

WELL PLATE SUPPORT

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] The present application claims the benefit of priority of U.S. Provisional Patent Application No. 63/585,696, filed September 27, 2023, the entire contents of which is incorporated herein by reference.

RELEVANT FIELD

[0002] Embodiments described herein relate to a support to prevent deformation of a well plate during centrifugation. More specifically, some embodiments relate to a support to prevent deformation of a well plate used in high resolution microscopy techniques, such as digital molecule counting, requiring a centrifugation step.

BACKGROUND

[0003] Many techniques in molecular biology, including digital molecule counting for immunoassays, require centrifugation of a well plate at speeds resulting in a force up to 4500 x gravity to be exerted on the well plate. During centrifugation, a well plate can become deformed, with maximum deformation typically at the center of the optical read surface for the digital counting system. Deformation can cause distortion of the optical read surfaces, delamination resulting in reagent leaking, or mechanical failure, also referred to as cracking, of the well plate.

[0004] Previously, there was no known device to support well plates to prevent deformation during centrifugation. If a well plate is prone to failure, a scientist may experiment with lower centrifugation forces thereby reducing the effectiveness of the centrifugation step. Alternatively, a scientist may also avoid centrifugation entirely and pipette the fluid into the bottom of the well plate while attempting to avoid air bubbles. Only a scientist with diligence and good technique can accomplish this repeatably, which is why centrifugation is so often recommended.

[0005] Researchers have previously used a lid, sometimes referred as a 'shoe', to protect the bottom of a well plate from dust and debris when on a lab bench, such as the Aurora plates (product number: ABB200160A; sold by MilliporeSigma, Burlington, MA) packaged with a lid that can be used to

protect the bottom of the plate or the Ultra Low Profile Lid for Microplates sold by Greiner Bio-One (product number: 691101) which can be used in a similar way with certain Greiner-brand well plates.

[0006] A support designed to physically support the optical read surface of a well plate to significantly reduce deformations and stresses, and thus diminish centrifugation issues would represent an advance in the art.

SUMMARY

[0007] The shortcomings of the prior art are overcome by embodiments described herein.

[0008] Some embodiments include a support for a well plate, the support comprising: a tiered rectangular structure comprising at least a top level and a lower level; a length and a width of the top level being less than a length and a width of the lower level, and the length and the width of the top level being at least the same as a length and a width of an optical read surface of the well plate; and the length and width of the lower level being greater than the length and the width of the top level, and the length and the width of the lower level are at least the same as a length and a width of the well plate.

[0009] In some embodiments, the length of the lower level is within the range of 120 mm to 140 mm. In some embodiments, the width of the lower level is within the range of 75 mm to 95 mm. In some embodiments, the length of the top level is within the range of 105 mm to 130 mm. In some embodiments, the width of the top level is within the range of 65 mm to 85 mm. In some embodiments, at least one dimension of the support is such that at least one open space is formed between a top or a side of the top level or the lower level when the support is contacted with a well plate for centrifugation. In some embodiments, the support further comprises a middle level. In some embodiments, a length and a width of the top level being less than a length and a width of the middle level. In some embodiments, at least one dimension of the support is such that at least one open space is formed between a top or a side of the middle level. In some embodiments, the length of the middle level is within the range of 120 mm to 130 mm. In some embodiments, the width of the middle level is within the range of 80 mm to 90 mm.

[0010] Some embodiments include a system formed by contacting an optical read surface of a well plate to the support described above.

[0011] Some embodiments include a method for reducing the frequency and degree of deformation or failure of a well plate during centrifugation compared to the risk of deformation or failure of the well plate without using the support of any one of claims 1-8 during centrifugation, the method comprising: contacting a well plate to an optical viewing area of the support; and centrifuging the well plate and support.

[0012] In some embodiments, centrifuging occurs prior to single molecule counting. In some embodiments, the method further comprises preventing delamination of an optical read surface from a frame of the well plate.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] FIG. 1 provides some embodiments of a well plate contacting a support.

[0014] FIG. 2 provides an exploded view of some embodiments shown in FIG. 1.

[0015] FIG. 3A provides a cross-section view of some embodiments shown in FIG. 1. FIG. 3B provides a line drawing enlarging the portion of FIG. 3A within the circle.

[0016] FIG. 4 is a line drawing of a side view of some embodiments of the support.

[0017] The appended drawings illustrate some embodiments of the disclosure herein and are therefore not to be considered limiting in scope, for the invention may admit to other equally effective embodiments. It is to be understood that elements and features of any embodiment may be found in other embodiments without further recitation and that, where possible, identical reference numerals have been used to indicate comparable elements that are common to the figures.

DETAILED DESCRIPTION

[0018] The present disclosure describes some embodiments of a support to significantly reduce the frequency and degree of failure of well plates during centrifugation. Some embodiments of the support are especially helpful for

reducing the frequency or degree of failure for glass bottom or transparent plastic bottom well plates, which are used in high resolution microscopy applications. Glass bottom or transparent plastic bottom well plates are generally more delicate than other types of well plates. In some embodiments of glass bottom or transparent plastic bottom well plates, the optical read surface is adhesively attached to the well plate frame. The optical read surface can become delaminated if the frame deformation becomes significant, as is prone to happen during centrifugation. In some embodiments, the objective lens is positioned below the optical read surface when the contents of the wells in the well plate are being viewed using an inverted microscope.

[0019] A typical well plate has a thin frame that can subject to extreme bending and eventual failure at high centrifugal forces. In some embodiments, the support is below an optical read surface resulting in the well plate being more uniformly supported. In some embodiments, the optical read surface is flat. In some embodiments, the optical read surface is large. In some embodiments, the support contacts the optical read surface. In some embodiments, the contact is not continuous with the optical read surface. In some embodiment, the support spreads centrifugal forces to a larger area than the centrifugal forces for a well plate not using the support. In some embodiments, use of the support reduces deformation of the well plate overall and/or the optical read surface. In some embodiments, use of a support results in a reduction in engineering stress during centrifugation. For example, engineering stress is significantly reduced for well plates using a support during centrifugation. In some embodiments, the support acts as a cover to prevent dust from getting on the imaging surface.

[0020] FIG. 1 provides a line drawing of some embodiments of a well plate **1** seated on a support **2**. The exploded view of some embodiments, shown in FIG. 2, shows the well plate **1** and support **2** as physically distinct components. In some embodiments, the support **2** comprises of at least three tiered levels: a top level **5**, a middle level **6**, a lower level **7** as shown in FIG. 4. In some embodiments, the support **2** comprises two tiered levels: a top level **5** and a lower level **7**. In some embodiments, the length and the width of the support **2** are the same as the length and the width of the lower level **7**.

[0021] In some embodiments, the length of the lower level **7** is within the range of 120 mm to 140 mm. In some embodiments, the length of the lower level **7** is within a range selected from the group consisting of: 120 mm to 121 mm, 121 mm to 122 mm, 122 mm to 123 mm, 123 mm to 124 mm, 124 mm to 125 mm, 125 mm to 126 mm, 126 mm to 127 mm, 127 mm to 128 mm, 128 mm to 129 mm, 129 mm to 130 mm, 130 mm to 131 mm, 131 mm to 132 mm, 132 mm to 133 mm, 133 mm to 134 mm, 134 mm to 135 mm, 135 mm to 136 mm, 136 mm to 137 mm, 137 mm to 138 mm, 138 mm to 139 mm, and 139 mm to 140 mm. In some embodiments, the length of the lower level **7** is 127.9 mm.

[0022] In some embodiments, the width of the lower level **7** is within the range of 75 mm to 95 mm. In some embodiments, the width of the lower level **7** is within a range selected from the group consisting of: 75 mm to 76 mm, 76 mm to 77 mm, 77 mm to 78 mm, 78 mm to 79 mm, 79 mm to 80 mm, 80 mm to 81 mm, 81 mm to 82 mm, 82 mm to 83 mm, 83 mm to 84 mm, 84 mm to 85 mm, 85 mm to 86 mm, 86 mm to 87 mm, 87 mm to 88 mm, 88 mm to 89 mm, 89 mm to 90 mm, 90 mm to 91 mm, 91 mm to 92 mm, 92 mm to 93 mm, 93 mm to 94 mm, and 94 mm to 95 mm. In some embodiments, the width of the lower level **7** is 85.5 mm.

[0023] In some embodiments, the length of the middle level **6** is less than the length of the lower level **7**. In some embodiments, the length of the middle level **6** is within a range of 115 mm to 135 mm. In some embodiments, the length of the lower level **7** is within a range selected from the group consisting of: 115 mm to 116 mm, 116 mm to 117 mm, 118 mm to 119 mm, 119 mm to 120 mm, 120 mm to 121 mm, 121 mm to 122 mm, 122 mm to 123 mm, 123 mm to 124 mm, 124 mm to 125 mm, 125 mm to 126 mm, 126 mm to 127 mm, 127 mm to 128 mm, 128 mm to 129 mm, 129 mm to 130 mm, 130 mm to 131 mm, 131 mm to 132 mm, 132 mm to 133 mm, 133 mm to 134 mm, and 134 mm to 135 mm. In some embodiments, the length of the middle level **6** is 125.1 mm.

[0024] In some embodiments, the width of the middle level **6** is less than the width of the lower level **7**. In some embodiments, the width of the middle level **6** is within a range of 70 mm to 90 mm. In some embodiments, the width of the middle level **6** is within a range selected from the group consisting of:

70 mm to 71 mm, 71 mm to 72 mm, 72 mm to 73 mm, 73 mm to 74 mm, 74 mm to 75 mm, 75 mm to 76 mm, 76 mm to 77 mm, 77 mm to 78 mm, 78 mm to 79 mm, 79 mm to 80 mm, 80 mm to 81 mm, 81 mm to 82 mm, 82 mm to 83 mm, 83 mm to 84 mm, 84 mm to 85 mm, 85 mm to 86 mm, 86 mm to 87 mm, 87 mm to 88 mm, 88 mm to 89 mm, and 89 mm to 90 mm. In some embodiments, the width of the middle level **6** is 82.8 mm.

[0025] In some embodiments, at least one of the middle level **6** and the lower level **7** guide the well plate **1** into place over the support **2**. In some embodiments, at least one of the middle level **6** and the lower level **7** prevent the well plate **1** from slipping off the support **2** during centrifugation or handling.

[0026] In some embodiments, the length of the top level **5** is less than the length of the middle level **6**. In some embodiments, the length of the top level **5** is less than the length of the lower level **7**. In some embodiments, the length of the top level **5** is within the range selected from 105 mm to 130 mm. In some embodiments, the length of the lower level **7** is within a range selected from the group consisting of: 105 mm to 106 mm, 106 mm to 107 mm, 107 mm to 108 mm, 108 mm to 109 mm, 109 mm to 110 mm, 110 mm to 111 mm, 111 mm to 112 mm, 112 mm to 113 mm, 113 mm to 114 mm, 114 mm to 115 mm, 115 mm to 116 mm, 116 mm to 117 mm, 118 mm to 119 mm, 119 mm to 120 mm, 121 mm to 122 mm, 122 mm to 123 mm, 123 mm to 124 mm, 124 mm to 125 mm, 125 mm to 126 mm, 126 mm to 127 mm, 127 mm to 128 mm, 128 mm to 129 mm, 129 mm to 130 mm. In some embodiments, the length of the top level **5** is 117.9 mm.

[0027] In some embodiments, the width of the top level **5** is less than the length of the middle level **6**. In some embodiments, the width of the top level **5** is less than the length of the lower level **7**. In some embodiments, the length of the top level **5** is within the range selected from 65 mm to 85 mm. In some embodiments, the width of the lower level **7** is within a range selected from the group consisting of: 65 mm to 66 mm, 66 mm to 67 mm, 67 mm to 68 mm, 68 mm to 69 mm, 69 mm to 70 mm, 70 mm to 71 mm, 71 mm to 72 mm, 72 mm to 73 mm, 73 mm to 74 mm, 74 mm to 75 mm, 75 mm to 76 mm, 76 mm to 77 mm, 77 mm to 78 mm, 78 mm to 79 mm, 79 mm to 80 mm, 80 mm to 81 mm, 81 mm to 82 mm, 82 mm to 83 mm, 83 mm to 84 mm, and 84 mm to 85

mm. In some embodiments, the length of the top level **5** is 79.5 mm.

[0028] In the cross-section view of an embodiment shown in FIG. 3A and FIG. 3B, the support **2** physically contacts the well plate **1**. In some embodiments as shown in Fig. 3A and FIG. 3B, the support **2** physically contacts the optical read surface **3** of the well plate **1**. In some embodiments, other surfaces **4** are not in contact with the support **2** and an open space exists between the support **2** and the well plate **1** to ensure the optical surface **3** is always supported by the top level **5** of the support **2**. In some embodiments, the other surfaces **4** comprise the lower level **7** and the middle level **6**. In some embodiments, the lower level **7** and the middle level **6** do not physically contact the well plate **1**. In some embodiments, the support **2** does not physically contact the side of the top level **5**. In some embodiments, the support **2** does not physically contact the side or the top of the middle level **6**. In some embodiments, the support **2** does not physically contact the top of the lower level **7**. In some embodiment, the lack of physical contact described above prevent over-constraint of the well plate **1**.

[0029] In some embodiments, the lack of physical contact results in empty space between the other surfaces **4** and the well plate **1**. In some embodiments, an empty space exists between the side of the top level **5** and the well plate **1**. In some embodiments, an empty space exists between the side of the middle level **6** and the well plate **1**. In some embodiments, an empty space exists between the top of the middle level **6** and the well plate **1**. In some embodiments, an empty space exists between the top of the lower level **7** and the well plate **1**.

[0030] In some embodiments, the support **2** enables a well plate **1** to be centrifuged with much lower risk of failure due to bending and stresses experienced during the centrifugation process compared to the risk during centrifugation of a well plate **1** without the support **2**.

[0031] In some embodiments, the support **2** is single-use. In some embodiments, the support **2** is multi-use. The design of the support **2** may be adjusted for the specific well plate **1** to be supported. In some embodiments, the support **2** is produced by any means appropriate. In some embodiments, the support **2** is produced by machining. In some embodiments, the support **2** is produced by injection-molding. In some embodiments, the support **2** is

produced by forming. In some embodiments, the support **2** is produced by three-dimensional (3D) printing.

[0032] In some embodiments, the support **2** is made of any appropriate material. In some embodiments, the support **2** is made of polyethylene terephthalate glycol (PETG) plastic. In some embodiments, the support **2** is made of polypropylene (PP) homopolymer plastic. In some embodiments, the support **2** is made of polystyrene (PS). In some embodiments, the support **2** is made of acrylonitrile butadiene styrene (ABS).

Methods

[0033] Some embodiments herein describe a support **2** designed to prevent deformation of a well plate **1** used in laboratory techniques requiring high centrifugation forces. In some embodiments, the support **2** is used during Millipore® (single molecule counting) SMC® Assays. In some embodiments, an eluted product is pipetted into a well plate such as Greiner #781892 or Aurora #ABB200160A. In some embodiments, after the well plate top is sealed, the plate is centrifuged the plate at 1000 x gravity to ensure that the reagent product is at the bottom of the well and there are no air bubbles. Such centrifugation can cause failure in well plates, especially high resolution imaging well plates including an optical read surface that is glass, such as Greiner #781892. Alternatively, the optical read surface is made of transparent plastic.

Definitions

[0034] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention pertains.

[0035] As used herein, the singular forms "a", "an," and "the" include plural unless the context clearly dictates otherwise.

EXAMPLES

Example 1

[0036] The discussed support enables a well plate to be centrifuged with much lower risk of failure due to bending and stresses experienced during the

centrifugation process. A Computer Aided Design (CAD) 3-D model representative of Greiner #781892 SensoPlate™, consisting of outer polystyrene plastic and an optical read surface, was simulated to be subject to 1000 x gravity centrifugal force using software from SolidWorks Corp. (Dassault Systems).

[0037] The simulation subjected the well plate to this force first without any support, and then with a support. Results show that the support reduced deformation more than 40X, from 215 µm at the center of the well plate without a support, to less than 5 µm when the support was utilized. Stresses were also reduced by approximately 15X, resulting in a process where material failure is less likely to occur.

[0038] The well plate simulated without a support at 1000 x gravity experienced a maximum deformation of 215 µm at the center of the plate and a maximum stress of 32.3 MPa in the optical read surface. In contrast, the well plate simulated with support at 1000 x gravity was observed to experience a deformation at the center of the plate of less than 5 µm and stress in the glass dropped to around 2 MPa.

Example 2

[0039] In additional testing, twelve Greiner #781892 well plates were subjected to high centrifugation forces (170 to 3400 x gravity) with and without the support. Only one Greiner well plate with the support showed evidence of delamination of the optical read surface, and these results were at the highest centrifugation of 3400 x g. In contrast, two Greiner well plates tested without the support showed evidence of delamination and cracking of the plastic frame when subjected to 2000 and 3400 x gravity centrifugation.

[0040] Simulations have shown similar high deformations and stresses in other well plates such as Aurora #ABB200160A. Testing of this model Aurora plate to high centrifugation forces has also shown failure of the frame, and customer complaints indicate potential for leaking and delamination of the optical read surface made of cyclo olefin polymer (COP).

EQUIVALENTS

[0041] All ranges for formulations recited herein include ranges therebetween and can be inclusive or exclusive of the endpoints. Optional included ranges are from integer values therebetween (or inclusive of one original endpoint), at the order of magnitude recited or the next smaller order of magnitude. For example, if the lower range value is 0.2, optional included endpoints can be 0.3, 0.4,... 1.1, 1.2, and the like, as well as 1, 2, 3 and the like; if the higher range is 8, optional included endpoints can be 7, 6, and the like, as well as 7.9, 7.8, and the like. One-sided boundaries, such as 3 or more, similarly include consistent boundaries (or ranges) starting at integer values at the recited order of magnitude or one lower. For example, 3 or more includes 4, or 3.1 or more.

[0042] Reference throughout this specification to “one embodiment,” “certain embodiments,” “one or more embodiments,” “some embodiments,” or “an embodiment” indicates that a feature, structure, material, or characteristic described is included some embodiments of the disclosure. Therefore, the appearances of the phrases such as “in one or more embodiments,” “in certain embodiments,” “in one embodiment,” “some embodiments,” or “in an embodiment” throughout this specification are not necessarily referring to the same embodiment.

[0043] Publications of patent applications and patents and other non-patent references, cited in this specification are herein incorporated by reference in their entirety in the entire portion cited as if each individual publication or reference were specifically and individually indicated to be incorporated by reference herein as being fully set forth. Any patent application to which this application claims priority is also incorporated by reference herein in the manner described above for publications and references.

CLAIMS

What is claimed is:

1. A support for a well plate, the support comprising:
 - a tiered rectangular structure comprising at least a top level and a lower level;
 - a length and a width of the top level being less than a length and a width of the lower level, and the length and the width of the top level being at least the same as a length and a width of an optical read surface of the well plate; and
 - the length and width of the lower level being greater than the length and the width of the top level, and the length and the width of the lower level are at least the same as a length and a width of the well plate.
2. The support of claim 1, wherein the length of the lower level is within the range of 120 mm to 140 mm.
3. The support of any one of claims 1 and 2, wherein the width of the lower level is within the range of 75 mm to 95 mm.
4. The support of any one of claims 1-3, wherein the length of the top level is within the range of 105 mm to 130 mm.
5. The support of any one of claims 1-4, wherein the width of the top level is within the range of 65 mm to 85 mm.
6. The support of any one of claims 1-5, wherein at least one dimension of the support is such that at least one open space is formed between a top or a side of the top level or the lower level when the support is contacted with a well plate for centrifugation.

7. The support of any one of claims 1-6, further comprising a middle level.
8. The support of any one of claims 1-7, wherein a length and a width of the top level being less than a length and a width of the middle level.
9. The support of any one of claims 1-8, wherein at least one dimension of the support is such that at least one open space is formed between a top or a side of the middle level.
10. The support of any one of claims 1-9, wherein the length of the middle level is within the range of 120 mm to 130 mm.
11. The support of any one of claims 1-10, wherein the width of the middle level is within the range of 80 mm to 90 mm.
12. A system formed by contacting an optical read surface of a well plate to the support of any one of claims 1-11.
13. A method for reducing the frequency and degree of deformation or failure of a well plate during centrifugation compared to the risk of deformation or failure of the well plate without using the support of any one of claims 1-8 during centrifugation, the method comprising:
 - contacting a well plate to an optical viewing area of the support;
 - and
 - centrifuging the well plate and support.
14. The method of claim 13, wherein centrifuging occurs prior to single molecule counting.

15. The method of any one of claims 13 and 14, further comprising preventing delamination of an optical read surface from a frame of the well plate.