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Comparison of power and exponential field programming in field-flow fractionation

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ABSTRACT

   Field programming in field-flow fractionation has the purpose of expanding the molecular weight or particle diameter range subject to a single analytical run. The two most widely used field programs are those in which the field strength decays with time according to an exponential function and a power function, respectively. The performances of these two programming functions are compared by obtaining limiting equations showing how retention time t_r, standard deviation in retention σ_t, and fractionating power F_d vary with particle diameter d. It is shown that uniform fractionating power (F_d independent of d) can be obtained with power programming but that in exponential programming F_d is always non-uniform, varying as $d^{-1/2}$. In exponential programming a linear relationship arises between t_r and log d. This particular relationship is impossible to realize in power programming but an alternative linear relationship can be obtained by plotting t_r *versus* $d^{1/3}$. These results are made more concrete by plotting and comparing field strength, relative field strength, F_d and t_r for specific programming cases.

INTRODUCTION

   Field-flow fractionation (FFF) is a family of techniques whose many system and operating variables make the methodology adaptable to virtually all classes of macromolecular and particulate materials. Given a system geometry, a carrier liquid, a flow-rate and field type, the field strength becomes the most important remaining variable influencing retention and resolution. The field strength can be varied widely and almost instantly to accommodate the requirements of samples of different molecular weights and particle sizes. Further, when the sample contains molecules or particles covering a very broad range of molecular weights or diameters, it becomes advantageous to change the field strength as the run proceeds so that eluting species at different times are subjected to different average field strengths that encourage their adequate resolution and timely elution. This approach is termed field-programmed FFF.
   Programming the field strength in FFF is analogous to, but simpler than, programming temperature or solvent strength in chromatography. All these programming methods are aimed at what Snyder [1] elegantly describes as the "general elution problem", the problem of adequately resolving the early components while avoiding the excessive elution time of the late components of wide ranging mixtures.
   The programming of field strength as a tool for the optimized application of

FFF to widely dispersed samples was first described by Yang *et al.* [2] in 1974. It was shown that different retention time relationships (describing retention time *versus* particle size) emerged for different programs (*i.e.*, different mathematical relationsips between field strength and time). Thus a variety of retention time relationsips have been obtained for linear, parabolic, exponential, power and other programs based on the concepts and fundamental equations of the 1974 paper [3–10]. Of particular note, exponential decay programs (and modifications thereof) produce nearly linear relationships when the logarithm of particle diameter is plotted against time [5,6,8].

Despite the early accessibility to quantitative retention time relationships, the effect of programming and variations in programming on FFF resolution was not delineated in the initial studies, thus making the search for optimized programming difficult if not impossible. This void was filled in 1987 by a paper [8] defining fractionating power F (a kind of specific resolution applicable to continuous distributions of macromolecules and particles) and providing the general equations needed to compute F under different programming conditions. The equations were initially applied to exponential programming, showing that F decreases as particle diameter increases (*i.e.*, resolution is non-uniform, less for large than small particles) [8]. Subsequently, a new form of programming was developed having the characteristic that a constant fractionating power could be obtained over a large range of particle diameters or molecular weights [9]. The new programs were called power programs and their use was described as power programming.

The two most widely used classes of programs at present are exponential programs and power programs. Both program forms are used in commercial FFF instrumentation, with exponential programming utilized in the DuPont (Wilmington, DE, USA) sedimentation FFF system and power programming provided as part of both sedimentation FFF and thermal FFF instrumentation from FFF fractionation (Salt Lake City, UT, USA). These two programming approaches have different origins and specific objectives, although the broader objective in both cases is to realize the general advantages of programming first stated in the 1974 paper [2]. In particular, exponential programming was developed mainly to provide linear log (particle diameter) *versus* retention time plots and power programming has the specific purpose of yielding a uniform fractionating power for all particle sizes. In order to understand these two programming systems better, it is useful to ascertain if either programming form can assume the specific role of the other, or if these objectives are instead mutually exclusive. These and other comparative features of these two principal programming approaches will be examined in this paper.

Although we focus below on the dependence of retention time and fractionating power on particle diameter, the same basic mathematics are involved in relating these parameters to molecular weight when polymer analysis is being considered.

THEORETICAL RELATIONSHIPS

Exponential programming

The exponential program is described by the function

$$S = S_0 \exp\left(-\frac{t - t_1}{\tau'}\right) \tag{1}$$

where S is the field strength at time t (when $t \geqslant t_1$), S_0 is the initial field strength, t_1 is a period of constant initial field strength before the start of field decay and τ' is the field decay constant.

The specific objective of this program, as noted, is to obtain a linear relationship between retention time and the logarithm of particle size (see refs. 5 and 6). One presumed advantage of this lies in the relatively simple data manipulation required to obtain particle size distributions. This advantage has become less compelling, however, with the development of computer programs for the transformation from time to particle size and the capability to acquire particle size distribution curves for arbitrary field decay programs.

For the exponential decay program it may be shown (e.g., refs. 8 and 11) that retention time, t_r, is given by

$$t_r = \tau' \ln \left[\frac{1}{2\lambda_0} (1 - B^{1/2}) \right] + t_1 \tag{2}$$

where λ_0 is the value of the retention parameter λ at the initial field strength and where

$$B \approx 1 - \frac{2t^0}{3\tau'} \tag{3}$$

Eqn. 2 is applicable for components significantly retained at the initial field strength (i.e., $\lambda_0 \ll 1$). The above expression for B is a best approximation when $t_1 = \tau'$, which corresponds to the special case of time delayed exponential (TDE) decay utilized by Yau and Kirkland [5]. For the TDE program, eqn.2 reduces to

$$t_r = \tau' \ln \left[\frac{e}{2\lambda_0} (1 - B^{1/2}) \right] \tag{4}$$

where $e = 2.718282$ is the natural logarithmic base. For each subtechnique of FFF carried out in the normal mode of retention, λ is given by (see, for example, ref. 8)

$$\lambda = \frac{\Lambda}{Swd^n} \tag{5}$$

where w is the channel thickness, d is the particle diameter and n depends on the field type (e.g., $n = 3$ for sedimentation FFF and $n = 1$ for flow FFF). The constant Λ is given by

$$\Lambda = \frac{kTd^n}{\phi} \tag{6}$$

where ϕ is the field–particle interaction parameter, which for sedimentation FFF is given by

$$\phi = \frac{\pi}{6} d^3 \Delta\rho \tag{7}$$

where $\Delta\rho$ is the density difference between the particles and the carrier fluid. The parameter Λ is independent of particle diameter for all FFF subtechniques.

It follows that for TDE programmed field decay,

$$\ln d = \frac{t_r}{n\tau'} - \frac{1}{n} \ln \left[\frac{eS_0 w}{2\Lambda} (1 - B^{1/2}) \right]$$ (8)

Thus, as first recognized by Yau and Kirkland [5], the theory predicts log–linear retention for TDE programming. Eqn. 8 shows that this relationship will hold for all normal mode separations subject to eqn. 5 under TDE programmed operation.

Assuming that B is given by eqn. 3 (which is a good approximation for significantly retained material), we can differentiate eqn. 8 with respect to d to obtain

$$\frac{dt_r}{dd} = \frac{n\tau'}{d}$$ (9)

It may be seen from eqn. 44 in ref. 8 that for significantly retained material (i.e., material for which $\lambda_0 < \lambda_r \ll 1$), the standard deviation in retention time, σ_t, is given by

$$\sigma_t \approx \frac{12w}{D^{1/2}R_r} \left(\frac{\tau'\lambda_r^4}{4} \right)^{1/2}$$ (10)

where D is the particle diffusion coefficient, R_r is the retention ratio at the time t_r of elution and λ_r is the value of λ also at time t_r. Replacing R_r with $6\lambda_r$ (a good approximation for well retained material), we obtain

$$\sigma_t \approx w \left(\frac{\tau'}{D} \right)^{1/2} \lambda_r$$ (11)

Eqn. 47 in ref. 8 states that

$$\lambda_r = \frac{1}{2} (1 - B^{1/2}) \approx \frac{1}{2} \left[1 - \left(1 - \frac{2t^0}{3\tau'} \right)^{1/2} \right]$$ (12)

where the second form substitutes for B using eqn. 3. If $\tau' \gg t^0$, eqn. 12 reduces to

$$\lambda_r \approx \frac{t^0}{6\tau'}$$ (13)

Thus, for eqn. 11 we obtain

$$\sigma_t \approx \frac{wt^0}{6(\tau'D)^{1/2}}$$ (14)

The diameter-based fractionating power, F_d, is defined by [8]

$$F_d = \frac{d}{4\sigma_t} \cdot \frac{dt_r}{dd} \tag{15}$$

Therefore, for significantly retained material eluted under a TDE field decay program, we obtain (by the substitution of eqns. 9 and 14 into eqn. 15) the expression

$$F_d \approx d \cdot \frac{6(\tau'D)^{1/2}}{4wt^0} \cdot \frac{n\tau'}{d} \tag{16}$$

or equivalently

$$F_d \approx \frac{3n}{2w} (t^0 D)^{1/2} \left(\frac{\tau'}{t^0}\right)^{3/2} \tag{17}$$

Of the parameters in eqn. 17, only the particle diffusion coefficient D varies with particle diameter d. Specifically, the Stokes–Einstein equation shows that

$$D = \frac{kT}{3\pi\eta d} \tag{18}$$

where k is the Boltzman constant, T is the system absolute temperature and η is the carrier fluid viscosity. As D is inversely proportional to d, it follows that

$$F_d \propto d^{-1/2} \tag{19}$$

Eqn. 19 provides a very general relationship for the dependence of F_d on d for well retained spherical or near-spherical particles subject to TDE programming, or more generally for any programming governed by eqn. 1. This relationship shows that F_d inevitably varies with d in exponential programming. Hence there is no possible combination of parameters that will provide a constant fractionating power over a significant range of d with the use of the TDE field decay or related exponential programs. (For non-spherical particles, a constant F_d, defined relative to the effective spherical diameter by eqn. 15, is possible only if particles of all sizes have the same D, which requires the unlikely situation that particles of different effective spherical diameters must have the same Stokes diameter as found in eqn. 18.)

Power programming
The power program is described by the function [9]

$$S = S_0 \left(\frac{t_1 - t_a}{t - t_a}\right)^p \tag{20}$$

where S, S_0, t_1 and t are identically defined as for the exponential decay program, t_a is a program parameter with units of time and p is the program power. For a programmed decay it is necessary that $t_a < t_1$ and $p > 0$.

The objective of this program is to obtain constant fractionating power over a wide range of particle diameters for material eluted in the normal mode of FFF [9].

It was shown by Williams and Giddings [9] that retention time for elution under such a field decay program is given by

$$t_r \approx t^0 \left[\frac{(p+1)}{6\lambda_0} \left(\frac{t_1 - t_a}{t^0} \right)^p \right]^{\frac{1}{p+1}} + t_a \tag{21}$$

It was also shown that the approximation holds over a greater range of λ_0 when $t_a = -pt_1$. It follows from eqns. 21 and 5 that

$$t_r - t_a \propto d^{\left(\frac{n}{p+1}\right)} \tag{22}$$

Differentiating eqn. 21 with respect to d gives

$$\frac{dt_r}{dd} \approx \frac{nt^0}{(p+1)d} \left[\frac{(p+1)}{6\lambda_0} \left(\frac{t_1 - t_a}{t^0} \right)^p \right]^{\frac{1}{p+1}} \tag{23}$$

so that

$$\frac{dt_r}{dd} \propto d^{\left(\frac{n}{p+1}-1\right)} \tag{24}$$

From eqn. 32 in ref. 9, it may be shown that for significantly retained material (*i.e.*, material for which $\lambda_0 < \lambda_r \ll 1$)

$$\sigma_t \approx \frac{12w}{D^{1/2}R_r} \left(\frac{t_r - t_a}{4p+1} \right)^{1/2} \lambda_r^2 \tag{25}$$

Substituting $6\lambda_r$ for R_r (good for well retained material), we have

$$\sigma_t \approx \frac{2w}{D^{1/2}} \left(\frac{t_r - t_a}{4p+1} \right)^{1/2} \lambda_r \tag{26}$$

and then replacing $(t_r - t_a)\lambda_r$ by $(p+1)t^0/6$ using eqn. 36 in ref. 9, we obtain

$$\sigma_t \approx \frac{2w}{D^{1/2}} \left[\frac{(p+1)t^0}{6(4p+1)} \right]^{1/2} \lambda_r^{1/2} \tag{27}$$

and finally, by using eqn. 43 in ref. 9 for λ_r, we are led to

$$\sigma_t \approx 2w \left[\frac{(p+1)t^0}{6(4p+1)D} \right]^{1/2} \left\{ \lambda_0 \left[\frac{(p+1)t^0}{6(t_1 - t_a)} \right]^p \right\}^{\frac{1}{2(p+1)}} \tag{28}$$

From the above equation together with eqns. 5 and 18 it follows that

$$\sigma_t \propto d^{\left(\frac{1}{2} - \frac{n}{2(p+1)}\right)} \tag{29}$$

Substituting eqns. 23 and 28 into the expression defining fractionating power, given by eqn. 15, and then rearranging gives

$$F_d \approx \frac{n}{48w} \left[\frac{6(4p+1)Dt^0}{(p+1)} \right]^{1/2} \left\{ \frac{1}{\lambda_0} \left[\frac{6(t_1-t_a)}{(p+1)t^0} \right]^p \right\}^{\frac{3}{2(p+1)}} \tag{30}$$

From eqn. 30 in combination with eqns. 5 and 18, it is seen that

$$F_d \propto d^{\left(\frac{3n}{2(p+1)} - \frac{1}{2}\right)} \tag{31}$$

We observe from the above equations that for power programmed field decay there is always a power dependence predicted for $t_r - t_a$, dt_r/dd, σ_t and F_d on d for well retained components. Further, if p is set equal to $3n - 1$, that is, to 8 for sedimentation FFF and to 2 for flow FFF, then eqns. 22, 24, 29 and 31 reduce to

$$t_r - t_a \propto d^{1/3} \tag{32}$$

$$\frac{dt_r}{dd} \propto d^{-2/3} \tag{33}$$

$$\sigma_t \propto d^{1/3} \tag{34}$$

$$F_d \propto d^0 \tag{35}$$

The final expression, eqn. 35, shows that F_d is predicted to be independent of d. All of the power dependences are also observed to be independent of n. These dependences will therefore hold for all subtechniques of normal mode FFF (subject to eqn. 5) when field strength is power programmed using power p equal to $3n - 1$.

COMPARISON OF TYPICAL FIELD DECAY PROGRAMS

Consider Fig. 1 in ref. 9, in which a power program (with $p = 8$ and $t_a = -8t_1$) is plotted together with an exponential program for which $\tau' = (5/4)\,t_1$ (note that it was incorrectly stated in ref. 9 that $\tau' = t_1/4$ for this figure). We take this figure (with an appearance much like that of Fig. 1 shown here) as a starting point for our more extended comparison of the program types.

We shall consider the case of sedimentation FFF and assume typical experimental parameters, specifically $S_0 = 100$ gravities, $w = 0.025$ cm, $t^0 = 100$ s, $\Delta\rho = 1.5$ g/ml, $\eta = 0.01$ P and $T = 298$ K. We have shown in the previous discussion and earlier (see ref. 9) that for a power programmed field decay a value of 8 for p is expected to give rise to constant fractionating power for a wide range of significantly retained particle sizes. The time parameters t_1 and t_a (fixed at $-8t_1$) may be adjusted according to eqn. 57 in ref. 9 to give some desired level of constant fractionating power. For the experimental parameters stated above, we calculate that the values of 9.27 and -74.16 min are required for t_1 and t_a, respectively, to obtain $F_d = 5.0$. For the exponential decay program we retain $t_1 = 9.27$ min and set $\tau' = (5/4)\,t_1 = 11.59$ min in order to match the power program as closely as possible. The resultant field decay
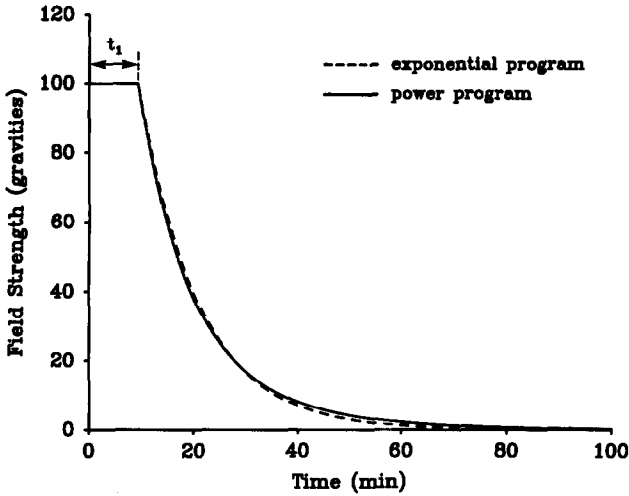
Fig. 1. Comparison of field strength decay for power and exponential programs.The programming parameters (see text) have been adjusted to give similar overall decay profiles.

programs are plotted together in Fig. 1 for elapsed times up to 100 min. The absolute difference between the curves is seen to be small over the full range of time shown. This comparison is deceptive, however. It is the relative difference in the programs that is of importance in comparing retention. The ratio of the field strengths (exponential/ power) is plotted in Fig. 2. The exponential program is seen to decay more slowly at first but at an elapsed time of 28.5 min the two decay programs are again equal. With the further passage of time the exponential program decays more rapidly than the
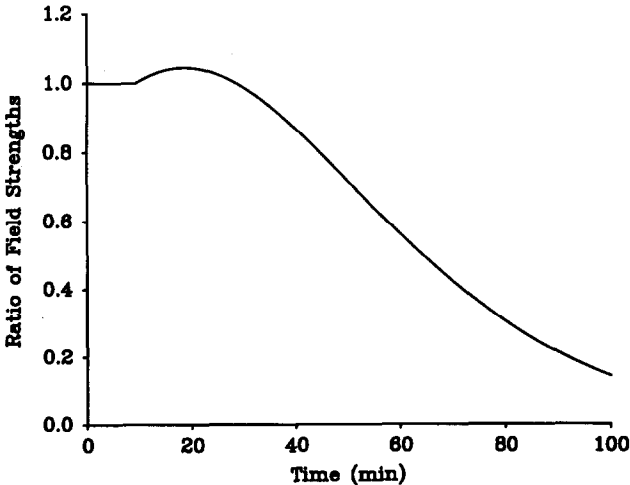

Fig. 2. Plot of the ratio of the field strength of the exponential decay program of Fig. 1 to the field strength of the power program shown in that figure.
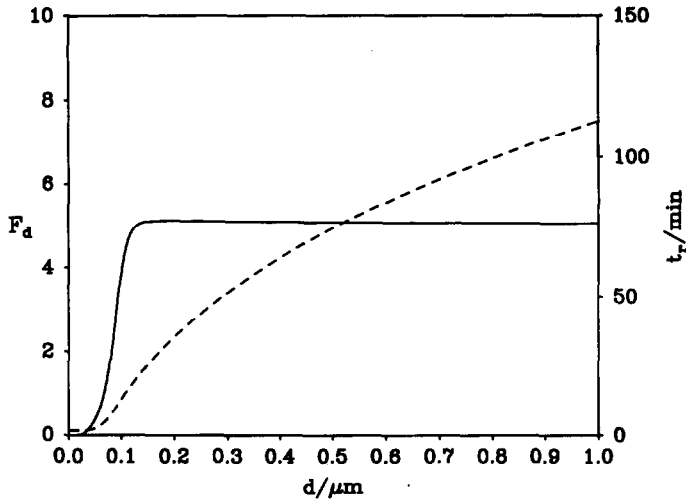
Fig. 3. Fractionating power F_d (solid line) and retention time t_r (dashed line) plotted as a function of particle diameter d for the power programming example described in the text.

power program, so that at a time of 64.2 min the field strength falls to half the strength of the power program, and at 100 min to one seventh of that of the power program.

Fig. 3 shows the variation of fractionating power (solid curve) and retention time (dashed curve) with particle diameter for the power program specified above and Fig. 4 the corresponding curves for the exponential example. The range of constant F_d (following an initial rise from $F_d = 0$) is apparent in Fig. 3 whereas F_d for significantly retained material (following a similar initial rise) is seen to decrease with $d^{-1/2}$ in Fig. 4, falling to a level of 3.7 for particles 1 μm in diameter. Note that retention times
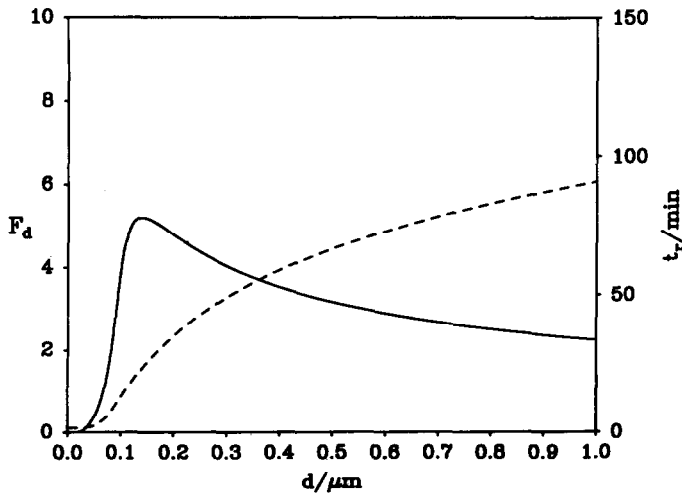

Fig. 4. Plot of the fractionating power (solid line) and the retention time (dashed line) against particle diameter for the exponential programming example described in the text.

for the larger components are lower for the exponential program chosen. This reflects the lower field strengths predicted with the passage of time for the exponential decay program and shows that the faster elution occurs at the expense of fractionating power.

It is clear from these examples that these two field decay programs, which superficially appear to be very similar, are actually different in relative terms and that the retention times and fractionating powers predicted for the two programs are consequently very different over a wide range of particle diameters.

CONCLUSIONS

The foregoing treatment shows that the fractionating power F_d of power programming can be made constant, independent of particle diameter d, by properly choosing the power p of the program, specifically $p = 3n - 1$, where n is defined by eqn. 5. The mathematics of programming, however, dictate that such a uniformity in fractionating power is not accessible through exponential (including time-delayed exponential) programming by any conceivable adjustment of parameters. Instead, F_d always decreases with increasing d through a dependence on $d^{-1/2}$. Power programming, by contrast, is sufficiently flexible that F_d can be made to depend on d, if desired, by choosing values of $p \neq 3n - 1$ in accordance with eqn. 31. Specifically, F_d can be made to increase or decrease with d (the choice depending on whether the highest resolution is needed for large or small particles) by setting $p < 3n - 1$ or $p > 3n - 1$, respectively. However, F_d cannot be made to decrease with d with a dependence as strong as that of the exponential program, $d^{-1/2}$, as this case corresponds to an infinitely high value for p (we note generally that F_d values in excess of those actually required for analysis have the disadvantage that they require more time than necessary for completion of the run).

Along with the constraints on F_d summarized above, there are similar constraints imposed by programming mathematics on the retention time (t_r)–diameter (d) relationships. For power programming, $t_r - t_a$ increases with some power of d (the power depending on the choice of p) in accordance with eqn. 22. This relationship cannot be converted into the log–linear relationship (see eqn. 8) characteristic of exponential programming. However, if a straight-line plot is desired for calibration purposes, a plot of $t_r - t_a$ (or simply t_r) versus $d^{n/p+1}$ is simple to construct and utilize. Similarly, a plot of log $(t_r - t_a)$ versus log d yields a straight line [a similar plot of log $(t_r - t_a)$ versus log (molecular weight, M) for polymers yields a straight line].

Various log–log plots in FFF more commonly yield straight calibration lines than any other type of plot; these plots, once established, can be readily used to obtain particle sizes or particle size distributions from experimental fractograms. In addition to power programming, where as we note a plot of log $(t_r - t_a)$ versus log d is linear (with slope $1/3$ when $p = 3n - 1$), non-programmed FFF yields a straight line (again for well retained materials) of slope n when log t_r [or, more exactly, log $(t_r - t^0/3)$] [12] is plotted against log d. In both sedimentation/steric and flow/hyperlayer FFF, straight-line calibration plots are produced by plotting log t_r versus log d. An advantage of such log–log plots is that the slope is equal to the selectivity S_d, the percentage change in t_r for two particles differing in diameter by 1%.

Programs other than power and exponential (e.g., linear and parabolic) have

their own unique F_d and t_r relationships [10]. Only the power program produces a uniform fractionating power across a wide range of d, but the other programs may prove useful in that they exhibit peak values of F_d that could be adjusted to focus on the most important constituents of a colloidal sample [10]. The possibilities for the flexible use of various programs to customize FFF separations to satisfy specific particle characterization holds considerable promise for future work.

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