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## Research Article

# Electrospinning Regimes for Tissue-Engineering Scaffolds: A Quantitative Synthesis of Reported Process Parameters

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## ABSTRACT

Electrospinning regimes are almost always reported as an applied voltage together with a working distance, which prevents direct comparison between laboratories because the same voltage produces different field strengths at different distances. This review collects the process parameters reported in thirteen studies of electrospun scaffolds for nerve, vascular, cardiac, cartilage, intervertebral-disc and bone tissue, converts them to a common basis, and analyses their distribution. When expressed as the normalised field strength  $E = U/H$ , the reported regimes occupy a narrow band:  $0.56\text{--}2.00\text{ kV cm}^{-1}$  with a mean of  $1.12 \pm 0.44\text{ kV cm}^{-1}$  and a median of  $1.09\text{ kV cm}^{-1}$ , the interquartile range being  $0.80\text{--}1.25\text{ kV cm}^{-1}$ . Working distances range from 10 to 25 cm (median 15 cm) and feed rates from  $0.6\text{ to }12\text{ mL h}^{-1}$  (median  $1.5\text{ mL h}^{-1}$ ), the latter spanning more than an order of magnitude. Fibre diameters reported for the same tissue class vary by up to an order of magnitude, and no correlation between normalised field strength and fibre diameter is detectable across the pooled data, indicating that diameter is controlled predominantly by the solution rather than by the field. The narrowness of the field-strength band is interpreted as an



empirically converged process window, and its use as a first-approximation starting point for new polymer systems is proposed, together with a minimum reporting set that would make future studies comparable.

## KEYWORDS

Electrospinning; process parameters; normalised field strength; tissue engineering; scaffold; fibre diameter; reporting standards.

## INTRODUCTION

Electrospinning has become the standard laboratory route to fibrous scaffolds for tissue engineering. Scaffolds for nerve, vascular, cardiac, cartilage and bone tissue have all been produced by the method, and for each tissue class several polymer systems have been reported [1–5]. The volume of this literature is now large enough that a newcomer working with a new polymer might reasonably expect to find guidance on where to begin — what voltage, what distance, what feed rate.

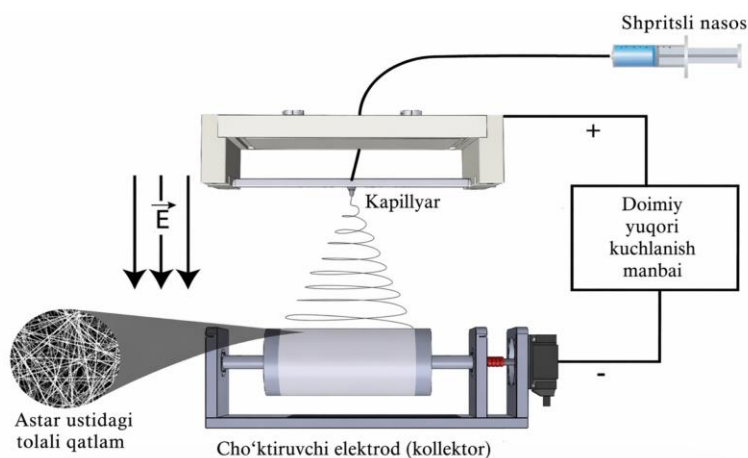
In practice that guidance is difficult to extract. The reason is a reporting convention rather than a scientific difficulty: applied voltage and working distance are reported as two independent numbers. A regime of 12 kV at 10 cm and a regime of 25 kV at 23 cm appear entirely different, although the mean field strength between the electrodes differs by less than 10%. Conversely, 5 kV and 25 kV quoted for the same study, without the corresponding distances, span a tenfold range of field strength. Comparison across studies therefore requires a conversion that authors rarely perform.

A second difficulty is that the parameters are reported selectively. Needle gauge is often

omitted; collector rotation speed is given only when orientation is the subject of the study; ambient temperature and humidity, which strongly affect solvent evaporation, are reported in a minority of papers. The result is a literature that is rich in individual regimes and poor in comparable ones.

The aim of this review is therefore narrow and practical: to collect the process parameters reported in a defined set of tissue-engineering studies, to convert them to a common basis, to describe their distribution quantitatively, and to establish whether any systematic relationship between the process parameters and the resulting fibre geometry can be detected in the pooled data. A secondary aim is to propose a minimum reporting set.

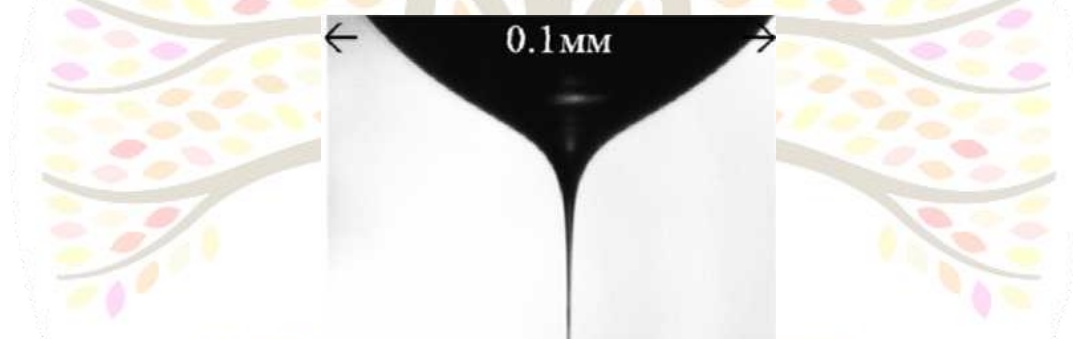
The parameters analysed here refer to the configuration shown schematically in Fig. 1, which is common to all the studies considered: a polymer solution is delivered through a capillary held at high potential, a jet is emitted from the conical meniscus at its tip, and the solidified fibres are deposited on a collector at the opposite potential.



**Fig. 1. Schematic diagram of the production of nanofibrous materials by electrospinning.**

Fig. 2 shows the conical meniscus — the Taylor cone — whose stability governs the first stage of

the process and whose geometry underlies the field-strength criterion discussed in Section 4.1.



**Fig. 2. Formation of the Taylor cone during emission of the primary jet.**

## METHOD

Studies were included if they reported an electrospun scaffold intended for a defined tissue class and gave at least the applied voltage and the working distance. Thirteen studies met this criterion, covering nerve (2), vascular (2), cardiac (3), cartilage (2), intervertebral disc (1) and bone (3) applications.

Three conversions were applied. First, the normalised field strength was computed as

$$E = U/H, \quad (1)$$

where  $U$  is the applied potential difference in kV and  $H$  the emitter-to-collector distance in cm. Where the source reported a range of voltages or distances, the midpoint was used. Where the source itself reported a normalised value (for instance 2 kV per 1 cm, or 0.56 kV per 1 cm of distance), that value was taken directly.

Second, needle gauge was converted to internal diameter using the standard Birmingham gauge scale, so that studies quoting a gauge and studies quoting a diameter in millimetres could be compared.

Third, fibre diameters were tabulated as reported, with the range given where a distribution was reported and the mean  $\pm$  standard deviation where those were given. Porosity data were recorded but not pooled, because the sources report total porosity, mean pore diameter and mean pore area interchangeably and these quantities are not interconvertible without additional assumptions. Descriptive statistics (mean, standard deviation, median, interquartile range) were computed for the normalised field strength, the working

distance and the feed rate. The association between normalised field strength and reported fibre diameter was examined on the subset of studies reporting both.

## RESULTS

### 1. Reported regimes

Table 1 collects the process parameters of the thirteen studies, ordered by tissue class.

**Table 1. Electrospinning parameters reported for tissue-engineering scaffolds, with the normalised field strength computed from Eq. (1).**

| Study (polymer system)               | Tissue    | U, kV | H, cm | E, kV cm <sup>-1</sup> | Feed rate, mL h <sup>-1</sup> | Needle    |
|--------------------------------------|-----------|-------|-------|------------------------|-------------------------------|-----------|
| Yang et al. (PLLA)                   | Nerve     | 12    | 10    | 1.20                   | n.r.                          | 18G / 22G |
| Prabhakaran et al. (PLCL + collagen) | Nerve     | 15    | 12    | 1.25                   | 1.0                           | 27G       |
| Vaz et al. (PCL / PLA bilayer)       | Vascular  | 13    | 20    | 0.65                   | 0.6–1.5                       | 26G       |
| Ju et al. (PCL + collagen)           | Vascular  | 5–25  | 10–20 | 1.00*                  | 1–10                          | n.r.      |
| Zong et al. (PLLA, PLGA)             | Cardiac   | n.r.  | 15    | 2.00†                  | 6.0                           | n.r.      |
| Prabhakaran et al. (PLGA + gelatin)  | Cardiac   | 14–16 | 12    | 1.25*                  | 1.0                           | 27G       |
| Hosseinkhani et al. (PGA + collagen) | Cardiac   | 25    | 23    | 1.09                   | 10.0                          | 0.7 mm    |
| Shin et al. (PLGA 50/50, 75/25)      | Cartilage | n.r.  | 25    | 0.56†                  | n.r.                          | 18G       |
| Nesti et al. (PLLA + HA gel)         | Disc      | n.r.  | n.r.  | 0.80†                  | 1.8                           | 18G       |
| Venugopal et al. (PCL/HA/gelatin)    | Bone      | 11–13 | 12    | 1.00*                  | 1.5                           | n.r.      |

| Study (polymer system)          | Tissue | U, kV | H, cm | E, kV cm <sup>-1</sup> | Feed rate, mL h <sup>-1</sup> | Needle  |
|---------------------------------|--------|-------|-------|------------------------|-------------------------------|---------|
| Zhang & Chen (PLGA/MWNT/HA)     | Bone   | 20    | 13    | 1.54                   | 12.0                          | 0.27 mm |
| BMP-2 containing systems        | Bone   | 20–30 | 15    | 1.67*                  | 8.4                           | n.r.    |
| Li et al. (PEO/silk/nHAP/BMP-2) | Bone   | 12    | 21.5  | 0.56                   | 1.2                           | n.r.    |

n.r. — not reported; \* computed from the midpoint of the reported range; † normalised value reported directly by the source.

## 2. Distribution of the normalised field strength

The thirteen values of E occupy the range 0.56–2.00 kV cm<sup>-1</sup>. The mean is 1.12 kV cm<sup>-1</sup> with a standard deviation of 0.44 kV cm<sup>-1</sup>, the median is 1.09 kV cm<sup>-1</sup> and the interquartile range is 0.80–1.25 kV cm<sup>-1</sup>. Eight of the thirteen values, that is 62%, lie between 0.80 and 1.30 kV cm<sup>-1</sup>.

This is a remarkably narrow band given the heterogeneity of the underlying work: the studies span six tissue classes, at least nine polymer systems, solvents ranging from water to hexafluoroisopropanol, and more than a decade of publication. The distribution is also approximately symmetric about its median, with a single value (2.00 kV cm<sup>-1</sup>) standing somewhat apart from the rest.

**Table 2. Descriptive statistics of the reported process parameters.**

| Parameter                                        | n  | Minimum | Maximum | Median | Mean ± SD   |
|--------------------------------------------------|----|---------|---------|--------|-------------|
| Normalised field strength E, kV cm <sup>-1</sup> | 13 | 0.56    | 2.00    | 1.09   | 1.12 ± 0.44 |
| Working distance H, cm                           | 12 | 10      | 25      | 15.0   | –           |
| Feed rate, mL h <sup>-1</sup>                    | 12 | 0.6     | 12.0    | 1.50   | –           |
| Reported fibre diameter, nm                      | 9  | 150     | 3000    | –      | –           |

## 3. Working distance and feed rate

Working distances cluster between 10 and 25 cm with a median of 15 cm. The narrowness of this range has a straightforward physical basis: the distance must be large enough for the solvent to evaporate before deposition, and small enough to

avoid electrical breakdown of the intervening air at the voltages used.

Feed rate, by contrast, spans more than an order of magnitude, from 0.6 to 12 mL h<sup>-1</sup>, with a median of 1.5 mL h<sup>-1</sup>. Nine of the twelve reported values lie at or below 2 mL h<sup>-1</sup>; the three higher values (6, 10 and 12 mL h<sup>-1</sup>) come from studies



using large-bore needles or aiming at higher throughput. This distribution suggests that feed rate is the parameter most often adjusted to the specific solution rather than taken from precedent, which is consistent with its role in setting the mass balance between delivery and jet extraction.

#### 4. Fibre diameter versus process parameters

Fibre diameters reported in the nine studies that give them span 150–3000 nm, that is a factor of twenty. Within a single tissue class the variation remains large: for nerve scaffolds, 150–500 nm and 800–3000 nm are reported in the same study, obtained by changing the polymer concentration while holding the field parameters constant [1]. For vascular scaffolds the inner layer is reported at  $600 \pm 400$  nm and the outer layer at 800–3000 nm within the same construct [3].

On the pooled data no association between the normalised field strength and the reported fibre diameter is detectable: the studies with the lowest field strengths report both the finest and

the coarsest fibres, and those at the median field strength span most of the observed diameter range. The inference is that within the range of field strengths actually used in practice, fibre diameter is governed predominantly by the solution — its polymer concentration and resulting viscosity — rather than by the field, a conclusion consistent with the concentration-dominated scaling reported in dedicated parametric studies [6, 7].

The same conclusion is supported by the way the sources themselves manipulate diameter: in every case where two fibre diameters are produced within a single study, the variable changed is the polymer concentration or the needle gauge, not the voltage.

#### 5. Additional structural data

Table 3 collects the structural characteristics reported alongside the process parameters. These are given for completeness; as noted in Section 2, the porosity descriptors are not interconvertible and are therefore not pooled.

**Table 3. Structural characteristics reported for the scaffolds of Table 1.**

| Study                      | Fibre diameter                      | Porosity descriptor         | Other reported outcome                                                    |
|----------------------------|-------------------------------------|-----------------------------|---------------------------------------------------------------------------|
| Yang et al.                | 150–500 nm; 800–3000 nm             | not reported                | neurite outgrowth 80% vs 40%                                              |
| Prabhakaran et al. (nerve) | not reported                        | not reported                | tensile strength $\times 3$ with collagen                                 |
| Vaz et al.                 | $600 \pm 400$ nm (inner)            | total porosity $79 \pm 4\%$ | pore size $\approx 15$ $\mu\text{m}$ (inner), $<10$ $\mu\text{m}$ (outer) |
| Ju et al.                  | 1–4.45 $\mu\text{m}$                | not reported                | Young's modulus $7.5 \rightarrow 2.7$ MPa                                 |
| Zong et al.                | $\approx 0.9$ – $1.0$ $\mu\text{m}$ | porosity 71–78%             | water contact angle $107^\circ$ and $85^\circ$                            |



| Study                        | Fibre diameter     | Porosity descriptor                       | Other reported outcome               |
|------------------------------|--------------------|-------------------------------------------|--------------------------------------|
| Prabhakaran et al. (cardiac) | 630 ± 51 nm (PLGA) | pore diameter 1.07 / 0.55 $\mu\text{m}$   | proliferation increased on composite |
| Shin et al.                  | 550 ± 150 nm       | porosity 80.7%                            | too compliant for cartilage          |
| Annabi et al.                | not reported       | mean pore diameter 540 ± 21 $\mu\text{m}$ | properties approach native cartilage |
| Venugopal et al.             | 411 ± 158 nm       | porosity 93%; pores 7–35 $\mu\text{m}$    | proliferation +88%, ALP +77%         |
| Collagen type II (cartilage) | 496 nm             | mean pore area 6.94 $\mu\text{m}^2$       | elongation at break only 1–2%        |

## 6. Collector configurations and deposition kinematics

Collector configuration is reported in only part of the sample, and almost exclusively where fibre orientation was itself a subject of the study. A stationary plate collector is used where random deposition is acceptable; a rotating cylindrical collector is used where alignment is sought. Three studies give rotational speeds explicitly: 1000  $\text{min}^{-1}$  for the parallel-fibre variants of a nerve scaffold, 300–2000  $\text{min}^{-1}$  for a bilayer vascular construct, and 1000  $\text{min}^{-1}$  for a poly(caprolactone)/collagen vascular scaffold [1, 3, 4]. One cartilage study reports the collector surface velocity directly, as 0.3  $\text{m s}^{-1}$  [10].

This mixture of units is itself an obstacle. A rotational speed is meaningful only in combination with the drum diameter, since it is the peripheral velocity that determines whether the collector can draw the arriving jet into alignment. For a drum of diameter  $D$  rotating at  $n$  revolutions per minute, the peripheral velocity is

$$v = \pi \cdot D \cdot n / 60. \quad (2)$$

Applying Eq. (2) to the reported speeds, and assuming the 100 mm drum diameter typical of laboratory systems, gives 5.2  $\text{m s}^{-1}$  for 1000  $\text{min}^{-1}$  and 1.6–10.5  $\text{m s}^{-1}$  for the 300–2000  $\text{min}^{-1}$  range. The cartilage study's 0.3  $\text{m s}^{-1}$  is thus an order of magnitude lower than the others, which is consistent with its stated aim of producing an isotropic web. Reporting peripheral velocity rather than rotational speed would make these regimes directly comparable, and is included in the minimum reporting set proposed below.

## 7. Solvent systems

Solvent choice is reported more consistently than collector configuration, and divides the sample cleanly. The synthetic polyesters are spun from chlorinated or fluorinated solvents — chloroform, dichloromethane, hexafluoroisopropanol — whose volatility is well matched to the 10–25 cm working distances of Table 1. The protein and polysaccharide systems are spun either from fluorinated solvents, with the attendant risk of denaturation, or from aqueous systems requiring a carrier polymer. The composite systems that combine a synthetic polyester with a natural polymer, which account

for six of the thirteen studies, therefore face a solvent-compatibility constraint that the single-polymer systems do not.

This division has a direct bearing on the field-strength window. Volatile organic solvents produce a jet that solidifies early, so that the extraction force required from the field is exerted over a shorter effective length; aqueous systems evaporate more slowly and tolerate — indeed require — longer flight times. That the two solvent families nevertheless converge on the same narrow field-strength band suggests that the window is set by jet initiation at the capillary rather than by jet solidification in flight.

## DISCUSSION

### 1. Physical basis of the observed process window

The convergence described in Section 3.2 can be related to the classical criterion for jet initiation. Following Taylor, a conical meniscus is in equilibrium between electrostatic and capillary forces when its semi-vertical angle reaches  $49.3^\circ$ , a value independent of the liquid [17]. The potential at which this equilibrium is reached depends on the surface tension of the liquid and on the geometry of the capillary, and scales as the square root of the surface tension:

$$U_c \propto \sqrt{\sigma \cdot R \cdot f(H, L, R)}, \quad (3)$$

where  $\sigma$  is the surface tension,  $R$  the capillary radius,  $L$  its length and  $H$  the working distance. Because the surface tensions of the solvents used across the sample differ by no more than a factor of about three — from roughly  $22 \text{ mN m}^{-1}$  for ethanol-rich systems to about  $73 \text{ mN m}^{-1}$  for water — the square-root dependence compresses this into a factor of about 1.7 in critical voltage. The observed spread of normalised field strengths, a factor of 3.6 between the extremes

and 1.6 across the interquartile range, is of the same order, which is consistent with surface tension being the dominant term and with the remaining spread arising from differences in capillary geometry.

The upper bound of the window has a different origin. As the field is raised beyond the level needed for stable single-jet emission, multiple jets appear at the meniscus, the deposition area broadens and, at higher fields still, corona discharge and eventually breakdown of the intervening air occur. In laboratory geometries with working distances of 10–25 cm these phenomena set in at field strengths of a few  $\text{kV cm}^{-1}$ , which places the upper edge of the practical window an order of magnitude below the breakdown strength of dry air and consistent with the highest value observed here.

It follows that the window is not a property of any particular polymer but of the electrode geometry and the range of surface tensions accessible to polymer solutions. This is why it has proved transferable across polymer systems that otherwise have little in common, and why it constitutes a defensible starting point for a new system.

The principal quantitative finding of this synthesis is the narrowness of the normalised field-strength band. Across six tissue classes, nine polymer systems and a decade of work, 62% of the reported regimes lie within  $\pm 0.25 \text{ kV cm}^{-1}$  of a common value near  $1.1 \text{ kV cm}^{-1}$ . This convergence is unlikely to be coincidental and is best interpreted as an empirically discovered process window, bounded below by the field needed to overcome the surface tension of the solution and initiate a stable jet, and above by the onset of multiple-jet emission, corona discharge and electrical breakdown.

Two practical consequences follow. The first is that a normalised field strength of approximately

$1.1 \text{ kV cm}^{-1}$  is a defensible first-approximation starting point for a new polymer system, to be refined by observing the Taylor cone. The second is that departures from this window should be reported as such and justified, because they indicate that the solution differs substantially from those on which the window was established — most often because its viscosity is considerably higher, requiring a larger electrostatic force to extract the jet.

A concrete illustration is provided by a silk fibroin / poly(vinyl alcohol) system whose dynamic viscosity is  $2139.6 \text{ mPa}\cdot\text{s}$ , an order of magnitude above that of the dilute solutions used in most of the studies of Table 1. The regime required for stable spinning of that solution corresponds to  $E = 3.8 \text{ kV cm}^{-1}$ , which is 3.4 times the mean of the present sample and lies more than six standard deviations above it. Reported simply as "29 kV at 10 cm", such a regime would appear unremarkable; expressed as a normalised field strength it is immediately recognisable as an outlier requiring explanation.

The absence of a detectable field-diameter association in the pooled data should be interpreted with care. It does not mean that field strength has no effect on diameter — dedicated parametric studies show that it does — but that within the narrow window actually used, and against the much larger variation in solution concentration between studies, the field contribution is not resolvable. For practical purposes this supports a design sequence in which diameter is set by formulation and the field is then chosen to make the process stable, rather than the reverse.

The synthesis has clear limitations. The sample is small (thirteen studies) and was assembled from studies cited within a single body of work rather than by exhaustive database searching, so it is not a systematic review in the formal sense and may

carry selection bias. Midpoints were substituted for reported ranges, which discards information about the width of the operating window in those studies. Ambient temperature and relative humidity, which affect solvent evaporation and hence fibre solidification, were reported too rarely to be included at all. Finally, the field strength of Eq. (1) is a mean value between the electrodes; the local field at the capillary tip, which actually governs jet initiation, is one to two orders of magnitude higher and depends on the emitter geometry, which is reported in fewer than half of the studies.

On the basis of these limitations, a minimum reporting set for electrospinning studies is proposed: applied potential difference and working distance together with their quotient; needle internal diameter in millimetres; volumetric feed rate; collector type and, for rotating collectors, peripheral velocity rather than rotational speed alone; ambient temperature and relative humidity; solution concentration in mass per cent and measured dynamic viscosity; and fibre diameter reported as a mean with its standard deviation and the number of measurements. Adoption of such a set would convert the existing body of individual regimes into a comparable one.

## CONCLUSIONS

Process parameters reported in thirteen studies of electrospun tissue-engineering scaffolds were converted to a common basis and analysed. Expressed as the normalised field strength  $E = U/H$ , the reported regimes occupy the narrow band  $0.56\text{--}2.00 \text{ kV cm}^{-1}$ , with a mean of  $1.12 \pm 0.44 \text{ kV cm}^{-1}$ , a median of  $1.09 \text{ kV cm}^{-1}$  and an interquartile range of  $0.80\text{--}1.25 \text{ kV cm}^{-1}$ .

Working distances cluster between 10 and 25 cm (median 15 cm), while feed rates span more than

an order of magnitude ( $0.6\text{--}12\text{ mL h}^{-1}$ , median  $1.5\text{ mL h}^{-1}$ ), indicating that the feed rate is adjusted to the individual solution whereas the field strength is effectively inherited from precedent. Reported fibre diameters span  $150\text{--}3000\text{ nm}$ , and no association between normalised field strength and fibre diameter is detectable in the pooled data. Within the field-strength window actually used, fibre diameter is therefore governed predominantly by the solution rather than by the field.

The convergence of reported regimes on a normalised field strength near  $1.1\text{ kV cm}^{-1}$  is interpreted as an empirically established process window, usable as a first-approximation starting point for new polymer systems; departures from it — such as the  $3.8\text{ kV cm}^{-1}$  required by a high-viscosity silk fibroin system — should be reported and justified explicitly. A minimum reporting set is proposed to make future studies comparable.

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**Declaration of competing interest.** The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

**Data availability.** The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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