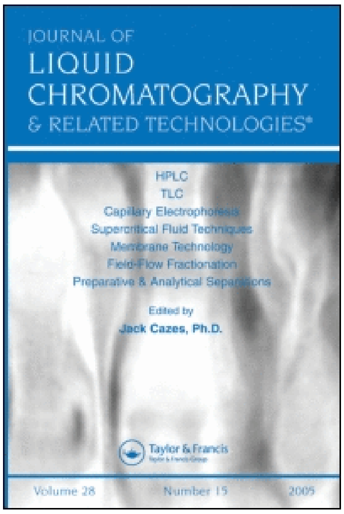

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A NEW HYPOTHESIS ON PHASE DISTRIBUTION IN COUNTERCURRENT CHROMATOGRAPHY

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A NEW HYPOTHESIS ON PHASE DISTRIBUTION IN COUNTERCURRENT CHROMATOGRAPHY

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ABSTRACT

This paper describes a new hypothesis on phase distribution in Countercurrent Chromatography, which, if proven to be true, will simplify the operation of CCC and greatly improve its predictability, efficiency, and reliability. It builds on the hydrodynamic distribution model first proposed by Ito[1] where "the radial force components act against the Archimedean force to establish a hydrostatic distribution of the two phases throughout the coil." This study postulates that these forces do not necessarily have to oppose one another and, depending on the geometry of the helical/spiral coils and the direction of rotation, can be arranged to work together.

INTRODUCTION

Countercurrent Chromatography is a form of liquid-liquid chromatography that takes place along a continuous length of tubing. One phase is held stationary, while the other is pumped through it in such a way that there is good retention of the stationary phase and a series of simultaneous mixing and settling zones along the length of the tubing. This results in the three important ingredients for successful high resolution liquid-liquid chromatography: mixing, settling, and transfer between the phases. In CCC, this continuous tubing is wound on a drum (called a bobbin) which is rotated in planetary motion (Figure 1A). A typical bobbin has 350 loops which results in 350 simultaneous mixing and settling zones. With the bobbin rotating, these mixing and settling

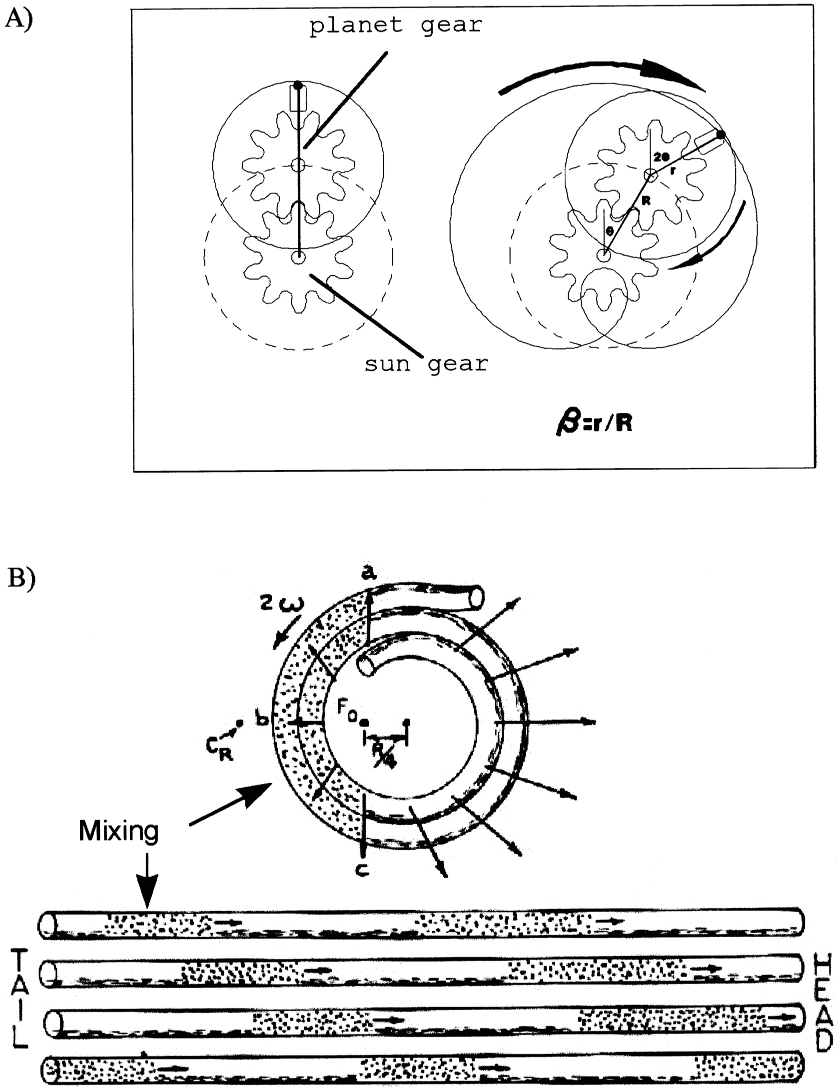

Figure 1. Planetary motion showing A) the geometry of the motion and B) the variable force field and movement of mixing and settling zones toward the "Head" end of the coil, after Conway.[2]

zones travel synchronously towards the head end of the tubing (Figure 1B). The head is defined as the end to which a bubble or bead would travel under Archimedean screw action.[2,3] Figure 2 shows a stroboscopic photograph of these mixing and settling zones in one spiral coil of a coil planet centrifuge. Mixing occurs toward the proximal node (nearest to the centre of rotation), while settling occurs toward the distal node (furthest from the centre of rotation). A sample injected into the mobile phase will experience 1000 mixing and settling steps a minute when the main rotor speed is 1000rpm.

CCC is proving a versatile, high resolution separation process that gives 100% sample recovery, has no non-specific adsorption to a solid support, and has the potential to be scaled up.[4]

CCC has benefited tremendously from the many phase distribution studies performed by Ito.[2,3] These studies have concluded that the heavy phase travels to different ends of the tubing according to: 1) which phase system is being used and 2) which set of operating conditions are chosen. Even when a head/tail end of the tubing is defined by the operating conditions, the phase travelling to the head end can still change with polarity, making the system difficult for the new user to interpret. Ito developed a hypothesis[1] that the heavy phase moved to the "tail" for hydrophobic phase systems, to the "head" for hydrophilic ones, and could go either way ("intermediate") for phase systems in between these two extremes.

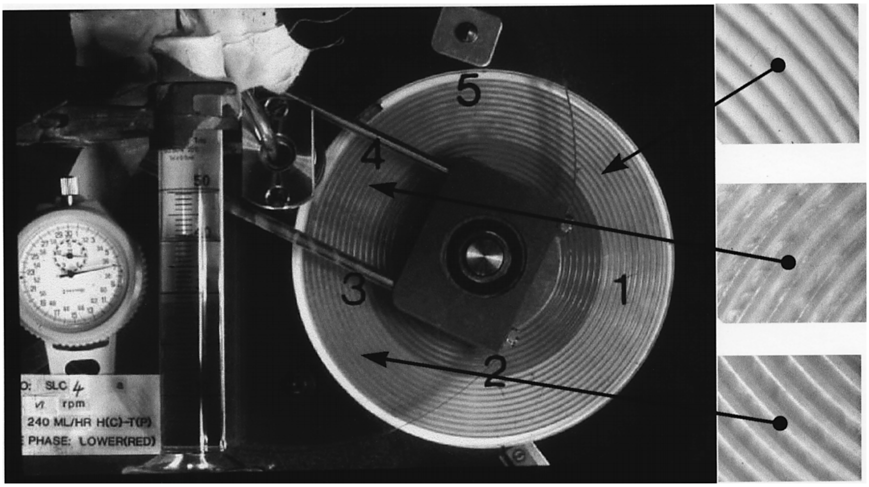

Figure 2. Stroboscopic photograph of mixing and settling zones in one spiral coil of a J1 coil planet centrifuge.

This paper examines the following hypothesis:

- The Archimedean screw action always forces the heavy phase toward the "Tail" end of the coil.

- Hydrostatic pressure forces the heavy phase to the "periphery" in multilayer coils.

As a consequence when the "Tail" is at the periphery, the Archimedean and Hydrostatic forces are working in the same direction and the heavy phase will always move to the "Tail" for all phase systems.

When the "Head" is at the periphery, the Archimedean and Hydrostatic forces are working in the opposite direction. Hence, the Archimedean effect dominates for hydrophobic phase systems where the density difference is high, and Hydrostatic forces dominate for hydrophilic phase systems, where the density difference is low.

Ito's retention studies[5] were with 1.6 mm and 2.6 mm diameter tubing, where viscous effects could have been masking the Head/Tail preferences of the hydrophobic phase systems. Half of Ito's results supported the situation[3] apart from the viscous phases, and half supported the situation[4] above, where the Archimedean and Hydrostatic forces are opposing one another. A fine example of the latter is illustrated in Figure 3, where an Archimedean screw is being used to raise water from a river against gravity. Notice how critical the angular tilt of the axis of rotation is in relation to the spiral angle. In this example, rotation will be counter-clockwise, looking from above, and water in each loop will settle toward the lower segment of each loop as it is lifted by the Archimedean screw action, hence, moving the water to the "Head" or top of the helical spiral. CCC works in a similar way, but there are some notable differences. The tubing is a closed system with both phases being screwed toward the head, but, one of them wins and displaces the other in the opposite direction. Archimedes was working with a uniform gravitational field (unit gravity - 1g), while in CCC, an artificial acceleration field is created with a "g" field distortion within one spiral loop creating a gravitational hollow for carrying liquids toward the "Head". These are acceleration fields produced by the constrained rotation of the tubing and not true "gravitational" fields which would act at a molecular level. However, it is convenient to reference the size of the acceleration field to unit gravity of "g" value.

Just as in Ito's earlier paper, the hypothesis presented here has been based on empirical observations and experimental studies. No attempt has yet been made to characterize the geometrical variables and phase system parameters that will affect these Archimedean and Hydrostatic forces; these are complex and are currently being evaluated as part of a Ph.D. thesis by one of the authors.[6]

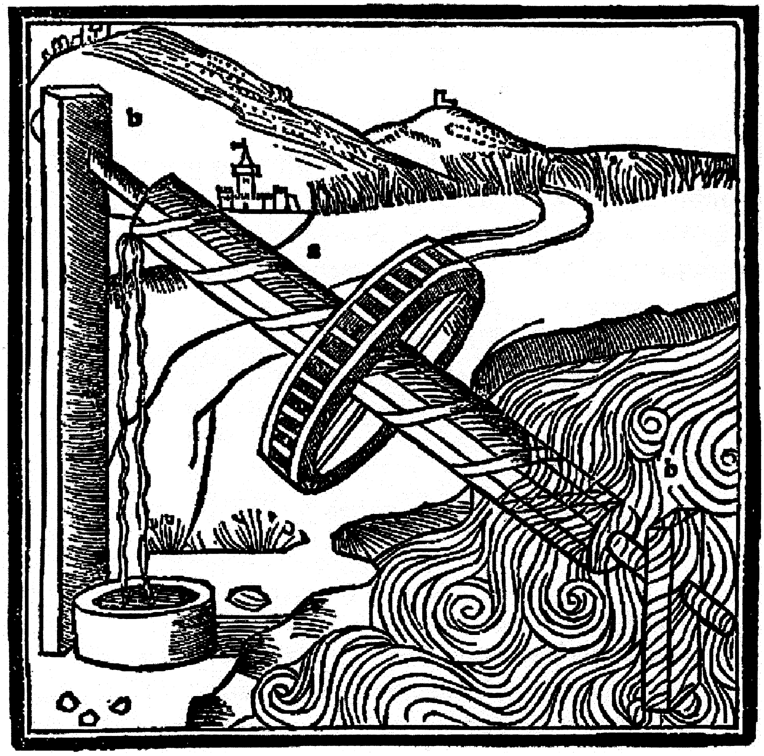

Figure 3. An Archimedean screw mechanism to gain potential energy for water collection from a river.

It is well known that the heavy phase goes to the "Head" in unit gravity Archimedean helical spirals, and to the "Tail" in gravitational systems like the J1 coil planet centrifuge.[1] This study has helped the authors understand why the heavy phase goes to the "Tail" and a theoretical analysis will be published in due course.

Another major difference to Ito's study of hydrodynamic distribution is the size of the tubing used. The tubing used in this study is twice the bore and about 1.5x the outside diameter. This will have two effects: 1) the increased bore will reduce viscous effects with respect to inertial ones by a factor four and 2) the Archimedean spiral angle will be increased by a factor 1.5x which will accentuate both the Archimedean effect and the Hydrostatic one in different ways, both of which are not yet understood. Another difference is that temperature in this study was controlled at 30°C, while Ito's observations[5] were at a room temperature (22°C ± 1).

EXPERIMENTAL

Experimental Apparatus

Figure 4A shows the coil planet centrifuge used for the Head/Tail experiments. It rotates in the vertical plane at speeds between 0-1200 rpm, either clockwise ("Head" centre) or anti-clockwise ("Head" periphery). The planet radius {R} is 10 cm. The single layer spiral coil was wound using 4.76 mm outside diameter tubing with an internal diameter of 3.18 mm, having 11 loops and a β range from 0.38 to 0.85 wound clockwise from centre to periphery. Coils were cantilevered outside the plane of rotation of the main rotor so that phase distribution could be observed using a stroboscope. The rotor and coils were enclosed in a temperature controlled housing, maintained at 30 ± 0.5°C for all experiments. The inlet filling tubing was fed through a coiled loop maintained at 30 ± 0.5°C to ensure the phase system was also at the same temperature as the centrifuge.

Phase Systems

Two groups of phase systems were chosen for this study. The first was a comparative set of three from Ito's hydrodynamic distribution study.[1] The second was a group of Heptane/Ethyl Acetate/Methanol/Water phase systems chosen to cross the polarity range without changing viscosity. This was achieved by varying the proportion of ethyl acetate. In this way, the contribution of viscosity could be examined; Ito's phase systems exhibiting a large variation in viscosity, the Heptane phase systems showing no variation in viscosity.

The three phase systems chosen from Ito's study on hydrodynamic distribution,[1] together with the physical properties as measured by Ito,[5] are listed in Table 1. One has been chosen from each part of the polarity range: hydrophobic, intermediate, and hydrophilic. The number in the first row refers to the Brunel phase system reference number and is only used as an abbreviation for the phase systems in figures and tables.

It can be seen that the density difference, density ratio, and viscosity ratios and interfacial tension of the Ito phase systems, decrease as they become more polar, whilst the viscosity increases.

To aid any comparison between Ito's observations and the ones presented here, Table 2 gives the physical properties of the phase systems, listed in Table 1, measured by Ito at room temperature (22°C), compared to measurements

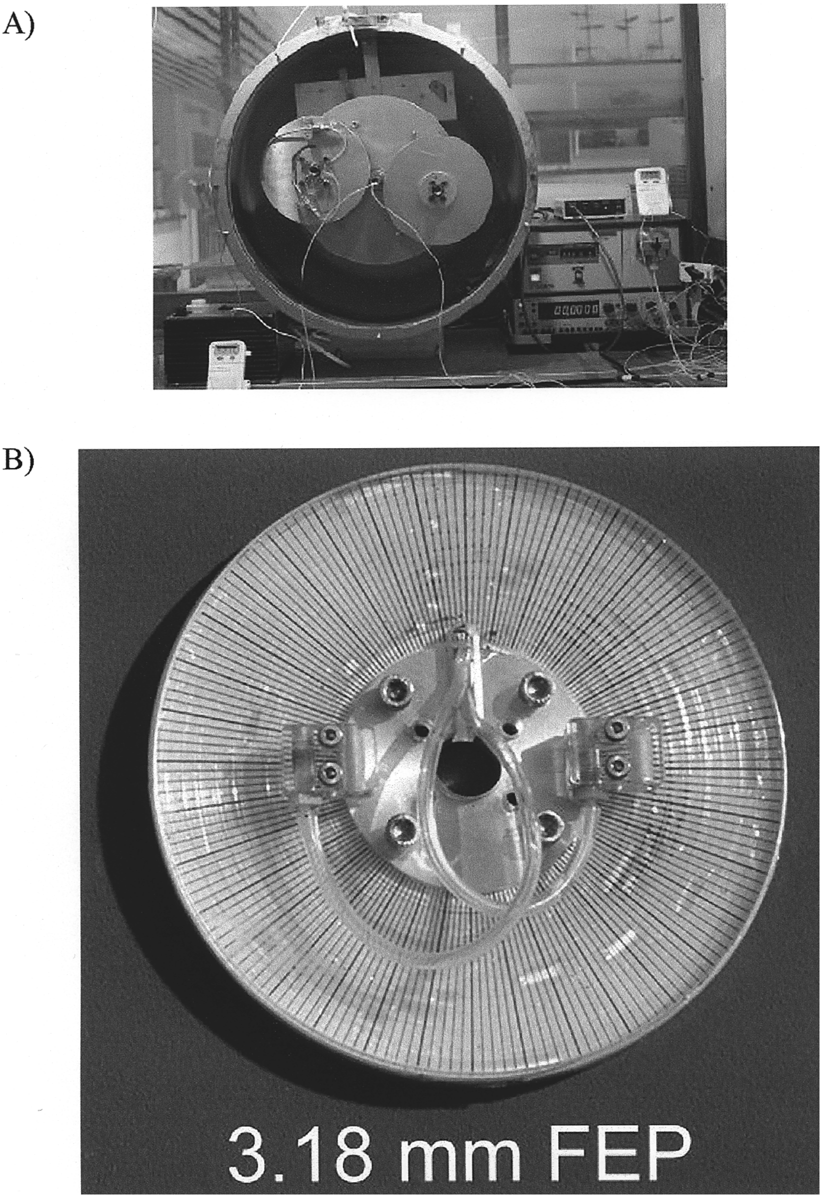

Figure 4. The J1 coil planet centrifuge showing A) the test rig and B) detail of the spiral coil with the transparent angle measurement template.

Table 1

The Physical Properties of the Ito Phase Systems Used, as Measured by Ito[5]

Brunel Code:	**2A**	**3B**	**3C**
Hydrophobicity:	**Hydrophobic**	**Intermediate**	**Hydrophilic**
Phase System:	**Heptane:Water (1:1)**	**Ethyl Acetate:Acetic Acid: Water (4:1:4)**	**n-Butanol:Acetic Acid:Water (4:1:5)**
Density Upper (ρ_1 - kg/m^3)	660	940	900
Density Lower (ρ_2 - kg/m^3)	1000	1010	950
Density Difference ($\rho_2 - \rho_1$)	340	70	50
Density Ratio (ρ_2/ρ_1)	1.515	1.074	1.055
Viscosity Upper (η_1 - cp)	0.41	0.76	1.63
Viscosity Lower (η_2 - cp)	0.95	0.81	1.40
Viscosity Ratio (η_2/η_1)	2.32	1.07	0.86
Kinematic Viscosity Ratio ($\eta_2\rho_1/\rho_2\eta_1$)	1.53	0.99	0.81
Interfacial Tension (τ_i - mNm)	52	16	<1

Table 2

Measured Physical Properties of Ito Phase Systems Used Taken at 25°C and 30°C

	Ito[5]	Measured	
	22 °C	25.0 °C	30.0 °C
	Density	Density (kg/m^3)	
Upper,2A	660	663	658
Upper,3B	940	932	926
Upper,3C	900	891	888
Lower,2A	1000	997	996
Lower,3B	1010	1012	1005
Lower,3C	950	994	990
		Viscosity (cP)	
Upper,2A	0.41	0.37	0.36
Upper,3B	0.76	0.74	0.68
Upper,3C	1.63	1.61	1.48
Lower,2A	0.95	0.92	0.87
Lower,3B	0.81	1.22	1.15
Lower,3C	1.40	1.46	1.32

made in this study at 25°C and 30°C. In general, these are comparable, apart from the density of the lower phase of 3C and the viscosity of the lower phase 3B.

The group of Heptane/Ethyl Acetate/Methanol/Water phase systems used for the Head/Tail studies at constant viscosity are listed in Table 3, with their physical properties given in Table 4. This results in density and viscosity ratios demonstrating constant kinematic viscosity ratios as shown in Table 5.

Preparing the Coil for a Phase Distribution Head/Tail Study

The phases were initially set up at the opposite ends of the coil to the way they would naturally distribute according to the hypothesis. This was achieved by filling the whole system, while stationary, with one phase, then pumping in the other phase until it occupied half the coil volume. Whether the heavy phase occupied the centre or periphery of the coil would be determined by which phase was chosen as the initial filling phase. Once completely filled, the dis-

Table 3

The Constant Viscosity Heptane Phase Systems

4B	Heptane/Ethyl Acetate/Methanol/Water	1.4 : 0.6 : 1.0 : 1.0
4F	Heptane/Ethyl Acetate/Methanol/Water	1.4 : 2.0 : 1.0 : 1.0
4H	Heptane/Ethyl Acetate/Methanol/Water	1.4 : 3.0 : 1.0 : 1.0
4C	Heptane/Ethyl Acetate/Methanol/Water	1.4 : 4.5 : 1.0 : 1.0

Table 4

The Physical Properties of the Ito Phase Systems Used as Measured by Ito[5]

	Density Upper (ρ_1 - kg/m^3)	**Density Lower (ρ_2 - kg/m^3)**	**Viscosity Upper (η_1 - cp)**	**Viscosity Lower (η_2 - cp)**	**Interfacial Tension (τ_i - mNm)**
4B	708	938	0.35	1.35	6.2
4F	782	920	0.39	1.33	2.1
4H	814	928	0.41	1.34	1.2
4C	833	931	0.42	1.35	1.0

Table 5

How Density and Viscosity Ratios Change Relative to Interfacial Tension for the Heptane Phase Systems

	Density Ratio (ρ_2/ρ_1)	**Viscosity Ratio (η_2/η_1)**	**Kinematic Viscosity Ratio ($\eta_2\rho_1/\rho_2\eta_1$)**	**Interfacial Tension (τ_i - mNm)**
4B	1.325	3.86	2.91	6.2
4F	1.176	3.41	2.90	2.1
4H	1.140	3.27	2.87	1.2
4C	1.118	3.21	2.88	1.0

tribution of the phases was recorded by allowing the phases to settle and measuring the phase distribution in each coil loop. This was done by using the transparent angle measurement template (Figure 4B) mounted in front of the coil and reading off the arc length of each phase. In this way, the mean phase distribution in each coil loop could be obtained for a given mean β value. The reading was an average one, since each loop has a spiral progression.

It was not always possible to completely place 0% heavy phase at one end and 100% at the other. This was very much dependent on the interfacial tension of the phase system. High interfacial tension phase systems would distribute in an ideal way as there would be plug flow. But, for low interfacial tension systems, plug flow could not always be guaranteed and hence, the starting distribution could be nearer 10% heavy phase at one end of the coil and 90% at the other.

Head/Tail Distribution Studies

Once the phases were distributed in the coil, a flow control valve was closed to guarantee there was a “no-flow” closed system. It is important to use a valve and not merely rely on the pump’s non-return valves. These have a one way action, and the Archimedean effects can act either way. Hence, in one direction it could overcome these valves.

Once the control valve was closed, the coil planet centrifuge was switched on to rotate at 800 rpm, the timer started, and the behaviour of the phases observed with the stroboscope. The time taken for the heavy phase to move from one side of the coil to the other was noted. After a set time limit of 5 minutes the rotor was switched off. The phase systems were then given time to settle, and the arc length of the stationary phase was then measured, and the retention in each loop (at a given β value) calculated.

RESULTS AND DISCUSSION

Ito Phase Systems - Heptane/Water (1:1)

The change in lower phase distribution for Ito’s Heptane/Water system is shown in Figures 5A and 5B, for clockwise and counter-clockwise rotation, respectively. In each case, there are equal volumes of upper and lower phase, with the lower phase initially occupying the “Head” end of the coil. Note, that in Figure 5A, the six loops at low β-value towards the centre of the coil containing lower phase (shown dotted), are equivalent in volume to the four containing upper phase at the higher β-values (shown as 0% lower phase distribution). In both cases, there is a strong tendency for the heavy phase to go to the “Tail” whether it is at the Periphery (Figure 5A) or at the Centre (Figure 5B).

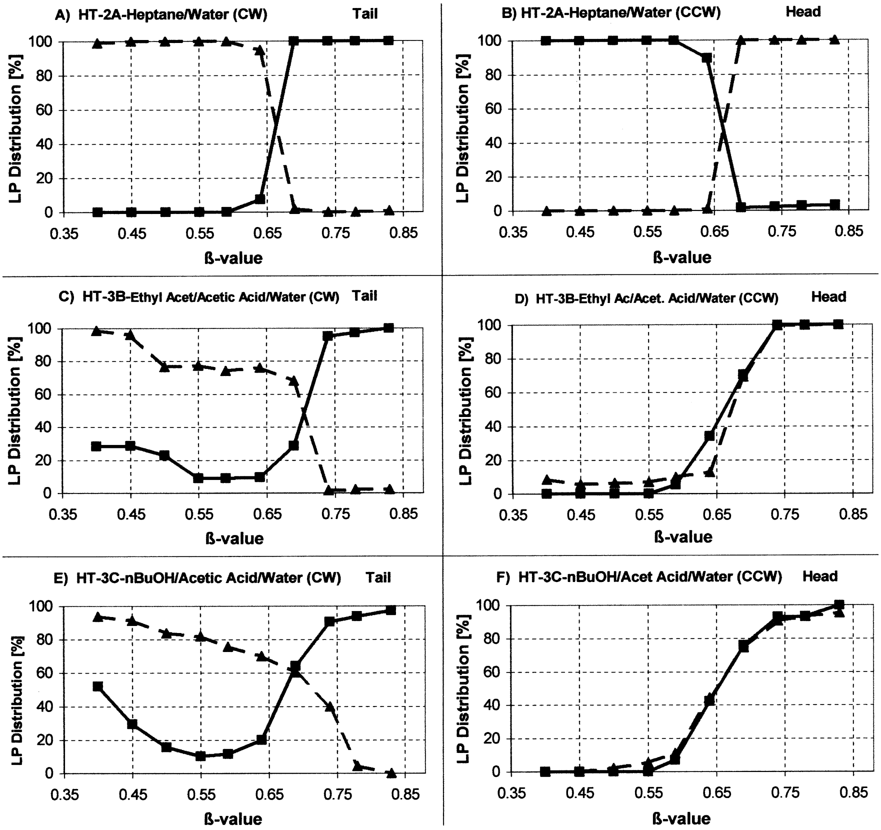

Figure 5. Change in Lower Phase Distribution from initial (dashed line) to final (solid line) for A) Heptane/Water (1:1) when Rotating Clockwise and B) Counter-Clockwise; C) for Ethyl Acetate/Acetic Acid/Water (4:1:4) when Rotating Clockwise and D) Counter-Clockwise; E) for n-BuOH/Acetic Acid/Water (4:1:5) when Rotating Clockwise and F) Counter-Clockwise. The Tail is at the Periphery for Clockwise Rotation and the Centre for Counter-Clockwise Rotation.

It was noted, that phase distribution occurred very quickly - less than 30 seconds for clockwise rotation (Figure 5A) and less than 40 seconds for counter-clockwise rotation (Figure 5B). There is no sign that hydrostatic forces are reducing the Archimedean effect in Figure 5B, but it is significant that phase distribution occurs more slowly in the latter case.

Ito Phase Systems - Ethyl Acetate/Acetic Acid/Water (4:1:4)

The change in lower phase distribution for Ito's Ethyl Acetate/Acetic Acid/Water system is shown in Figures 5C and 5D, for clockwise and counter-clockwise rotation, respectively. In this test, it was not possible (due to the lower interfacial tension) to get the phases to distribute 100% at one end and 100% at the other. Nevertheless, it can still be seen that for clockwise rotation the heavy phase moves to the tail, but below a β -value of 0.55 movement is much more sluggish, suggesting there may a "g" level threshold below which phase distribution is difficult. In contrast, for counter-clockwise rotation, the heavier lower phase stays at the "Head" end of the coil. At lower β -values there is a hint of lower phase moving toward the "Head" suggesting that, in this instant, the Hydrostatic forces are exceeding the Archimedean ones. These results are after 5 minutes of rotation at 800 rpm.

Ito Phase Systems - n-Butyl Alcohol/Acetic Acid/Water (4:1:5)

The change in lower phase distribution for Ito's n-Butyl Alcohol/Acetic Acid/Water system is shown in Figures 5E and 5F, for clockwise and counter-clockwise rotation, respectively. Again, it was not possible to get a phase distribution with 100% at one end and 0% at the other. Nevertheless, it can be seen that for clockwise rotation the heavy phase still moves to the tail, and again, below a β-value of 0.55, there are remnants of lower phase lingering at the "Head". Again, for counter-clockwise rotation, the heavier lower phase stays at the "Head" end of the coil. There is also a hint of lower phase moving toward the "Head" suggesting that the Hydrostatic forces are exceeding the Archimedean ones. These results are also obtained after 5 minutes of rotation at 800 rpm.

Comparison with Ito's Results[1]

When rotating clockwise, the lower heavy phase <u>always</u> goes to the tail, supporting the hypothesis for when the Archimedean and Hydrostatic forces are additive. (Clockwise rotation is in the same direction as the coil winding and the "Tail" is at the periphery). This is accentuated in the case of Heptane/Water when the density difference is large. Phase re-distribution can occur very quickly (less than 30 seconds) which, with a coil volume of 30 mL, is equivalent to each phase flowing at 30 mL/min (i.e., a relative flow of 60ml/min). Phase distribution takes longer when the density difference is small. For example, the Ethyl Acetate/Acetic Acid/Water and n-BuOH/Acetic Acid/Water systems, where the phase systems take 5 minutes for re-distribution, imply relative flows an order of magnitude less at 6 mL/min. Nevertheless, these results indicate that much higher flows are possible with CCC than are currently being used, but the magnitude would depend on the density difference of the phase systems.

When rotating counter-clockwise, the lower heavy phase goes to the tail for the high density difference phase systems, like Heptane/Water, but to the "head" for low density phase systems, like Ethyl Acetate/Acetic Acid/Water and n-BuOH/Acetic Acid/Water. (Counter-clockwise rotation is in the opposite direction to the coil winding and the "Head" is at the Periphery). These observations are very similar to those of Ito,[1] except the switch over point may be different due to the larger tubing bore and higher temperature, both giving less viscous effects.

Experiments Using Heptane/Ethyl Acetate/Methanol/Water Phase Systems

Figure 6 details the head/tail results obtained using the Heptane/Ethyl Acetate/Methanol/Water quaternary phase systems with fixed proportions of Heptane, Methanol, and water, and with Ethyl Acetate proportions increasing from 0.6 to 4.5. This has the effect of reducing the hydrophobicity, density, and interfacial tension of the phase systems, while keeping the viscosity approximately constant.

In all cases of clockwise rotation, where the Archimedean and Hydrostatic forces are additive and the "Tail" is at the periphery, the lower heavy phase always goes to the "Tail". When rotating counter-clockwise, where the Archimedean and Hydrostatic forces are opposed and the "Head" is at the periphery, then the lower heavy phase goes to the "Tail" when the density ratio (ρ_2/ρ_1) is over 1.15 and to the "Head" when the density ratio is less than 1.15.

It is interesting to compare these constant viscosity results with those using Ito's phase systems where the viscosity varies considerably. Figures 5A and B and 6A and B exhibit virtually identical behaviour, so do Figures 5C and D and 6E and F and Figures 5E and F and 6G and H. In the case of Ito's phase systems, the kinematic viscosity ratio varies from 1.53 to 0.81 (Table 1), with the most viscous phase changing from the lower phase (Heptane/Water) to the upper phase (n-BuOH/Acetic Acid/Water). With the quaternary phase systems, the kinematic viscosity ratio was constant at 2.9. This suggests that phase distribution for preparative scale tubing (3.2 mm diameter used in this study) is driven primarily by the density difference of the phase systems, and that viscosity has little effect. This is particularly important for scale up when viscous wall effects become less dominant as the tubing bore increases. The role viscosity plays in analytical CCC, when the tubing size is small, is less clear. In this case, distribution of the phases to one end of the coil has to initially work against the viscous drag of the tubing walls and then hold its own against the incoming flow of the mobile phase. The kinematics may well be defined by the density ratio of the phase systems, but distribution can still be influenced by viscous drag on the tubing walls, as, Ito's results for hydrophilic phase systems suggest.[1] This is one good reason why higher speed and higher "g" fields may be important for the smaller tubing used for analytical work.

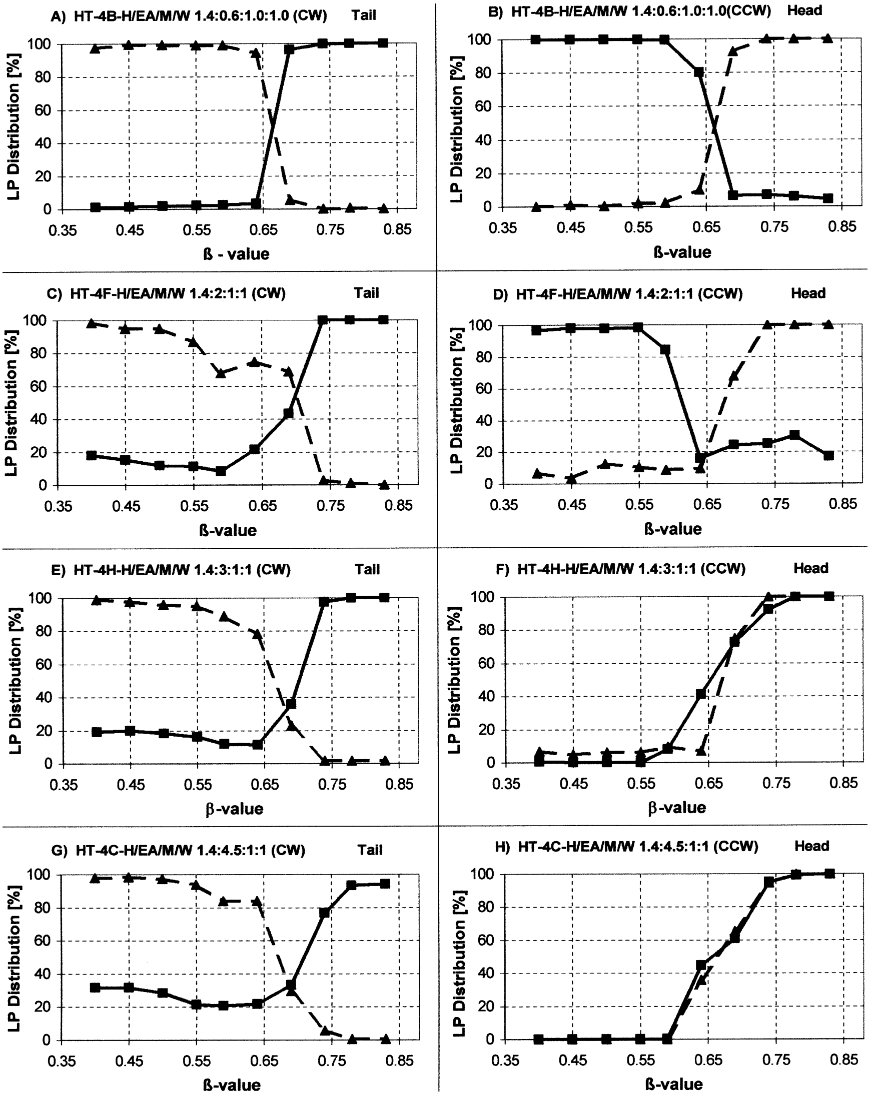

Figure 6. Change in Lower Phase Distribution from initial (dashed line) to final (solid line) for A) Heptane/Ethyl Acetate/Methanol/Water (1.4:0.6:1.0:1.0) when Rotating Clockwise and B) Counter-Clockwise; for C) Heptane/Ethyl Acetate/Methanol/Water (1.4:2.0:1.0:1.0) when Rotating Clockwise and D) Counter-Clockwise; for E) Heptane/Ethyl Acetate/Methanol/Water (1.4:3.0:1.0:1.0) when Rotating Clockwise and F) Counter-Clockwise; for G) Heptane/Ethyl Acetate/Methanol/Water (1.4:4.5:1.0:1.0) when Rotating Clockwise and H) Counter-Clockwise. The Tail is at the Periphery for Clockwise Rotation and the Centre for Counter-Clockwise Rotation.

It is also interesting to speculate on the reasons why, for counter-clockwise rotation, where the Archimedean and Hydrostatic forces work against one another, the Archimedean effect dominates when high density ratio phase systems are used, whereas, the Hydrostatics dominate when low density ratio phase systems are used. Comparing Figures 6C and D and 6E and F, there is a very significant difference in phase distribution between the two when rotating counter-clockwise. But, the difference in density ratio for the one where the lower phase goes to the "Tail" is 1.17, and for the one that goes to the "Head" 1.14; a difference of only 0.03. One must not forget, that mixing and settling is still taking place while these phase systems are distributing themselves (Figure 2). The fact that the interfacial tension of these two phase systems has virtually halved, may make a difference. It may also be significant that Figures 5C and D and 6E and F convey the same phase partition behaviour when one has a density ratio of 1.07 and interfacial tension of 16 mNm, compared to the other with a density ratio of 1.14 and interfacial tension of 1.2 mNm.

CONCLUSIONS

The hypothesis that the lower heavy phase always goes to the "Tail" when the "Tail" is at the periphery of a coil planet centrifuge bobbin, is supported by experiments using a range of phase systems, including some of those used earlier by Ito[1] for the study of hydrodynamic phase distribution. This will hopefully lead to an improvement of current CCC practice, as it is common for CCC instruments to be built and to operate with the "Head" at the periphery to prevent coils unwinding in use. The following is recommended:

All CCC instruments should be marketed with only one direction of rotation, which, is in the same direction as the coils are wound, so that the "Tail" is at the periphery. The lower, heavy phase will always want to go to the Tail (Periphery) and the upper, lighter phase, to the Head (Centre).

Authors of CCC papers on existing instruments should state the direction of rotation relative to the way the coil is wound (i.e., whether the "Head" is at the "Periphery" or "Centre").

Bobbin/coil manufacturers should be encouraged to make coils in such a way that they do not unwind. This is not easy, and will need some investment by the industry before truly reliable bobbins/coils are available.

Always flow the mobile phase in the direction it wants to go - lower, heavy phase toward the "Tail" (Head(Centre)>Tail(Periphery)) and the upper, lighter phase toward the "Head" (Tail (Periphery)>Head(Centre)).

If these rules are followed, CCC will become an extremely competitive separation process with the prospect of both analytical and preparative scale applications.

NOMENCLATURE

Definition of Terms

"Head"	The end of the tubing to which a bubble or bead would move under the action of Archimedean screw action.
"Tail"	The opposite end of the tubing to the "Head."
"Periphery"	The outside of the coil of tubing with the highest β value.
"Centre"	The inside of the coil of tubing with the lowest β value.

Symbols Used

R	Distance from centre of main rotor to the planetary axis.
r	Distance from the planetary axis to a given point on the planetary rotor (bobbin.)
β	The ratio r/R.
ρ	Density of phase system (suffix 1 upper, suffix 2 lower).
η	Viscosity of phase system (suffix 1 upper, suffix 2 lower).
τ_i	Interfacial tension.
η/ρ	Kinematic viscosity.

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REFERENCES

1. Y. Ito, "Speculation on the Mechanism of Unilateral Hydrodynamic Distribution of two Immiscible Solvent Phases in the Rotating Coil," J. Liq. Chromatog., **15**, 2639-75 (1992).

2. W. D. Conway **Counter Current Chromatography: Apparatus, Theory and Applications**, ISBN 0-89573-331-5, VCH Publishers, NY, 1990.

3. Y. Ito, "Principle, Apparatus, and Methodology of High-Speed Countercurrent Chromatography." in **High Speed Countercurrent Chromatography**, Y. Ito, W. D. Conway, eds., Chemical Analysis Series, John Wiley & Sons, Vol 132, Chapter 1, 1996, pp. 3-44.

4. I. A. Sutherland, L. Brown, S. Forbes, D. Games, D. Hawes, K. Hostettmann, E. H. McKerrell, A. Marston, D. Wheatley, P. Wood "Countercurrent Chromatography (CCC) and its Versatile Application as an Industrial Purification & Production Process," J. Liq. Chromatog., **21(3)**, 279-298 (1998).

5. Y. Ito, "Principles and Instrumentation of Countercurrent Chromatography," in **Countercurrent Chromatography - Theory and Practice**, N.B. Mandava, Y. Ito eds., Marcel Dekker Inc, New York, 1988, pp. 370.

6. P. Wood, PhD Dissertation, "The Hydrodynamics of CCC."

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