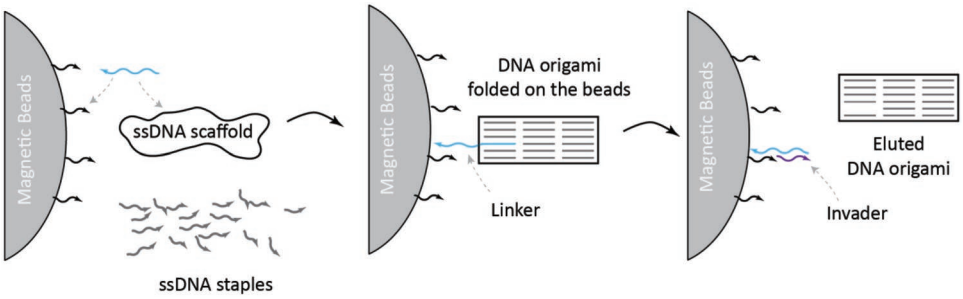

Figure 1. Schematic representation of folding DNA origami with the solid phase synthesis technique. Magnetic beads with oligo $(dT)_{25}$ coating were used to capture the DNA origami, through Linker oligonucleotides (blue), during folding. Linker strand contains an oligo adenine tail, a toehold sequence and a sequence complementary to the DNA origami scaffold. A magnet was used to capture the beads and excess of folding material, present in the liquid, can be removed. Pure DNA origami eluted, in desired buffer and volume, by using an invader strand (purple), complementary to the toehold and scaffold- paired part of the linker DNA strand (blue).

stirring. After completion of the reaction, the solution is removed, and the bead is washed. Recovery of the final product occurs by cleavage from the bead.

In this study we develop a method for synthesizing DNA origami by using the advantages of solid phase synthesis (**Figure 1**). To circumvent the stirring step, which is normally important during solid phase synthesis, we use a chemical called sodium polytungstate (SPT) responsible for creating a dense liquid environment to keep the beads in suspension during folding. As solid support we use magnetic beads conjugated with oligothymine that bind with DNA origami during folding through a linker with an oligo-adenine tail. After successful removal of unused folding material, the final pure product can be eluted using toehold mediated strand displacement. Using this strategy, we hereby introduce a new high yield method to fold DNA origami directly on solid supports. As mentioned above, DNA origami often need to be functionalized with other molecules for use in downstream applications and a different purification method is recruited to remove to functional molecules. With our solid phase synthesis protocol, in a one-pot reaction DNA origami can both fold, then subsequently being purified from excess of folding material, undergo modifications, and then again be purified from excess of these additional molecules.

2. Results and Discussion

The reaction mixture for folding DNA origami with solid phase synthesis technique includes; scaffold, staples strands, magnetic beads, and SPT (**Figure 2**a). After thermal annealing of the mixture in Tris-EDTA buffer, the desired DNA origami is formed on the magnetic beads. An external magnet can capture the beads while the remaining solution, which contains excess staples and a fraction of DNA origami that failed to bind to the beads, can be easily removed. To assure a final product with high purity, the captured DNA origami on beads washed in washing buffer (methods) three times. Finally, the magnetic beads were dispersed in elution buffer (methods) and addition of invasion strand was used to elute the folded DNA origami from the beads by toehold mediated strand displacement.[23,24] A magnet can separate the beads from the solution that contains pure DNA origami ready to use in other applications. To start synthesis of DNA origami on solid support, we need to assure that magnetic beads will remain in suspension for a few hours. For this purpose, we resuspended magnetic beads in Tris-EDTA buffer and SPT and imaged after 30 min, 1, 2, and 3 h (Figure 2b). We observed that magnetic beads at 0 mM SPT precipitated in less than 30 min, at 250 to 270 mM remained in suspension up to 3 hours and 280 to 300 mM floated on top of heavy liquid after 1 h. Concentrations from 250 to 300 mM SPT were used to test the folding of a rod-like 18 Helix-bundle (18HB) DNA origami (Figure 2c). Folding mixture containing scaffold, staples strands, magnetic beads, and SPT run on three different folding programs where the 16hours program gave better reaction yields (Figure S1, Supporting information). This program starts with denaturation during 5 min from 65 to 50 °C and then drops 1 °C per hour. To compare the production efficiency under different SPT concentrations, we ran agarose gels containing reference structures and fractions of unbound, wash and elution steps. As reference structure we used 18HB structure that was folded using a classic (non-bead) folding protocol and subsequently purified using ultrafiltration. We adjusted the concentration of this reference sample to 10 nM and loaded 4 µL (or 186 ng) on the agarose gels. In parallel, we used 10 nM of scaffold and added magnetic beads at a ratio of 23.33 ng scaffold per µL beads to fold the 18HB with the solid phase technique. We then loaded 8 µL of each fraction on the agarose gels. Relative intensity of each main band to reference structure is shown in a bar plot (Figure 2d). We observe that the lanes that correspond to unbound (U) sample appear to migrate slower compared to the other samples. We attribute this to the existence of SPT in the solution of the U samples, which increases the ionic strength of these samples. We clearly see that a small fraction of the DNA origami remained unbound from the bead (<10%) and that excess of the staples effectively removed from the samples. To conclude, 18HB origami is folding in all SPT concentrations tested without any addition of magnesium salts, but more efficiently between 250–280 mM.

To further optimize our solid phase synthesis technique, for high folding yield at the shortest possible time, we investigated five different factors: addition of $MgCl_2$, linker concentration, invader concentration, invader time and the ratio between the amount of scaffold and the amount of magnetic beads. Typically, close-packed DNA origami, needs to be supplemented with $MgCl_2$ solution for negatively charged phosphate backbone

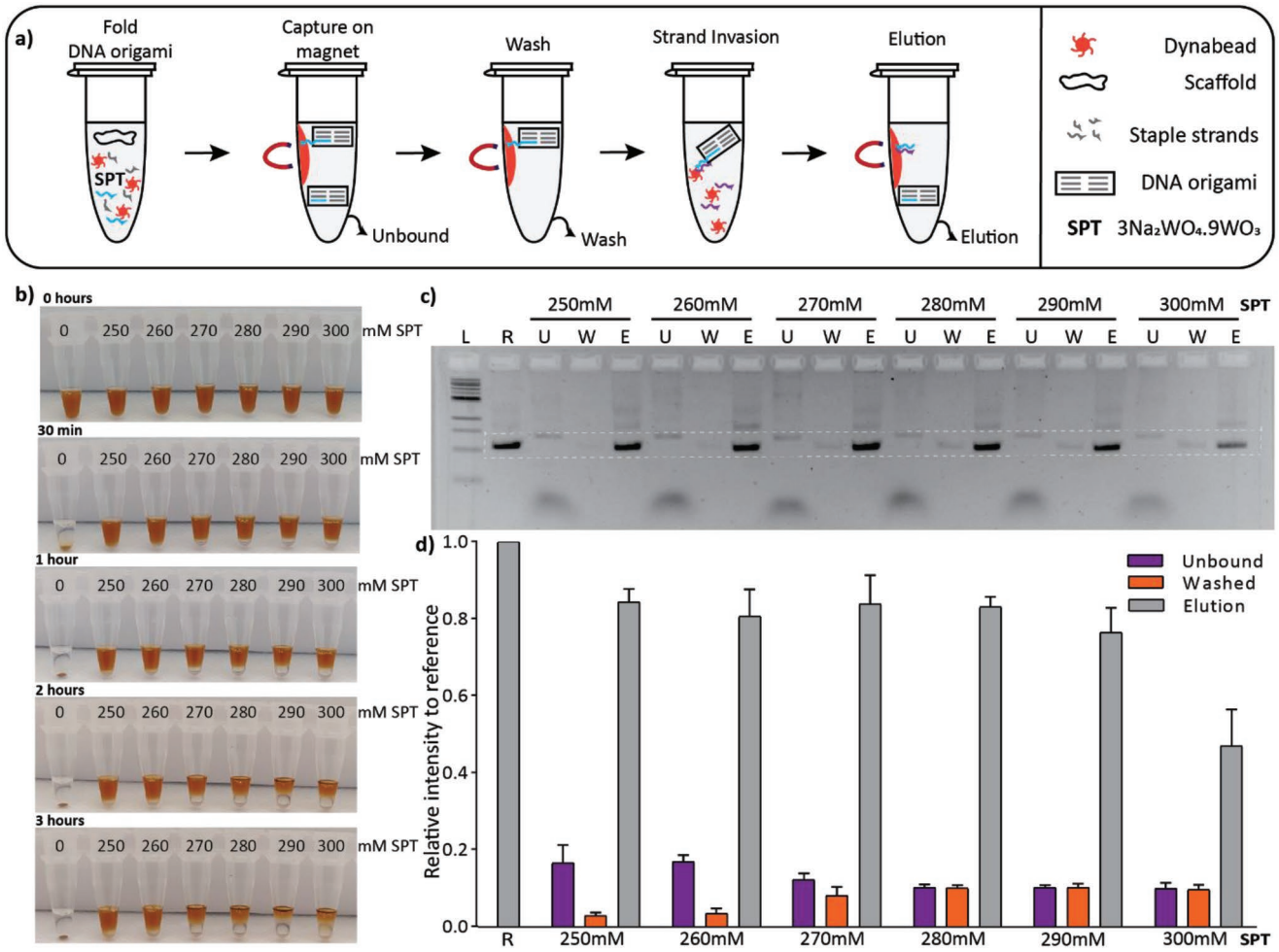

Figure 2. Folding of DNA origami on magnetic beads in suspension, induced by SPT. a) DNA origami is folded by mixing magnetic beads, scaffold, staple strands and SPT in Tris-EDTA buffer. After folding, a magnet was used to capture magnetics beads with the origami, and the unbound origami and excess of staples are removed (Unbound). Additionally, washing buffer added to the beads, to assure that excess of material was removed (Wash). Magnetic beads with captured DNA origami re-suspend in elution buffer containing invasion strands. By placing a magnet, we capture only the beads, and the eluted DNA origami remains in solution (Elution). b) Images of magnetic beads re-suspended in 0 mM and 250–300 mM SPT on folding buffer at different time points up to 3 h. c) Agarose gel of an 18HB DNA origami folded in 250, 260, 270, 280, 290, and 300 mM SPT. Ladder 1 kb (L), reference structures (R) and fractions of unbound (U), wash (W), and elution (E) steps ran on agarose gel. d) Intensity of each band inside the white dashed box (Figure 2c) measured and compared to a reference 18HB structure folded with a standard procedure. Standard deviations shown in bar plots from 4 individual experiments.

of the DNA helixes to stay in close proximity.[3] The DNA origamis used in this paper seem to fold in 4 to 20 mM $MgCl_2$ in magnesium screening experiments (Figure S2, Supporting Information). From results in Figure 2 we observe that SPT, which is composed of sodium, not only facilitates the suspension of the beads for several hours but also provides the necessary positive charge needed for DNA origami folding. Nevertheless, we tested if supplementing with extra $MgCl_2$ would result in highest folding yield. Concentrations between 5 and 20 mM $MgCl_2$ tested during solid phase synthesis of 18HB with no evidence of further folding (**Figure 3**a). These results are in agreement with previous studies for folding DNA origami in monovalent cation solutions.[25] Another factor able to affect the folding reaction is the linker concentration. Given that during folding we always use 5 times excess of staple strands to scaffold concentration, we tested 5, 10, 25, and 50 times excess of linker concentration to scaffold (Figure 3b). We surprisingly observed that 5 and 10 times gave the highest folding yield while 25 and 50 times, lowered it significantly. We believe that high concentrations of linker due to mutually hybridization to both origami and magnetic beads, prevent them from linking together. The linker is composed of an oligo adenine tail that enables binding on magnetic beads, a toehold sequence and a region complementary to the scaffold sequence. The toehold sequence is used for toehold mediated strand displacement during the elution step. We chose two sequences rich in GC content and a third sequence containing all bases. Their pairwise free energy with their respective complement sequences were calculated in NUPACK (using parameters DNA 0 mM Mg^{2+} and 1 M Na^{+}). Different toehold sequences tested and showed similar folding yields for most of the different linker positions designed on 18HB DNA origami (Figure S3,

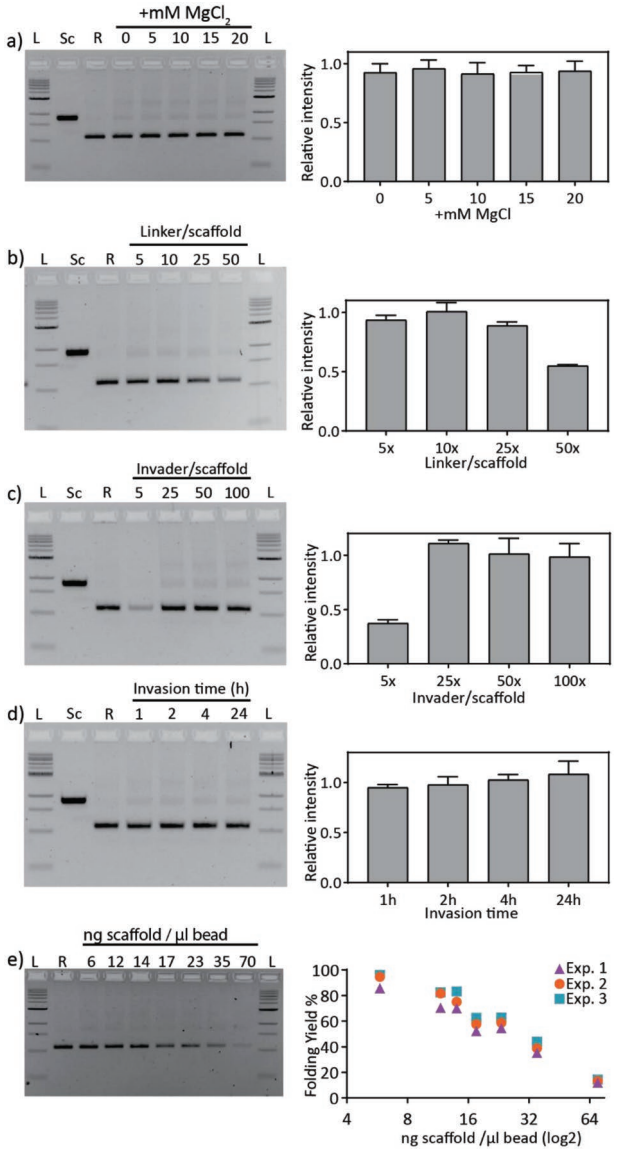

Figure 3. Optimization steps on solid phase synthesis of DNA origami. Five factors that affect the reaction process tested on 18HB structure and fractions of elution samples ran on agarose gel. Intensity of the bands were measured and plotted according to their relative intensity compared to the reference structure. In agarose gels we ran 1 kb ladder (L), scaffold (Sc), reference structure (R), and fractions of solid phase synthesis samples as described in each experiment: a) SPT in folding buffer supplemented with 5–20 mM $MgCl_2$ during solid phase synthesis. b) 5–50 times excess of Linker to scaffold concentration tested during folding. c) 5–100 times excess of invader to scaffold concentration was used during strand invasion step. d) Strand invasion performed for 1–24 h after solid phase synthesis. Standard deviations are shown in bar plots from 3 individual experiments. e) 6–70 ng of scaffold per µL of magnetic beads tested during folding and yield was calculated from the intensity of the bands compared to the intensity of reference product. Purple triangles, blue squares and red dot symbols correspond to individual experiments.

Supporting Information). Elution of DNA origami from the magnetic beads is achieved when an invader strand initiates the toehold mediated strand displacement process. To optimize that step, we tested the invader strand in 5, 25, 50, and 100 times excess to scaffold concentration, where 25 times resulted in sufficient DNA origami elution from the beads (Figure 3c). We then tested invader over time for 1, 2, 4, and 24 h under rotation at room temperature, where 1 hour was enough for eluting a good amount of DNA origami (Figure 3d). To achieve the maximum folding yield, we explored the effect of the ratio between the amount of scaffold and the amount of magnetic beads. According to the suppliers' instructions these magnetic beads are widely used to capture mRNA from pools of RNA sample at 10 ng μL^{-1} of beads. We folded 10 nM of scaffold with solid phase technique at 5.83, 11.66, 14, 17.49, 23.33, 34.99, and 69.98 ng of scaffold per µL magnetic beads. We loaded 4 µL of 10 nM reference 18HB structure and 4 µL of each elution sample on agarose gels (Figure 3e). To calculate the folding yield, we estimated the final concentrations from the intensities of the bands relative to the reference, multiplied by the final reaction volume and divided with the calculated nominal concentration and initial volume. This experiment revealed that 5.83 ng scaffold per µL bead can result in up to 90% folding yield. Step-wise assembly of multiple origami using beads both for folding and for subsequent multimerization,[26] could be used to facilitate the emerging work on DNA origami superstructures.[27–29] To further develop a cost-efficient method for folding and purifying DNA origami, we tried to regenerate the magnetic beads after elution. In this approach we used an invader DNA strand that is complementary to the full linker sequence. The experiment repeated three times where we conclude that magnetic beads can be used again for a few rounds of folding with solid phase synthesis (Figure S4, Supporting Information). An additional advantage of our method is that during elution step we can use buffers suitable for downstream applications without the need of separate buffer exchange techniques. We tested several different buffers during elution and their compatibility with our method confirmed (Figure S9, Supporting Information).

All the optimization steps for folding DNA origami with solid phase synthesis technique described above, were assessed with the 18HB structure. A small proportion seems to remain unbound to the beads that is removed already during the first wash with the excess staples as shown on agarose gels (**Figure 4**a). Migration speed for reference, unbound, wash and elution samples are shown in plots where same migration of reference and elution sample indicates that the structure is correctly folded (Figure 4b). Successful production of the right shape is confirmed by negative stain transmission electron microscopy (TEM) for reference and elution from the solid phase technique with structures whose shapes are identical with respect to the resolution of TEM (Figure 4c; Figure S11a, Supporting Information). To demonstrate that our method works with other DNA origami shapes we tested a 2D rectangle (R) and a 3D hollow brick (HB) structure. Agarose gel for R (Figure 4d) and HB (Figure 4g) show identical results to 18HB. By plotting the migration of gel bands, we see that reference and elution samples for R (Figure 4e) and HB (Figure 4h) also have identical mobilities. Finally, successful folding for both reference and elution samples confirmed by negative stain TEM for R (Figure 4f; Figure S11b, Supporting Information) and HB (Figure 4i; Figure S11c, Supporting Information) DNA nanostructures. Both structures were also validated for several linker

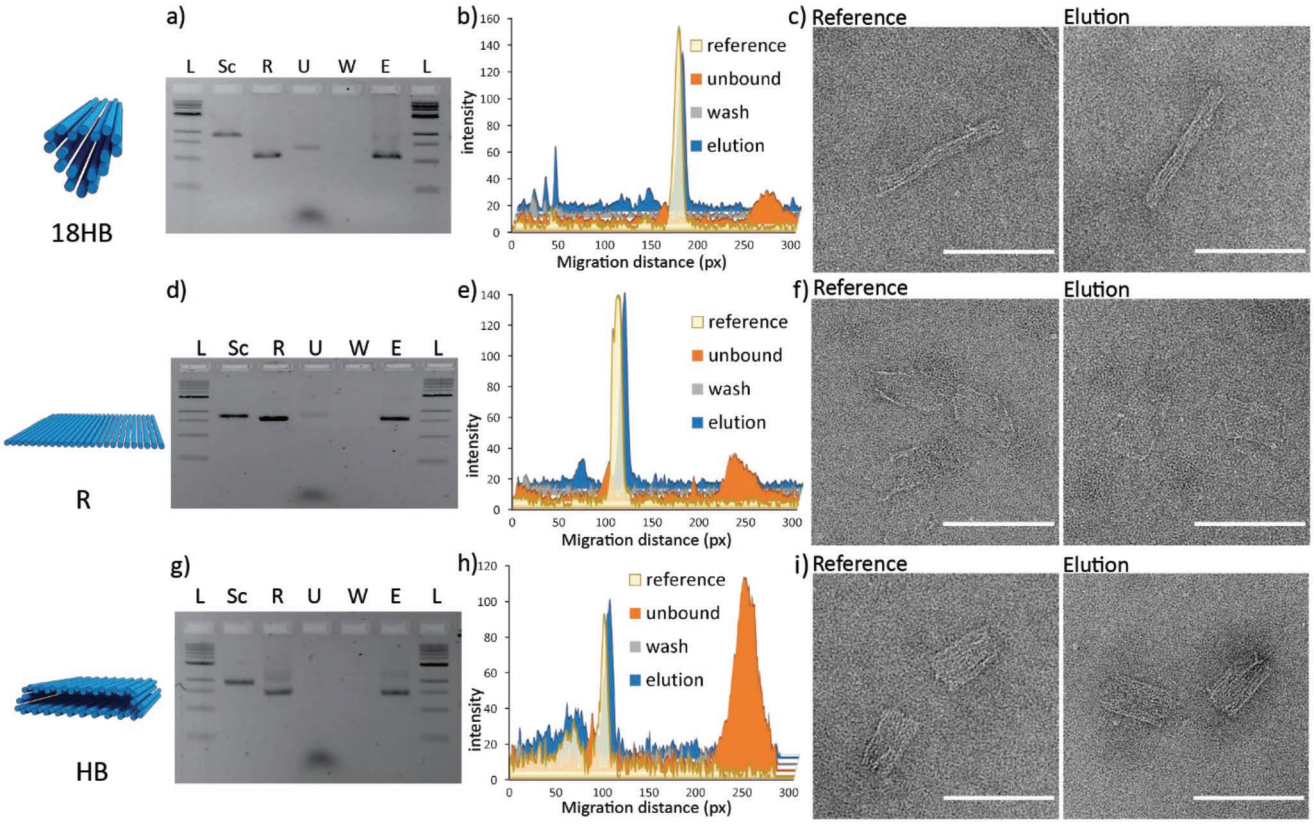

Figure 4. Different structures folded with the solid phase synthesis technique. Agarose gels for a) 18HB, d) R, and g) HB structures showing the migration of: 1 kb ladder (L), scaffold (Sc), reference (R), unbound (U), wash (W), and elution (E) samples. b,e,h) Migration distance of each lane from agarose gels are shown on a plot. c,f,i) Sample TEM pictures of reference structures and structures from the solid phase synthesis for each case (scale bar 100 nm). Zoomed out pictures of the same samples are provided in Figure S11 (Supporting Information).

positions (Figures S5 and S6, Supporting Information) and similar folding yield was found.

One aspect of many applications of DNA-origami is the incorporation of additional modifications on the structures, this step is often limiting both in terms of achievable purity and yield. If a solid-phase protocol could be used also for post-folding modification of origami, this could greatly reduce the experimental burden in many DNA-origami applications. For this purpose, we folded 18HB conjugated with two haptens (digoxigenin, DIG) and solid phase synthesis technique. These haptens serve as antigens for a commercially available high-affinity rabbit anti-DIG IgG. We folded and purified the DNA origami with solid phase technique but before the elution step an antibody was added to the solution in high excess for 1 h. The excess of unbound antibody was removed, and three extra washes assure no remaining amount of antibody is left. We ran reference structures without and with antibodies and elution samples, from solid phase synthesis technique, without and with antibodies on an agarose gel, and similar mobilities of the same samples between the two different folding methods were observed (**Figure 5**a). A shift on the gel after adding an antibody to the DNA origami indicates changes at the molecular weight and charge of DNA origami, compatible with an antibody-modified structure. Using TEM, we confirmed the successful production of antibody modified structures for normal folded samples (Figure 5b) and with solid phase synthesis samples (Figure 5c). The same assay repeated with the HB structure where a shift on the agarose gel for nanostructures modified with antibodies compared to unmodified DNA origami was found (Figure 5d). Successful production of the antibody modified nanostructures with the two different methods was verified on TEM images (Figure 5e,f). For many applications of DNA origami, it is important that all unbound modifications are removed. For this purpose, purified and unpurified samples were analyzed using gel electrophoresis and imaging with TEM. The two samples run at the same speed in the gel and successful removal of antibodies can be observed on TEM images (Figure S7, Supporting Information). To validate our technique for other modifications, we also used the solid phase technique to fold an 18HB with protruding oligo. Before elution step we added a complementary Cy5 oligo for 1 h and washed three times. Successful removal of excess of staples and modification of the structure was revealed on agarose gel (Figure S8, Supporting Information). Furthermore, a major advantage of our technique is the ability to modify DNA origami sequentially with different functionalized molecules and at the same time be able to remove the excess of those different modifications in a one pot reaction (Figure S10, Supporting Information). We believe that this characteristic of the solid phase synthesis technique will impact specifically applications that study co-localization of different types of proteins on the same DNA origami.

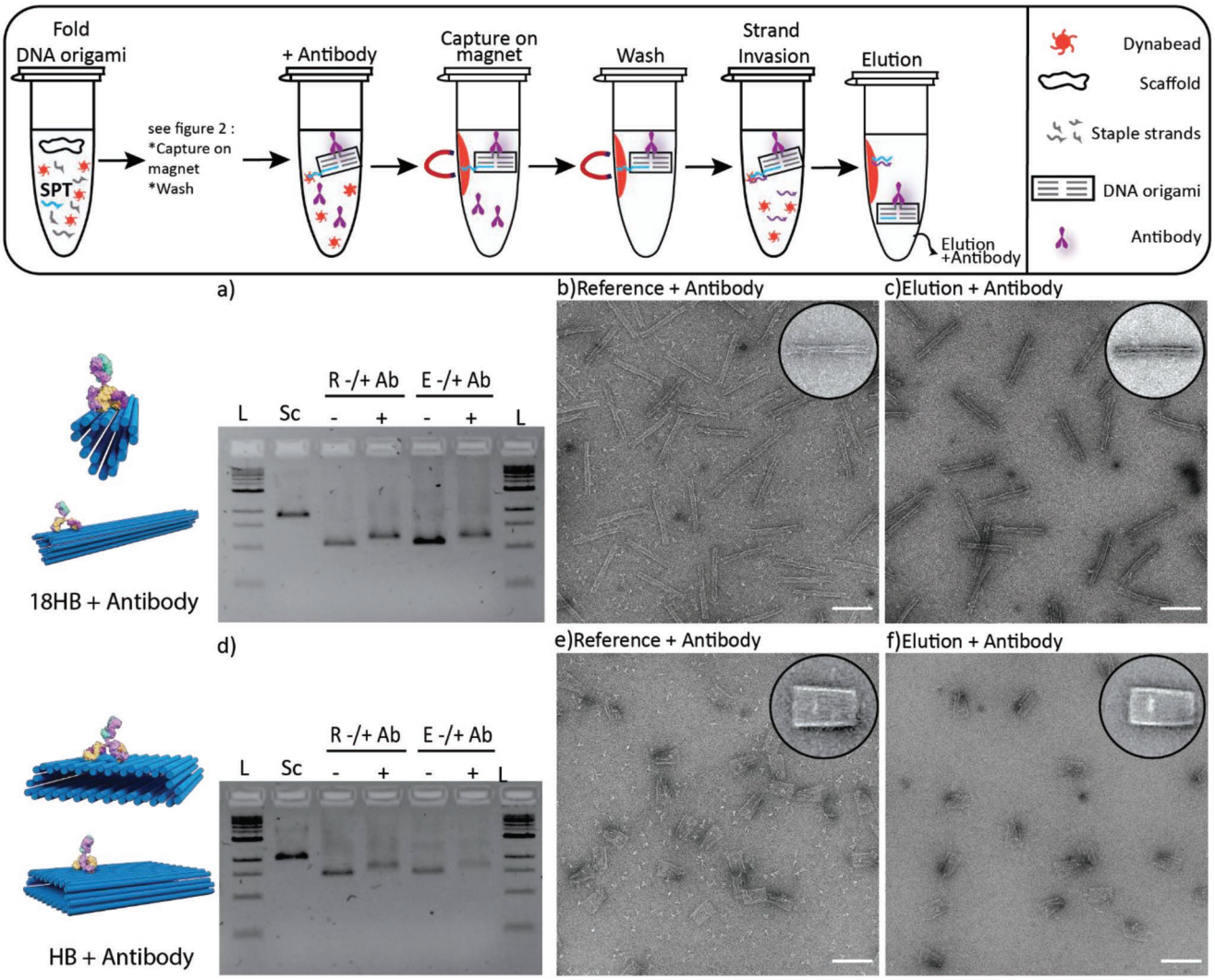

Figure 5. Production of directly purified protein-modified DNA nanostructures using solid-phase synthesis. a) Agarose gels showing the migration of: 1 kb ladder (L), scaffold (Sc), reference structure (R), reference structure with antibody (R+Ab), elution sample (E) and elution sample with antibody (E+Ab) for a) 18HB. TEM pictures of b) reference nanostructures modified with antibody and c) eluted samples modified with antibody for 18HB. d) Agarose gel showing the same samples as in (a) for HB structures. TEM micrographs of e) reference nanostructures modified with antibody and f) eluted sample modified with antibody for HB structures. In all TEM pictures a class average from 100 TEM micrographs are shown in the upper right corner HB (scale bar 100 nm).

3. Conclusion

In this study, we report the development of a new high yield method to directly fold DNA origami on solid support for fast purification from excess of folding material and functionalization molecules. The method offers production and purification in one go and also offers complementary advantages depending on the other purification methods for functionalized DNA origami that one would consider as a comparison (Figure S12, Supporting Information). We use the inorganic compound SPT, due to its ability to produce dense aqueous solutions, to keep magnetic beads in suspension for longer periods. We found that 250 to 280 mM of SPT is sufficient to suspend magnetic beads for several hours and, at the same time, provides an ionic strength appropriate for DNA origami folding, with no need of $MgCl_2$ addition during folding. We further optimize a protocol for high purification yield of DNA origami. During folding we use magnetic beads at the ratio 5.83 ng scaffold per µL bead, scaffold, 5x excess of staples, 10x excess of linker and SPT in Tris-EDTA buffer at thermal cycler for 16 h folding program. After folding we can easily remove excess folding materials in a few seconds. To elute our structures from the solid support, we use 25x excess of invader for at least 1 h. Additionally, we validate our method with three different DNA origami with similar folding yields. Using the magnetic beads and SPT during folding we not only achieve high folding yields but also speed up the purification process significantly. Furthermore, we demonstrate stepwise assembly and purification of modified origami. We introduced modifications at the DNA origami after folding, and purification of the excess material removed successfully in all cases. With existing methods for removal of non-integrated folding material and functionalization molecules we

would need to combine different methods for each step. In this study we develop a method that can be used to purify the DNA origami from excess of folding material with up to 90% yield and from additional functionalized molecules with high purity. Another advantage of this technique is that final product can elute in any desired buffer suitable for downstream applications without the need of extra steps. To summarize, we believe that our method will create new opportunities for scientists to produce pure functionalized DNA origami easily which in turn will facilitate the development of new applications for DNA nanotechnology.

4. Experimental Section

Sodium Polytungstate Preparation: Sodium polytungstate(3.1 grams) (Sigma, 71 913) was dissolved in water at a final concentration of ≈800 mM and placed at 37 °C until is completely dissolved. The final concentration of SPT to fold DNA origami is 270 mM unless otherwise specified in the experiment.

Folding DNA Origami for Reference: Circular single stranded DNA that serves as scaffold for DNA origami folding was produced, extracted and purified from E. coli JM109 inoculated with M13 phage variants.[8] Single strand DNA staples, were purchased from Integrated DNA Technologies. DNA origami structures were folded in folding buffer containing Tris buffer [5 mM Tris (VWR, 77-86-1), 1 mM EDTA (VWR, 20 301.290) at ph 7.8] supplemented with 10 mM $MgCl_2$ (Sigma, M2670). Scaffold at 10 nM and staple strand mixture at 50 nM staple were mixed in folding buffer and placed at a pcr machine. DNA origami was folded by annealing at 65 °C for 4 min, then 65 °C to 50 °C for 1 min per 0.7 °C, 50 °C to 35 °C for 1 h per 1 °C and 20 °C forever until retrieved.

Solid Phase Synthesis of DNA Origami: The folding mixture for solid phase synthesis of DNA origami contains oligo dT_{25} magnetic beads (Thermo, 61 005), Tris buffer (same as in the reference origami), 10 nM scaffold, 50 nM staple strand mixture, 100 nM ssDNA linker, and SPT at a final concentration of 270 mM. The magnetic beads had previously been placed on a magnet to remove their storage buffer and were resuspended in the Tris buffer, before adding the other components. The ratio of DNA scaffold to beads used in most of the experiments is 5.83 ng μL^{-1}. The mixture was placed in a PCR machine and folded by annealing at 65 °C for 4 min, then 65 °C to 50 °C for 1 min per 0.7 °C, 50 °C to 35 °C for 1 h per 1 °C and 20 °C forever until retrieved. Then, the tube was placed on a magnet where the solution was removed and kept for agarose gel analysis. This solution is called unbound in this study, because it contains the unbound DNA origami and the excess of folding material. The beads were subsequently washed with washing buffer containing 1x PBS (Sigma, 806 552) supplemented with 10 mM $MgCl_2$ without removing the tube from the magnet in order to avoid the formation of dimers and multimers. The first wash was also kept for agarose gel analysis. The magnetic beads were re-suspended in elution buffer containing 1x PBS supplemented with 10 mM $MgCl_2$ and invasion strand at 250 nM for at least 1 h. Finally, the tube was placed on a magnet to separate the beads from the solution that contains the pure DNA origami.

Ultrafiltration Method for Reference DNA Origami Purification: The excess of staple strands in the reference structure samples, was removed by molecular weight cut-off filters, 100k columns 0.5 mL Amicon (Sigma, UFC5100). Folded DNA origami at 100 µL was diluted with PBS buffer supplemented with 10 mM $MgCl_2$ to 400 µL, placed on the filter tube, spun down for 1 min at 10.000 rpm and then re-diluted to 400uL.This procedure was repeated 7 times or until no excess of staples detected at the flow throw using a spectrophotometer (Nano-Drop, Thermo Fisher). The final concentration was measured using Nano-Drop and adjusted to 10 nM for direct application on the agarose gel electrophoresis.

Agarose Gel Electrophoresis: Agarose gels were casted by mixing 2% w/v agarose, 0.5x Tris-Borate-EDTA (TBE) (VWR, 0658), 10 mM $MgCl_2$ and 0.5 mg mL^{-1} ethidium bromide (Invitrogen, 15585-011). Gels were run in a buffer containing 0.5x TBE supplemented with 10 mM $MgCl_2$ at 90 V for 2–3 h. The gel tank was placed on ice water bath during the run for cooling. The gels were imaged on a GE Image Quant LAS 4000 system.

Negative-Stain TEM: The concentration of samples was first adjusted to 5 nM and then 3uL were applied on glow discharged, carbon-coated, formvar resin grid (Electron Microscopy Sciences) for 20 seconds. Then the grid was blotted on filter paper and stained with 2% w/v aqueous solution of uranyl formate supplemented with 20 mM NaOH. The negative stained samples were imaged by Talos 120 V microscope at 73 000x, 92 000x, and 150 000x magnification.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

Acknowledgements

The authors would like to acknowledge support from the Knut and Alice Wallenberg Foundation for B.H. (Grants KAW 2017.0114 and KAW 2017.0276), from the European Research Council ERC for B.H. (Acronym: Cell Track GA No. 724872), from Swedish research council for B.H. (grant no. 2019-01474), and from Academy of Finland for B.S. (grant no. 341908).

Conflict of Interest

The authors declare no conflict of interest.

Author Contributions

I.S., A.S., and B.H. conceived the study and designed experiments. I.S. performed most of the experimental work. A.S contributed to initial solid phase synthesis experiments. Y.Y. and B.S contributed to transmission electron microscopy experiments. All of the authors contributed to writing the manuscript. All authors have given approval to the final version of the manuscript.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords

DNA nanostructures, DNA origami, purification, sodium polytungstate, solid phase synthesis

Received: July 21, 2022
Revised: October 25, 2022
Published online:

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