24 well multichannel pipetting using standard 96 well multichannel pipettors

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Abstract

High throughput cell culture using 96 well and 384 well tissue culture plates is becoming more commonplace with the advent of affordable multichannel pipettors and robotic technologies. However, expansion into 24 well plates is often necessary following initial screens or assays and can significantly impede the high throughput process. We describe here a simple and cost effective method for adapting multichannel pipettors designed for a 96 well format into a useable 24 well format. This technique can be applied to both manual 8 or 12 channel pipettors, as well as robotic liquid handlers equipped with 96 channels.

The success of targeted drug therapies has lead to a resurgence in the use of high throughput cell based assays for the identification of clinically efficacious compounds [reviewed in (1)]. Although these screens have not been historically performed in academic medical centers, the declining cost of cell culture reagents and equipment has made it possible for even modestly funded laboratories to perform cell based assays in a relatively high throughput fashion. Although most academic laboratories still do not have the financial resources to afford robotic equipment for these purposes, more and more laboratories are turning to the use of multichannel pipettors as an affordable alternative to perform rapid and cost effective large-scale cell culture. The development of 12 and even 24 channel pipettors capable of volume deliveries between 0.5μl to 1.2 ml emphasizes the reality of being able to execute high throughput cell culture on a limited budget.

During our own experience performing large-scale high throughput cell culture, we encountered a “bottleneck” that is most likely not unique among researchers using multichannel pipettors for this purpose. Very often, initial screening in our 96 well plates yielded a number of potential positive colonies that required further expansion into 24 well plates. After transfer of these putative candidate colonies, we found it frustrating that we could no longer process and manipulate these colonies in rapid fashion, as we did not have access to multichannel pipettors capable of delivering volumes in a 24 well

format. Moreover, the only multichannel pipettor we could locate capable of delivering volumes in this format required purchase of a variable spacing pipettor with proprietary tips at significant cost (Matrix Technologies, Hudson NH). We therefore devised a simple, cost effective method for adapting our exiting 96 well format multichannel pipettors into a 24 well format.

We first measured the spacing between our 12 channel pipettors and discovered that skipping every other channel when loading the pipette tips allows for a perfect fit across a six well row in a 24 well plate (Figure 1).
Although one could manually equip every other channel with a pipet tip, this would make the high throughput nature of multichannel pipetting less efficient and could compromise sterility. Therefore, we next developed a method of Bypassing Every odD Row In a Box or the BEDRI Box. We initially obtained an empty tip box that would have otherwise been discarded (Figure 2A). We then used our multichannel pipettor to sterilely transfer every odd column (8 tips) from a full tip box to the empty box (Figure 2B-D). This procedure yields two boxes in which every other column is empty, allowing fast loading of the tips to be used in a 24 well format (Figure 2E-F). In addition, one could also array both rows and columns to give four BEDRI Boxes each with 24 tips (Figure 2G-H). We envision this to be useful for 96 well robotic liquid handlers fashioned with 96 channels that can then be used for 24 well plates. We have created and utilized BEDRI Boxes with our Rainin LTS multichannel pipettors, but since the 96 and 24 well formats are universal, this procedure should work for any standard 96 well format multichannel pipettor. Moreover, we have found that BEDRI boxes work equally well for both small and large volume multichannel pipettors and their respective tip sizes (data not shown).

In summary, we present a cost efficient method for preserving the high throughput nature of large-scale cell culture even when expanded to a 24 well plate format. With practice, BEDRI Boxes can be arrayed quite quickly and stored until needed. The creation of BEDRI Boxes should facilitate more researchers to embrace the use of large-scale cell based screening assays.

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References

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Figure 1

A

B

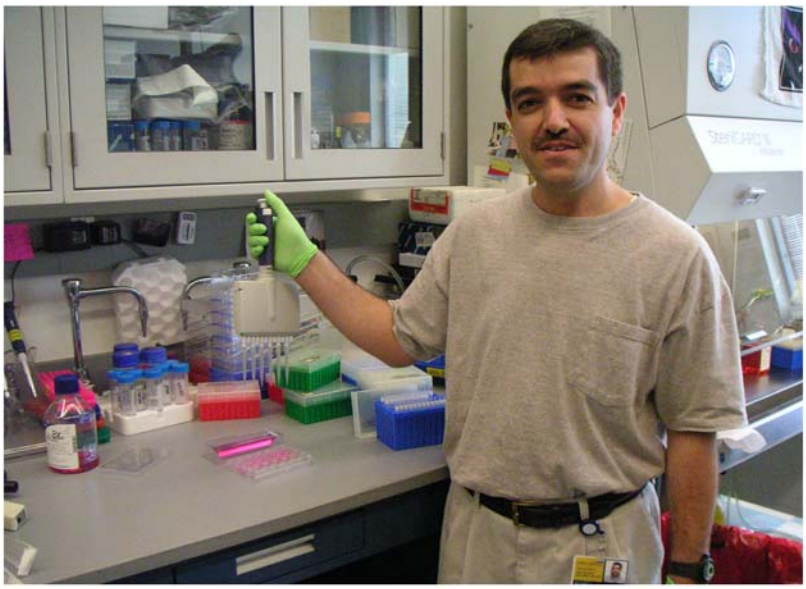

Figure 1. 24 well multichannel pipetting. (A) Every other tip loading fits a 24 well plate. (B) Bedri's inadvertent invention.

Figure 2

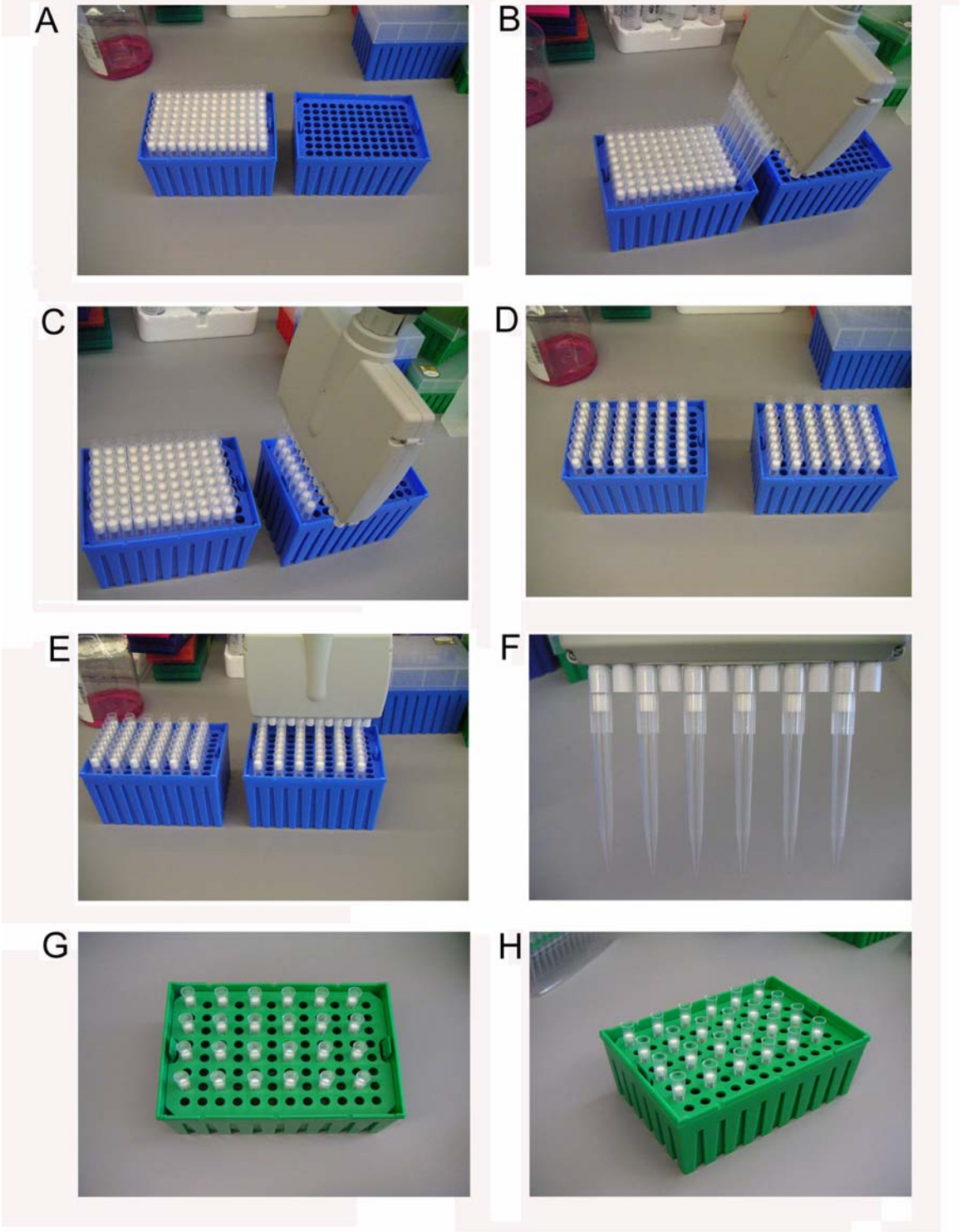

Figure 2. Making BEDRI Boxes. (A) thru (F) Creating BEDRI boxes and loading the tips. (G) thru (H) BEDRI Boxes XL for a 96 well channel robotic liquid handler now adapted for 24 well use.